Clinical Infectious Diseases

IDSA GUIDELINE

2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis*

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The Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee collaborated with partner organizations to convene a panel of 10 experts on healthcare-associated ventriculitis and meningitis. The panel represented pediatric and adult specialists in the field of infectious diseases and represented other organizations whose members care for patients with healthcare-associated ventriculitis and meningitis (American Academy of Neurology, American Association of Neurological Surgeons, and Neurocritical Care Society). The panel reviewed articles based on literature reviews, review articles and book chapters, evaluated the evidence and drafted recommendations. Questions were reviewed and approved by panel members. Subcategories were included for some questions based on specific populations of patients who may develop healthcare-associated ventriculitis and meningitis after the following procedures or situations: cerebrospinal fluid shunts, cerebrospinal fluid drains, implantation of intrathecal infusion pumps, implantation of deep brain stimulation hardware, and general neurosurgery and head trauma. Recommendations were followed by the strength of the recommendation and the quality of the evidence supporting the recommendation. Many recommendations, however, were based on expert opinion because rigorous clinical data are not available. These guidelines represent a practical and useful approach to assist practicing clinicians in the management of these challenging infections.

Keywords. ventriculitis; meningitis; cerebrospinal fluid shunts; cerebrospinal fluid drains; central nervous system infections.

EXECUTIVE SUMMARY

Meningitis may not only be acquired in the community setting, but may be associated with a variety of invasive procedures or head trauma. The latter group has often been classified as nosocomial meningitis because a different spectrum of microorganisms (ie, resistant gram-negative bacilli and staphylococci) is the more likely the etiologic agents, and different pathogenic mechanisms are associated with the development of this disease. Although many of these patients present with clinical symptoms during hospitalization, ventriculitis and meningitis may develop after hospital discharge or even many years later. We, therefore, prefer the term "healthcare-associated ventriculitis and meningitis" to be more representative of the diverse mechanisms (that include placement of devices) that can lead to these serious illnesses.

Summarized below are recommendations for the evaluation, diagnosis, and management of healthcare-associated ventriculitis and meningitis, specifically addressing the approach to infections associated with cerebrospinal fluid shunts, cerebrospinal fluid drains, intrathecal drug (eg, baclofen) therapy, deep brain stimulation hardware, and neurosurgery and head trauma. These infections may be difficult to diagnose because changes in cerebrospinal fluid parameters are often subtle, making it hard to determine if the abnormalities are related to infection, related to placement of devices, or following neurosurgery. Many of our recommendations are based on expert opinion because rigorous clinical data are not available and the likelihood that clinical trials will be conducted to answer some of these questions is low. Our goal was to develop guidelines that offered a practical and useful approach to assist practicing clinicians in the management of these challenging infections. The panel followed a process used in the development of other IDSA guidelines that

Received 12 December 2016; editorial decision 12 December 2016; accepted 16 December 2016.

*It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situations. The Infectious Diseases Society of America considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

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Clinical Infectious Diseases® 2017;64(6):701–6

DOI: 10.1093/cid/cix152

included a systematic weighting of the strength of recommendations and quality of evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system (Figure 1) [1–5]. A detailed description of the methods, background, and evidence summaries that support each recommendation can be found in the full text of the guidelines.

I. What Are the Typical Symptoms and Signs in Patients With Healthcare-Associated Ventriculitis and Meningitis?

Cerebrospinal Fluid Shunts and Drains

Recommendations

1. New headache, nausea, lethargy, and/or change in mental status are suggestive of cerebrospinal fluid (CSF) shunt infection (strong, moderate).
2. Erythema and tenderness over the subcutaneous shunt tubing are suggestive of CSF shunt infection (strong, moderate).
3. Fever, in the absence of another clear source of infection, could be suggestive of CSF shunt infection (weak, low).
4. Symptoms and signs of peritonitis or abdominal tenderness in patients with ventriculoperitoneal shunts, in the absence of another clear etiology, are indicative of CSF shunt infection (strong, moderate).
5. Symptoms and signs of pleuritis in patients with ventriculopleural shunts, in the absence of another clear etiology, are indicative of CSF shunt infection (strong, moderate).
6. Demonstration of bacteremia in a patient with a ventriculoatrial shunt, in the absence of another clear source of bacteremia, is evidence of CSF shunt infection (strong, moderate).
7. Demonstration of glomerulonephritis in a patient with a ventriculoatrial shunt is suggestive of CSF shunt infection (weak, low).
8. New or worsening altered mental status in patients with external ventricular drains is suggestive of infection (weak, low).
9. New fever and increased CSF white blood cell count in patients with external ventricular drains could be suggestive of infection (weak, low).

Neurosurgery or Head Trauma

Recommendations

10. New headache, fever, evidence of meningeal irritation, seizures, and/or worsening mental status are suggestive of ventriculitis or meningitis in the setting of recent trauma or neurosurgery (strong, moderate).

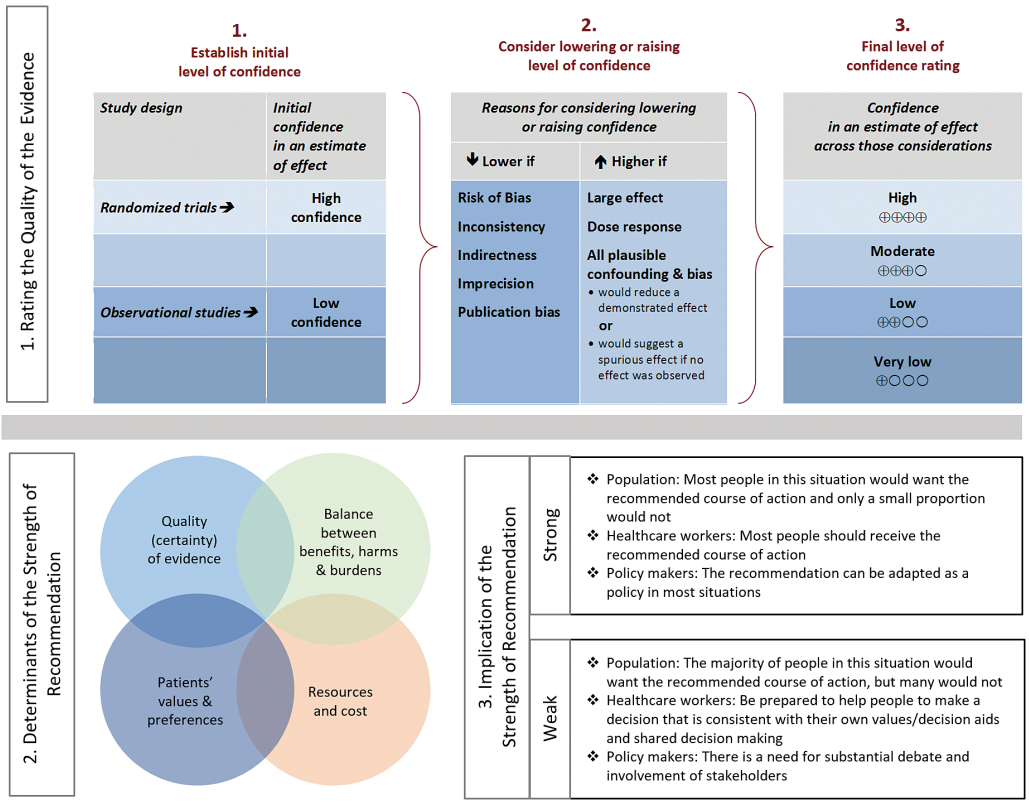

Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology (unrestricted use of the figure granted by the US GRADE Network).

11. Fever, in the absence of another clear source of infection, is suggestive of central nervous system (CNS) infection in the setting of recent head trauma or neurosurgery (weak, low).

Intrathecal Infusion Pumps
Recommendation

12. New fever and drainage from the surgical site in patients with intrathecal infusion pumps are suggestive of wound infection (weak, low).

II. What are the Typical Cerebrospinal Fluid Findings in Patients with Healthcare-Associated Ventriculitis and Meningitis?

Cell Count, Glucose, and Protein
Recommendations

13. Abnormalities of CSF cell count, glucose, and/or protein may not be reliable indicators for the presence of infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate).
14. Normal CSF cell count, glucose, and protein may not reliably exclude infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate).
15. A negative CSF Gram stain does not exclude the presence of infection, especially in patients who have received previous antimicrobial therapy (strong, moderate).

Culture
Recommendations

16. CSF cultures are the most important test to establish the diagnosis of healthcare-associated ventriculitis and meningitis (strong, high).
17. If initial CSF cultures are negative in patients with CSF shunts or drains with suspected infection, it is recommended that cultures be held for at least 10 days in an attempt to identify organisms such as *Propionibacterium acnes* (strong, high).
18. If a CSF shunt or drain is removed in patients suspected of having infection, cultures of shunt and drain components are recommended (strong, moderate).
19. If a CSF shunt or drain is removed for indications other than infection, cultures of shunt or drain components are not recommended (strong, moderate).
20. Blood cultures are recommended in patients with suspected ventriculoatrial shunt infections (strong, high).
21. Blood cultures may be considered in patients with ventriculoperitoneal and ventriculopleural shunts (weak, low).
22. Single or multiple positive CSF cultures in patients with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis, is indicative of CSF drain infection (strong, high).
23. CSF and blood cultures in selected patients should be obtained before the administration of antimicrobial therapy; a negative CSF culture in the setting of previous antimicrobial therapy does not exclude healthcare-associated ventriculitis and meningitis (strong, moderate).

Neurosurgery or Head Trauma
Recommendations

24. CSF pleocytosis with a positive culture and symptoms of infection are indicative of a diagnosis of healthcare-associated ventriculitis or meningitis (strong, high).
25. Hypoglycorrhachia and elevated CSF protein concentrations are suggestive of the diagnosis of healthcare-associated ventriculitis or meningitis (weak, low).
26. Growth of an organism that is commonly considered a contaminant (eg, coagulase-negative staphylococcus) in enrichment broth only or on just 1 of multiple cultures in a patient with normal CSF and no fever is not indicative of healthcare-associated ventriculitis or meningitis (strong, low).
27. CSF cultures with multiple organisms from a single sample may be contaminants in patients with no symptoms of infection or CSF pleocytosis (weak, low).
28. CSF cultures that grow *Staphylococcus aureus* or aerobic gram-negative bacilli are indicative of infection (strong, moderate).
29. CSF cultures that grow a fungal pathogen are indicative of infection (strong, moderate).

III. What Specific Tests of Cerebrospinal Fluid can be used to Confirm the Patient has Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

30. An elevated CSF lactate or an elevated CSF procalcitonin, or the combination of both, may be useful in the diagnosis of healthcare-associated bacterial ventriculitis and meningitis (weak, moderate).
31. An elevated serum procalcitonin may be useful in differentiating between CSF abnormalities due to surgery or intracranial hemorrhage from those due to bacterial infection (weak, low).
32. Nucleic acid amplification tests, such as polymerase chain reaction, on CSF may both increase the ability to identify a pathogen and decrease the time to making a specific diagnosis (weak, low).
33. Detection of β–D-glucan and galactomannan in CSF may be useful in the diagnosis of fungal ventriculitis and meningitis (strong, moderate).

IV. What is the Role of Imaging in Patients with Suspected Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

34. Neuroimaging is recommended in patients with suspected healthcare-associated ventriculitis and meningitis (strong, moderate).

35. Magnetic resonance imaging with gadolinium enhancement and diffusion-weighted imaging is recommended for detecting abnormalities in patients with healthcare-associated ventriculitis and meningitis (strong, moderate).
36. In patients with infected ventriculoperitoneal shunts and abdominal symptoms (eg, pain or tenderness), an ultrasound or computed tomography of the abdomen is recommended to detect CSF loculations at the shunt terminus (strong, moderate).

V. What is the Empiric Antimicrobial Approach for Patients with Suspected Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

37. Vancomycin plus an anti-pseudomonal beta-lactam (such as cefepime, ceftazidime, or meropenem) is recommended as empiric therapy for healthcare-associated ventriculitis and meningitis; the choice of empiric beta-lactam agent should be based on local in vitro susceptibility patterns (strong, low).
38. In seriously ill adult patients with healthcare-associated ventriculitis and meningitis, the vancomycin trough concentration should be maintained at 15–20 μg/mL in those who receive intermittent bolus administration (strong, low).
39. For patients with healthcare-associated ventriculitis and meningitis who have experienced anaphylaxis to beta-lactam antimicrobial agents and in whom meropenem is contraindicated, aztreonam or ciprofloxacin is recommended for gram-negative coverage (strong, low).
40. For patients with healthcare-associated ventriculitis and meningitis who are colonized or infected elsewhere with a highly antimicrobial-resistant pathogen, adjusting the empiric regimen to treat for this pathogen is recommended (strong, low).

VI. Once a Pathogen is Identified, What Specific Antimicrobial Agent(s) Should be Administered?

Recommendations

41. For treatment of infection caused by methicillin-susceptible *S. aureus*, nafcillin or oxacillin is recommended (strong, moderate). If the patient cannot receive beta-lactam agents, the patient can be desensitized or may receive vancomycin as an alternative agent (weak, moderate).
42. For treatment of infection caused by methicillin-resistant *S. aureus*, vancomycin is recommended as first-line therapy (strong, moderate), with consideration for an alternative antimicrobial agent if the vancomycin minimal inhibitory concentration (MIC) is ≥1 μg/mL (strong, moderate).
43. For treatment of infection caused by coagulase-negative staphylococci, the recommended therapy should be similar to that for *S. aureus* and based on in vitro susceptibility testing (strong, moderate).
44. If the staphylococcal isolate is susceptible to rifampin, this agent may be considered in combination with other antimicrobial agents for staphylococcal ventriculitis and meningitis (weak, low); rifampin is recommended as part of combination therapy for any patient with intracranial or spinal hardware such as a CSF shunt or drain (strong, low).
45. For treatment of patients with healthcare-associated ventriculitis and meningitis caused by staphylococci in whom beta-lactam agents or vancomycin cannot be used, linezolid (strong, low), daptomycin (strong, low), or trimethoprim-sulfamethoxazole (strong, low) is recommended, with selection of a specific agent based on in vitro susceptibility testing.
46. For treatment of infection caused by *Propionibacterium acnes*, penicillin G is recommended (strong, moderate).
47. For treatment of infection caused by gram-negative bacilli, therapy should be based on in vitro susceptibility testing with agents that achieve good CNS penetration (strong, moderate).
48. For treatment of infection caused by gram-negative bacilli susceptible to third-generation cephalosporins, ceftriaxone or cefotaxime is recommended (strong, moderate).
49. For treatment of infection caused by *Pseudomonas* species, the recommended therapy is cefepime, ceftazidime, or meropenem (strong, moderate); recommended alternative antimicrobial agents are aztreonam or a fluoroquinolone with in vitro activity (strong, moderate).
50. For treatment of infection caused by extended-spectrum beta-lactamase–producing gram-negative bacilli, meropenem should be used if this isolate demonstrates in vitro susceptibility (strong, moderate).
51. For treatment of infection caused by *Acinetobacter* species, meropenem is recommended (strong, moderate); for strains that demonstrate carbapenem resistance, colistimethate sodium or polymyxin B (either agent administered by the intravenous and intraventricular routes) is recommended (strong, moderate).
52. Prolonged infusion of meropenem (each dose administered over 3 hours) may be successful in treating resistant gram-negative organisms (weak, low).
53. For treatment of infection caused by *Candid*a species, based on in vitro susceptibility testing, liposomal amphotericin B, often combined with 5-flucytosine, is recommended (strong, moderate); once the patient shows clinical improvement, therapy can be changed to fluconazole if the isolated species is susceptible (weak, low).
54. For treatment of infection caused by *Aspergillus* or *Exserohilum* species, voriconazole is recommended (strong, low).

VII. What is the Role of Intraventricular Antimicrobial Therapy in Patients with Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

55. Intraventricular antimicrobial therapy should be considered for patients with healthcare-associated ventriculitis and meningitis in which the infection responds poorly to systemic antimicrobial therapy alone (strong, low).
56. When antimicrobial therapy is administered via a ventricular drain, the drain should be clamped for 15–60 minutes to allow the agent to equilibrate throughout the CSF (strong, low).
57. Dosages and intervals of intraventricular antimicrobial therapy should be adjusted based on CSF antimicrobial concentrations to 10–20 times the MIC of the causative microorganism (strong, low), ventricular size (strong, low), and daily output from the ventricular drain (strong, low).

VIII. What is the Optimal Duration of Antimicrobial Therapy in Patients with Healthcare-Associated Ventriculitis and Meningitis?

Recommendations

58. Infections caused by a coagulase-negative staphylococcus or *P. acnes* with no or minimal CSF pleocytosis, normal CSF glucose, and few clinical symptoms or systemic features should be treated for 10 days (strong, low).
59. Infections caused by a coagulase-negative staphylococcus or *P. acnes* with significant CSF pleocytosis, CSF hypoglycorrhachia, or clinical symptoms or systemic features should be treated for 10–14 days (strong, low).
60. Infections caused by *S. aureus* or gram-negative bacilli with or without significant CSF pleocytosis, CSF hypoglycorrhachia, or clinical symptoms or systemic features should be treated for 10–14 days (strong, low); some experts suggest treatment of infection caused by gram-negative bacilli for 21 days (weak, low).
61. In patients with repeatedly positive CSF cultures on appropriate antimicrobial therapy, treatment should be continued for 10–14 after the last positive culture (strong, low).

IX. What is the Role of Catheter Removal in Patients with Cerebrospinal Fluid Shunts or Drains?

Recommendations

62. Complete removal of an infected CSF shunt and replacement with an external ventricular drain combined with intravenous antimicrobial therapy is recommended in patients with infected CSF shunts (strong, moderate).
63. Removal of an infected CSF drain is recommended (strong, moderate).
64. Removal of an infected intrathecal infusion pump is recommended (strong, moderate).
65. Removal of infected hardware in patients with deep brain stimulation infections is recommended (strong, moderate).

X. How are Patients Monitored for Response to Treatment?

Recommendations

66. Patients with healthcare-associated ventriculitis and meningitis should be monitored for response to treatment based on clinical parameters (strong, low).
67. In patients with healthcare-associated ventriculitis and meningitis and an external drainage device, monitoring of CSF cultures is recommended to ensure that they become negative (strong, low).
68. In patients with no definitive clinical improvement, additional CSF analysis is recommended to ensure that the CSF parameters have improved and the cultures become negative (strong, low).
69. For external CSF drains not being used in the treatment of CSF shunt infection, daily CSF cultures and analysis are not recommended unless clinically indicated (strong, low).

XI. In Patients with Cerebrospinal Fluid Shunts Who Develop Ventriculitis and Meningitis, When can a New Shunt be Reimplanted?

Recommendations

70. In patients with infection caused by coagulase-negative staphylococci or *P. acnes*, with no associated CSF abnormalities and with negative CSF cultures for 48 hours after externalization, a new shunt should be reimplanted as soon as the third day after removal (strong, low).
71. In patients with infection caused by a coagulase-negative staphylococcus or *P. acnes*, with associated CSF abnormalities but negative repeat CSF cultures, a new shunt should be reimplanted after 7 days of antimicrobial therapy (strong, low); if repeat cultures are positive, antimicrobial treatment is recommended until CSF cultures remain negative for 7–10 consecutive days before a new shunt is placed (strong, low).
72. In patients with infection caused by *S. aureus* or gram-negative bacilli, a new shunt should be reimplanted 10 days after CSF cultures are negative (strong, low).
73. A period off antimicrobial therapy is not recommended to verify clearing of the infection before shunt reimplantation (strong, low).

XII. What is the Best Approach to Prevent Infection in Patients Who are Receiving Cerebrospinal Fluid Shunts?

Recommendations

74. Periprocedural prophylactic antimicrobial administration is recommended for patients undergoing CSF shunt or drain insertion (strong, moderate).
75. Periprocedural prophylactic antimicrobial administration is recommended for patients undergoing placement of external ventricular drains (strong, moderate).
76. Prolonged antimicrobial prophylaxis for the duration of the external ventricular drain is of uncertain benefit and not recommended (strong, moderate).

77. Use of antimicrobial-impregnated CSF shunts and CSF drains is recommended (strong, moderate).
78. In patients with external ventricular drains, fixed interval exchange is not recommended (strong, moderate).
79. Use of a standardized protocol for insertion of CSF shunts and drains is recommended (strong, moderate).

XIII. Is there a Role for Prophylactic Antimicrobial Therapy in Patients Undergoing Neurosurgery or in those with Cerebrospinal Fluid Leak?

Recommendation

80. For neurosurgical patients, perioperative antimicrobial agents are recommended to prevent infections of the incision (strong, high).
81. In patients with basilar skull fractures and a CSF leak, prophylactic antimicrobial agents are not recommended (strong, moderate).
82. In patients with basilar skull fractures and a prolonged CSF leakage (>7 days), an attempt to repair the leak is recommended (strong, low).
83. In patients with basilar skull fractures and a CSF leak, pneumococcal vaccination is recommended (strong, moderate).

Notes

Acknowledgments. The expert panel expresses its gratitude for thoughtful reviews of an earlier version by Drs Naomi O'Grady, Richard Whitley, William E. Whitehead, and Ram Yogev. The panel thanks Vita Washington for her guidance and preparation of the manuscript.

Financial support. Support for these guidelines was provided by the Infectious Diseases Society of America (IDSA).

Potential conflicts of interest. The following is a reflection of what has been reported to the IDSA regarding potential conflicts of interest (COI). In order to provide thorough transparency, the IDSA requires full disclosure of all relationships, regardless of relevancy to the guideline topic. Such relationships as potential conflicts of interest are determined by a review process that includes assessment by the Standards and Practice Guidelines Committee (SPGC) chair, the SPGC liaison to the development panel, and the Board of Directors (BOD) liaison to the SPGC, and, if necessary, the COI Task Force of the Board. This assessment of disclosed relationships for possible COI is based on the relative weight of the financial relationship (ie, monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The reader should be mindful of this when the list of disclosures is reviewed. A. T. received royalties from UpToDate and Elsevier and honoraria from ACP and Merck. A. B. received research support from Cubist. R. H. has received personal fees for speaker bureau participation with Pfizer, Medicine's Company and Biofire; he has served as a consultant for Biomeriaux. S. K. served as a consultant for Pfizer; received royalties from UpToDate and Elsevier; and received research grants from Pfizer, Forest Laboratories, Cubist, and Merck. W. M. S. received research grants from the National Institutes of Health, Pfizer, and Wyeth. D. v. d. B received research grants from the Netherlands Organization for Health Research and Development, Netherlands Scientific Organization, European Research Council, FP-7, Horizon 2020, and Omeros and served as a consultant for GSK. All other authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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