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Prophylactic antibiotics in pediatric neurological surgery

Friederike Knerlich-Lukoschus[1] · Martina Messing-Jünger[1]

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Abstract

Purpose Surgical antibiotic prophylaxis (SAP) in pediatric neurosurgery has poorly been characterized until now. This review gives an overview on the current literature extracting recommendations and guidelines.

Methods The current literature on SAP with special forcus on pediatric neurosurgerical procedures was reviewed. Further, available recommendations in online databases were checked. Clean neurosurgical, shunt, and implant surgeries are considered separately.

Results To date, evidence-based data on SAP in pediatric neurosurgery remain sparse and there are no standardized approaches to an adequate use of antimicrobial agents for SSI prevention for this age group.

Conclusion Due to statistical needs, multi-center surveillance studies are needed for implementing SAP recommendations in pediatric neurosurgery.

Keywords Surgical antibiotic prophylaxis · Pediatric neurosurgery · Surgical side infection

Abbreviations
SAP Surgical antibiotic prophylaxis
SSI Surgical side infection

Introduction

Despite their low incidence, surgical side infection (SSI) remains one of the most feared hospital-acquired infections in neurosurgery due to their potentially serious consequences. Accordingly, SSI may complicate the patient's post-operative course by increasing morbidity and mortality, prolongation of hospitalization, which results in considerable more costs, a nowadays critical factor for all health care systems [1, 2]. In neuro-oncology patients, SSI may additionally delay adjuvant therapies, which leads to an increased risk of adverse medical and psychosocial outcome [3].

SSI rates range on second to fourth position of hospital-acquired infections with a considerably large range of reported incidences between institutions and countries [4, 5]. In a multi-center analysis by the ACS-NSQIP (American College of Surgeons—National Surgical Quality Improvement Program), the overall neurosurgical post-operative infection rate was 5.3% from 2006 to 2014 in 132,063 neurosurgery adult (i.e., > 18 year of age) cases [6]. In respect to pediatric neurosurgery, there are no comparable large studies available on SSI rates to date.

To prevent SSI, surgical antimicrobial prophylaxis (SAP) was introduced early as a short-term application of an antibiotic just before a surgical procedure to avoid pathogen multiplication in the operative field [7]. Since the availability of prospectively randomized studies on prophylactic antibiotic application, demonstrating the overall potential of SAP to effectively reduce SSI, peri-operative antibiosis was widely acknowledged [8–15]. In regard to "clean" neurosurgical procedures, the prospective surveillance study by Korinek et al. demonstrated that SAP effectively decreased infection rates in low-risk patients (i.e., clean craniotomy cases) [16]. It is of note that no effectiveness in SAP could be shown for high-risk patients (those undergoing emergency, clean contaminated, and dirty procedures; or reoperation or with operative times exceeding 4 h) [16, 17].

Even though SAP is not a substitute for evidence-based hygiene measures, aseptic handling and tissue-conserving surgical techniques (https://www.nice.org.uk/guidance/CG74/chapter/1-Guidance, as of March 30, 2018), it has the potential to essentially reduce complication rates and costs. Thus, SAP is recommended currently for adult and pediatric neurosurgery [18]. However, evidence-based recommendations, specifically for pediatric neurosurgery, remain problematic. Placebo-controlled and randomized studies on SAP in pediatric

✉ Friederike Knerlich-Lukoschus
f.knerlich@asklepios.com; knerlich-cns@lukoschus.de

[1] Department of Pediatric Neurosurgery, Asklepios Klinik Sankt Augustin GmbH, Arnold-Janssen-Str. 29, 53757 Sankt Augustin, Germany

neurosurgery are missing to date and current guidelines on “clean” neurosurgery for this specific patient group were largely derived from adult (neuro)-surgical databases not taking into account the specific needs of preterm, newborns, and children [18]. In regard to the pediatric population, SAP-specific age-related studies are mainly limited to shunt-related procedures.

This review will summarize current data situation and SAP recommendations in clean surgery and shunt-surgery—as far as available—with special focus on pediatric neurosurgery.

General considerations

Surgical site infections (SSI) are defined as infections of the superficial or deep tissue or organs at the surgical site or related to the site of the surgical procedure. Regardless of age, a national nosocomial infection surveillance (NNIS) risk index was defined for assessing patients at risk for SSI [19]. It ranges from 0 to 3, based on the American Anesthesiologists score, surgical wound classification (Altemeier score), and duration of the surgical procedure [20]. Narotam et al. provided a classification system for neurosurgery in which procedures are divided into five categories: clean, clean with foreign body, clean contaminated, contaminated, and dirty [21]. Risk factors for post-operative infections after neurosurgical procedures are considered an ASA classification of ≥ 2, invasive post-operative intracranial pressure monitoring, ventricular drains for five or more days, cerebrospinal fluid (CSF) leak, procedure duration of more than 2 to 4 h, repeat or additional neurosurgical procedures, concurrent or previous shunt infection, emergency procedures, and metabolic comorbidity (like diabetes). In regard to pediatric neurosurgery, age might also be a relevant factor and comorbidities, which are related to developmental disorders like spina bifida-associated problems [22, 23].

Current recommendations on SAP refer to Bratzler’s et al. (2013) comprehensive analyses of the literature and recommendations. This consortium of different organizations provided analyses of the current literature on meta-analyses and studies, which investigated antimicrobial prophylaxis versus no prophylaxis among others in clean neurosurgical procedures [18]. Assuming less infection-related complications like meningitis, scalp infections, bone flap osteitis, and abscess or empyema with antimicrobial prophylaxis compared to surgery without prophylaxis, they provided recommendations on different aspects of SAP [18]. However, pediatric particularities could not be addressed for neurosurgery (instead of for example cardiac surgeries) due to the current data situation.

Surgical antibiotic prophylaxis (SAP) in clean neurosurgical procedures

Crucial aspects of SAP include the time-point of application, appropriate antibiotic selection, duration, and SAP re-dosing during longer procedures. Establishing antibiotic stewardship programs were shown to increase the compliance to these points, as well as correctly performed team-time outs before starting the surgical procedure [24].

Pre-operative dosing time Applying the antibiotic shortly before skin incision is considered effective SSI prevention as the applied antibiotic lowers bacterial inoculation before incision and prevents proliferation during surgery [25, 26]. In the current recommendations, the optimal time-point for SAP administration is given when applied within 60 min before surgical incision [18, 27]. This point seems to be often ignored during daily clinical practice and SAP application “at induction of anesthesia” is not an adequate approach [28]. Here, a correctly performed team-time out may be a helpful tool for a constructive interdisciplinary interaction and adherence to standards and recommendations [29, 30].

Choice of antibiotic for SAP SSI in neurosurgical procedures is mainly due to gram-positive organisms, *Staphylococcus aureus*, and coagulase-negative staphylococci, and other skin organisms (for review, see [18]. One major problem is the current high rate of infection with MRSA and coagulase-negative staphylococci, with a reported rate of 75–80% isolated patients (among others [16, 17, 31–34]).

In regard to the antibiotic choice, different antimicrobial regimens were reported to be effective in SSI prevention including clindamycin, vancomycin, cefotiam, piperacillin, cloxacillin, oxacillin, cefuroxime, cefotaxime, sulfamethoxazole–trimethoprim, cefazolin, penicillin G, and amoxicillin–clavulanate [9, 16, 17, 33–38].

Currently, a single dose of cefazolin (not followed by further antimicrobiotic administration) is recommended by the AAHP/IDSA/SIS/SHEA (American Society of Health-System Pharmacists, the Infection Disease Society if America, Surgical Infection Society, the Society for Healthcare Epidemiology of America) for patients undergoing clean neurosurgical procedures, i.e., “elective craniotomy and cerebrospinal fluid-shunting procedures” (strength of evidence A) and “implantation of intrathecal pumps” (strength of evidence C) [18], as this first-generation cephalosporin is active against a variety of staphylococci and streptococci [39]. These recommendations were followed in studies evaluating SAP for different neurosurgical procedures—in regard to pediatric neurosurgery—including vagus nerve stimulator implantation and external ventricular drains, and found to be effective in reducing or preventing SSI [40–42]. Thereby, clindamycin or vancomycin should be reserved as an alternative agent for patients with a documented β-lactam allergy or for MRSA-colonized patients (vancomycin) [18]. In a further meta-analysis, third-generation cephalosporins did not show superiority over first-generation cephalosporins in regard to incisional- and organ-related SSI [43].

To ensure sufficient serum and tissue antibiotic concentration level, SAPs have to be given in a weight-based manner. Further, there is the need of re-dosing during longer procedures if the duration exceeds two half-lives of the drug or there is excessive blood loss during the procedure. For cefazolin, current recommendations are 30 mg/kg children with a re-dosing interval of 4 h (after initiation of the pre-operative dose) [18].

Duration of SAP Further care has to be taken regarding duration and choice as arbitrary usage can lead to resistant microorganisms (European Center for Disease Prevention and Control; https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Perioperative%20antibiotic%20prophylaxis%20-%20June%202013.pdf; accessed May 16, 2018). There is a great variety in clinical practice regarding this point. In the recent literature, SAP is recommended for a shortened post-operative course, i.e., a single dose or continuation for less than 24 h. There is no evidence that prolonged AB application bears any benefit for the patient (National Institute of Health and Clinical Excellence. Surgical site infection is www.nice.org.uk/CG74, [17].

Antibiotic prophylaxis for shunt-related procedures

Deleterious sequelae resulting from shunt infections are well known and feared complications. The role of SAP in such shunt-related procedures has been studied in various early trials (among others [44, 45]). Despite ongoing efforts to prevent these infections, there is still no consensus met about application and duration of SAP in pediatric shunt surgeries. However, SAP application in shunt surgery for children is recommended and integrated as one crucial step in current shunt infection prevention protocols (among others [46–49]. Thereby, reported shunt infection rates themselves vary widely between different institutions and countries and depend on individual medical preconditions like prematurity, age, previous shunt infection and others. The major source of shunt infections are bacteria of the patient's own skin. Hence, infection often occurs during the first post-operative month and is most often due to infections with Staphylococcus species (90%) [50].

Due to small patient numbers of single institutional studies, the SAP problematic for shunt surgeries has been approached by meta-analyses of multiple individual studies. By doing so, Langeley et al. [45], found that SAP significantly (up to 50%) reduced shunt related infection rates similar to Haines and Walter 1994 who demonstrated relative effectiveness of SAP depending on the initial infection rate [44]. Ratilal et al. performed meta-analyses of 17 trials with 2134 participants to evaluate the use of SAP in shunt procedures. They came to the conclusion that systemic SAP within the first 24 h post-operatively was effective to prevent shunt infection regardless of patients' characteristics (age, type of shunt) [51]. Xu et al. recently performed a meta-analysis for effectiveness of SAP in pediatric shunt surgery; they concluded that shunt prophylaxis is effective, again pointing out that more evidence from advanced multi-center studies are necessary [52].

Like in other clean procedures benefit of SAP beyond 24 h after surgery in shunt-related procedures is nowadays discussed controversial and there are no general recommendations available on SAP duration after surgery. Some institutions follow Kestle et al.'s protocol and apply a further dose of cafazolin 6 h after surgery (first author's experience at two different hospitals), in others antibiotics are applied during 3 following days after surgery (authors' institution) or are limited to the single dose before surgery. In their meta-analyzes of trials with 2134 patients, Ratilal et al. demonstrated a beneficial effect of SAP for the first 24 h post-operatively to prevent shunt infections; they stated that the benefit of its use after this period remains uncertain [51].

Due to the widespread inconsistency regarding SAP choice, SAP application time and duration and recommending specific antibiotics remains problematic [53]. Antibiotics used for SAP in shunt surgery included first-generation cephalosporins, second-generation cephalosporin, and vancomycin (in different forms from i.v. or local powder administration). Thereby, none of these antibiotics showed any better effect compared to the other. Another aspect not cleared to date is if the antimicrobiotic's ability to penetrate the blood-brain-barrier has an impact on the prevention of CNS infections after shunting procedures [18]. In their latest shunt infection prevention protocol, Kestle et al. recommended cefazolin (30 mg/kg) application before surgery ("before incision") and one further application of this dose after surgery [48].

However, large cohort studies on SAP in pediatric shunt surgeries are not available and evidence-based protocols for SAP choice and application times are lacking. Accordingly, we are not past the stage of often arbitrary application of prophylactic antibiotics for shunt-related procedures in children. Same applies to the use of antimicrobial-impregnated shunts. There are hints from published case series and few randomized controlled studies that the use of these shunts along with SAP decreases the rate of shunt infections [50, 54–56]. However, data from further well-designed studies are needed to define the role of antimicrobial-impregnated shunts in SAP in pediatric neurosurgery.

In regard to SAP for ventricular drains or baclofen pumps or other devices, the factual situation is even unclear. There are minimal published trial data regarding appropriate prophylaxis for these procedures. Thus, there are no recommendations available for children, which can be deduced from the literature right now [18]. However, considering publications of the current literature, SAP is

Table 1 Suggested standard operation procedures (SOP) for peri-operative antibiotic prophylaxis by the European Center for Disease Prevention and Control (details are provided in the text)

Current recommendation for surgical antibiotic prophylaxis (SAP) in clean neurosurgical procedures	Responsibilities for appropriate application of SAP
SAP: cefazolin 30 mg/kg i.v.	SAP before and during surgery should is controlled by the anesthesiologist* ➔Control: team-time out
Timing of peri-operative antibiotic prophylaxis	
SAP should be administered within 60 min before incision	Application trough anesthesiologist ➔ Control: team-time out
Dosing and duration of SAP	
Single dose of SAP	➔ Performed by anesthesiologist
Repeat for longer duration after initial SAP dose (for cefazolin re-dosing interval is 4 h)	
Duration and termination of SAP	
Continuing SAP after the end of surgery is not recommended*	➔ Control by surgical team

mostly performed like in clean or shunt-procedures (i.e., application of an antibiotic before incision).

Perspective

In addition to the lack of evidence, authors increasingly raised concerns about clinicians' compliance in adhering to current available SAP recommendations. In Ciofi degli Atti et al.'s prospective study on adherence to SAP-indication, SAP-choice, SAP-timing, and SAP-duration in pediatric surgical procedures, there was an underuse of SAP when it was indicated and an overuse was it was not indicated [28]. Also in case of application, there was a quite arbitrary manner in the choice of antibiotics, timing, and duration.

To address this point, the European Center for Disease Prevention and Control proposed five key SAP modalities that were shown to improve compliance of healthcare professionals in regard to appropriate administration, timing, dosage, and duration of SAP. These modalities included (1) forming a multidisciplinary team to develop, implement and update a SAP protocol, conduct an audit of compliance, and provide feedback; (2) ensuring administration of SAP within 60 min prior to incision; (3) assigning responsibility for timely administration of SAP to the anesthesiologist; (4) administering only a single dose of SAP; and (5) to discontinue SAP at the end of surgery (https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/Perioperative%20antibiotic%20prophylaxis%20-%20June%202013.pdf, accessed May 16, 2018; summarized in Table 1).

However, despite these efforts, Weiss et al. demonstrated a lacking compliance and fostered individualism in regard to adherence to internal institutional standard operation procedures (SOPs). Despite a formulated SOP which was developed by a multidisciplinary team (neurosurgeons, neurooncologists, microbiologists) based on a medline search, different antibiotic agents were found to be used other than recommended or different time-periods and different doses [57].

These observations again reflected the dilemma of missing evidence-based and thus accepted best practice workflows. Thereby, critical points that challenged randomized controlled studies on antimicrobial prophylaxis in children is the low SSI rates for neurosurgical procedures resulting in low numbers with an increase in the likelihood of type II errors and difficulty in establishing controls (including placebo, no treatment, or other antimicrobial agents) due to study design.

Conclusion

Controlled randomized multicenter studies are urgently needed for implementing SAP guidelines in pediatric neurosurgical procedures. In regard to shunt-related procedures, which have been addressed more frequently compared to other neurosurgical interventions, adherence to existing protocols is desirable. This emphasizes the need for a robust surveillance programs to provide valid data for SAP. Other procedures like clean craniotomies have to be addressed at all for the pediatric population in order to meet the needs of this age group and prevent inappropriate use of SAP, which promotes selection of multi-resistant microorganisms. Due to statistical needs, multi-center surveillance studies are needed for implementing SAP evidence-based recommendations in pediatric neurosurgery, which is the prerequisite to overcome traditions and arbitrary individual decisions that may endanger the patient's safety.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

1. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R (2003) Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis 9:196–203
2. Plowman R (2000) The socioeconomic burden of hospital acquired infection. Euro Surveill 5:49–50
3. Woodgate RL, Tailor K, Yanofsky R, Vanan MI (2016) Childhood brain cancer and its psychosocial impact on survivors and their parents: a qualitative thematic synthesis. Eur J Oncol Nurs 20: 140–149
4. Davies BM, Jones A, Patel HC (2016) Surgical-site infection surveillance in cranial neurosurgery. Br J Neurosurg 30:35–37
5. Nichols RL (2004) Preventing surgical site infections. Clin Med Res 2:115–118
6. Karhade AV, Cote DJ, Larsen AM, Smith TR (2017) Neurosurgical infection rates and risk factors: a National Surgical Quality Improvement Program Analysis of 132,000 patients, 2006–2014. World Neurosurg 97:205–212
7. Malis LI (1979) Prevention of neurosurgical infection by intraoperative antibiotics. Neurosurgery 5:339–343
8. Cruse PJ, Foord R (1980) The epidemiology of wound infection. A 10-year prospective study of 62,939 wounds. Surg Clin North Am 60:27–40
9. Barker FG 2nd (1994) Efficacy of prophylactic antibiotics for craniotomy: a meta-analysis. Neurosurgery 35:484–490 discussion 491–482
10. Blomstedt GC, Kytta J (1988) Results of a randomized trial of vancomycin prophylaxis in craniotomy. J Neurosurg 69:216–220
11. Bullock R, van Dellen JR, Ketelbey W, Reinach SG (1988) A double-blind placebo-controlled trial of perioperative prophylactic antibiotics for elective neurosurgery. J Neurosurg 69:687–691
12. Gaillard T, Gilsbach JM (1991) Intra-operative antibiotic prophylaxis in neurosurgery. A prospective, randomized, controlled study on cefotiam. Acta Neurochir 113:103–109
13. Geraghty J, Feely M (1984) Antibiotic prophylaxis in neurosurgery. A randomized controlled trial. J Neurosurg 60:724–726
14. van Ek B, Dijkmans BA, van Dulken H, van Furth R (1988) Antibiotic prophylaxis in craniotomy: a prospective double-blind placebo-controlled study. Scand J Infect Dis 20:633–639
15. Young RF, Lawner PM (1987) Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomized clinical trial. J Neurosurg 66:701–705
16. Korinek AM, Golmard JL, Elcheick A, Bismuth R, van Effenterre R, Coriat P, Puybasset L (2005) Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. Br J Neurosurg 19:155–162
17. Korinek AM, Baugnon T, Golmard JL, van Effenterre R, Coriat P, Puybasset L (2006) Risk factors for adult nosocomial meningitis after craniotomy: role of antibiotic prophylaxis. Neurosurgery 59: 126–133 discussion 126-133
18. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RG, Slain D, Steinberg JP, Weinstein RA (2013) Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 70: 195–283
19. Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM (1985) Identifying patients at high risk of surgical wound infection. A simple multivariate index of patient susceptibility and wound contamination. Am J Epidemiol 121:206–215
20. Kourbeti IS, Jacobs AV, Koslow M, Karabetsos D, Holzman RS (2007) Risk factors associated with postcraniotomy meningitis. Neurosurgery 60:317–325 discussion 325-316
21. Narotam PK, van Dellen JR, du Trevou MD, Gouws E (1994) Operative sepsis in neurosurgery: a method of classifying surgical cases. Neurosurgery 34:409–415 discussion 415–406
22. Spader HS, Hertzler DA, Kestle JR, Riva-Cambrin J (2015) Risk factors for infection and the effect of an institutional shunt protocol on the incidence of ventricular access device infections in preterm infants. J Neurosurg Pediatr 15:156–160
23. Lee JK, Seok JY, Lee JH, Choi EH, Phi JH, Kim SK, Wang KC, Lee HJ (2012) Incidence and risk factors of ventriculoperitoneal shunt infections in children: a study of 333 consecutive shunts in 6 years. J Korean Med Sci 27:1563–1568
24. Liu J, Li N, Hao J, Li Y, Liu A, Wu Y, Cai M (2018) Impact of the antibiotic stewardship program on prevention and control of surgical site infection during peri-operative clean surgery. Surg Infect 19: 326–333
25. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP (1992) The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med 326: 281–286
26. van Ek B, Dijkmans BA, van Dulken H, Mouton RP, Hermans J, van Furth R (1990) Effect of cloxacillin prophylaxis on the bacterial flora of craniotomy wounds. Scand J Infect Dis 22:345–352
27. Steinberg JP, Braun BI, Hellinger WC, Kusek L, Bozikis MR, Bush AJ, Dellinger EP, Burke JP, Simmons B, Kritchevsky SB, Trial to Reduce Antimicrobial Prophylaxis Errors Study G (2009) Timing of antimicrobial prophylaxis and the risk of surgical site infections: results from the trial to reduce antimicrobial prophylaxis errors. Ann Surg 250:10–16
28. Ciofi degli Atti M, Spila Alegiani S, Raschetti R, Arace P, Giusti A, Spiazzi R, Raponi M, Group AS (2015) Surgical antibiotic prophylaxis in children: adherence to indication, choice of agent, timing, and duration. Eur J Clin Pharmacol 71:483–488
29. Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AH, Dellinger EP, Herbosa T, Joseph S, Kibatala PL, Lapitan MC, Merry AF, Moorthy K, Reznick RK, Taylor B, Gawande AA, Safe Surgery Saves Lives Study G (2009) A surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med 360:491–499
30. Oszvald A, Vatter H, Byhahn C, Seifert V, Guresir E (2012) "Team time-out" and surgical safety-experiences in 12,390 neurosurgical patients. Neurosurg Focus 33:E6
31. Tacconelli E, Cataldo MA, Albanese A, Tumbarello M, Arduini E, Spanu T, Fadda G, Anile C, Maira G, Federico G, Cauda R (2008) Vancomycin versus cefazolin prophylaxis for cerebrospinal shunt placement in a hospital with a high prevalence of meticillin-resistant Staphylococcus aureus. J Hosp Infect 69:337–344
32. Lietard C, Thebaud V, Besson G, Lejeune B (2008) Risk factors for neurosurgical site infections: an 18-month prospective survey. J Neurosurg 109:729–734
33. Whitby M, Johnson BC, Atkinson RL, Stuart G (2000) The comparative efficacy of intravenous cefotaxime and trimethoprim/sulfamethoxazole in preventing infection after neurosurgery: a prospective, randomized study. Brisbane Neurosurgical Infection Group. Br J Neurosurg 14:13–18
34. Valentini LG, Casali C, Chatenoud L, Chiaffarino F, Uberti-Foppa C, Broggi G (2008) Surgical site infections after elective neurosurgery: a survey of 1747 patients. Neurosurgery 62:88–95 discussion 95-86
35. Barker FG 2nd (2002) Efficacy of prophylactic antibiotic therapy in spinal surgery: a meta-analysis. Neurosurgery 51:391–400 discussion 400-391
36. Barker FG 2nd (2007) Efficacy of prophylactic antibiotics against meningitis after craniotomy: a meta-analysis. Neurosurgery 60: 887–894 discussion 887–894
37. Holloway KL, Smith KW, Wilberger JE Jr, Jemsek JG, Giguere GC, Collins JJ (1996) Antibiotic prophylaxis during clean

neurosurgery: a large, multicenter study using cefuroxime. Clin Ther 18:84–94
38. Korinek AM (1997) Risk factors for neurosurgical site infections after craniotomy: a prospective multicenter study of 2944 patients. The French study Group of Neurosurgical Infections, the SEHP, and the C-CLIN Paris-Nord. Service Epidemiologie hygiene et prevention. Neurosurgery 41:1073–1079 discussion 1079-1081
39. Scher KS (1997) Studies on the duration of antibiotic administration for surgical prophylaxis. Am Surg 63:59–62
40. Ifeachor AP, Nichols KR, Morris JL, Cox EG, Smith JL, Sinclair EA (2015) Antimicrobial prophylaxis for external ventricular drains in pediatric neurosurgical patients. Paediatr Drugs 17:239–244
41. Raskin JS, Hansen D, Mohan A, Pan IW, Curry DJ, Lam S (2017) Perioperative antibiotic use in vagus nerve stimulator implantation: a clinical series. Childs Nerv Syst 33:801–804
42. Somma T, Maraolo AE, Esposito F, Cavallo LM, Tosone G, Orlando R, Cappabianca P (2015) Efficacy of ultra-short single agent regimen antibiotic chemo-prophylaxis in reducing the risk of meningitis in patients undergoing endoscopic endonasal transsphenoidal surgery. Clin Neurol Neurosurg 139:206–209
43. Liu W, Neidert MC, Groen RJ, Woernle CM, Grundmann H (2014) Third-generation cephalosporins as antibiotic prophylaxis in neurosurgery: what's the evidence? Clin Neurol Neurosurg 116:13–19
44. Haines SJ, Walters BC (1994) Antibiotic prophylaxis for cerebrospinal fluid shunts: a metanalysis. Neurosurgery 34:87–92
45. Langley JM, LeBlanc JC, Drake J, Milner R (1993) Efficacy of antimicrobial prophylaxis in placement of cerebrospinal fluid shunts: meta-analysis. Clin Infect Dis 17:98–103
46. van Lindert EJ, Bilsen MV, Flier MV, Kolwijck E, Delye H, Oever JT (2018) Topical vancomycin reduces the cerebrospinal fluid shunt infection rate: a retrospective cohort study. PLoS One 13:e0190249
47. Kestle JR, Riva-Cambrin J, Wellons JC 3rd, Kulkarni AV, Whitehead WE, Walker ML, Oakes WJ, Drake JM, Luerssen TG, Simon TD, Holubkov R, Hydrocephalus Clinical Research N (2011) A standardized protocol to reduce cerebrospinal fluid shunt infection: the hydrocephalus clinical research network quality improvement initiative. J Neurosurg Pediatr 8:22–29
48. Kestle JR, Holubkov R, Douglas Cochrane D, Kulkarni AV, Limbrick DD Jr, Luerssen TG, Jerry Oakes W, Riva-Cambrin J, Rozzelle C, Simon TD, Walker ML, Wellons JC 3rd, Browd SR, Drake JM, Shannon CN, Tamber MS, Whitehead WE, Hydrocephalus Clinical Research N (2016) A new hydrocephalus clinical research network protocol to reduce cerebrospinal fluid shunt infection. J Neurosurg Pediatr 17:391–396
49. Klimo P Jr, Van Poppel M, Thompson CJ, Baird LC, Duhaime AC, Flannery AM, Pediatric Hydrocephalus Systematic R, Evidence-Based Guidelines Task F (2014) Pediatric hydrocephalus: systematic literature review and evidence-based guidelines. Part 6: preoperative antibiotics for shunt surgery in children with hydrocephalus: a systematic review and meta-analysis. J Neurosurg Pediatr 14(Suppl 1):44–52
50. Parker SL, McGirt MJ, Murphy JA, Megerian JT, Stout M, Engelhart L (2015) Comparative effectiveness of antibiotic-impregnated shunt catheters in the treatment of adult and pediatric hydrocephalus: analysis of 12,589 consecutive cases from 287 US hospital systems. J Neurosurg 122:443–448
51. Ratilal B, Costa J, Sampaio C (2008) Antibiotic prophylaxis for surgical introduction of intracranial ventricular shunts: a systematic review. J Neurosurg Pediatr 1:48–56
52. Xu H, Hu F, Hu H, Sun W, Jiao W, Li R, Lei T (2016) Antibiotic prophylaxis for shunt surgery of children: a systematic review. Childs Nerv Syst 32:253–258
53. Biyani N, Grisaru-Soen G, Steinbok P, Sgouros S, Constantini S (2006) Prophylactic antibiotics in pediatric shunt surgery. Childs Nerv Syst 22:1465–1471
54. Jaeger W, Lee S, Vineet D, Keil A, Agarwal N, Rao S (2017) Ventriculoperitoneal shunts in neonates: a retrospective study of outcomes with antibiotic-impregnated catheters and a modified peri-operative antibiotic protocol. Br J Neurosurg 31:672–676
55. Govender ST, Nathoo N, van Dellen JR (2003) Evaluation of an antibiotic-impregnated shunt system for the treatment of hydrocephalus. J Neurosurg 99:831–839
56. Sorar M, Er U, Ozisik P, Ozeren E, Simsek S (2014) The impact of antibiotic-impregnated catheters on ventriculoperitoneal shunt infection. Turk J Med Sci 44:393–396
57. Weiss K, Simon A, Graf N, Schope J, Oertel J, Linsler S (2017) Clinical practice audit concerning antimicrobial prophylaxis in paediatric neurosurgery: results from a German paediatric oncology unit. Childs Nerv Syst 33:159–169