Acute Meningitis

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Meningitis Basics

I. Generally refers to inflammation of the leptomeninges (pia mater and arachnoid mater)
II. CSF runs between these two meningeal layers, making it ideal for diagnostic purposes

Diagnosis	Opening Pressure (cm H2O)	WBC Count (cells/uL)	WBC Differential	Glucose (mg/dL)	Total Protein (mg/dL)
Normal	<20	<5 (corrected for RBC)	N/A	50 – 100 (≥2/3 serum)	15 – 60 (lab dependent)
Bacterial Meningitis	Very high; often >30	Very high; often >1K	Strong neutrophilic predominance	<40% serum; often very low	Very high; often >500
Viral/aseptic Meningitis	Usually normal	High; teens to hundreds	Strong mononuclear predominance*	Usually normal	Normal to high
Fungal/TB Meningitis	High to very high	Variably high; teens to hundreds to thousands	Neutrophilic or mononuclear	Low to very low	High to very high

III. MRI findings are neither sensitive nor specific (nor acquired in a timely fashion) but include FLAIR sulcal hyperintensities and/or abnormal uptake of gadolinium within the leptomeninges
IV. Coverage for most common bacterial agents (van de Beek *ESCMID* 2016):

TABLE 4.2. Specific antibiotic in-hospital treatment for community-acquired bacterial meningitis[a]

Microorganism	Standard treatment	Alternatives	Duration
Streptococcus pneumoniae			
Penicillin susceptible (MIC <0.1 µg/mL)	Penicillin or amoxicillin/ampicillin	Ceftriaxone, cefotaxime, chloramphenicol	10–14 days
Penicillin resistant (MIC >0.1 µg/mL), third-generation cephalosporin susceptible (MIC <2 µg/mL)	Ceftriaxone or cefotaxime	Cefepime, meropenem, moxifloxacin[b]	10–14 days
Cephalosporin resistant (MIC ≥2 µg/mL)	Vancomycin plus rifampicin, or vancomycin plus ceftriaxone or cefotaxime, or rifampicin plus ceftriaxone or cefotaxime[c]	Vancomycin plus moxifloxacin,[b] linezolid	10–14 days
Neisseria meningitidis			
Penicillin susceptible (MIC <0.1 µg/mL)	Penicillin or amoxicillin/ampicillin	Ceftriaxone, cefotaxime, chloramphenicol	7 days
Penicillin resistant (MIC ≥0.1 µg/mL)	Ceftriaxone or cefotaxime	Cefipime, meropenem, ciprofloxacin or chloramphenicol	7 days
Listeria monocytogenes	Amoxicillin or ampicillin, penicillin G[d]	trimethoprim-sulfamethoxazole, moxifloxacin,[b] meropenem, linezolid	At least 21 days
Haemophilus influenzae			
β-Lactamase negative	Amoxicillin or ampicillin	Ceftriaxone, cefotaxime or chloramphenicol	7–10 days
β-Lactamase positive	Ceftriaxone or cefotaxim	Cefepime, ciprofloxacin, chloramphenicol	7–10 days
β-Lactamase negative ampicillin resistant	Ceftriaxone or cefotaxime plus meropenem	Ciprofloxacin	7–10 days
Staphylococcus aureus			
Methicillin sensitive	Flucloxacillin, nafcillin, oxacillin	Vancomycin, linezolid, rifampicin,[e] fosfomycin,[e] daptomycin[b]	At least 14 days
Methicillin resistant	Vancomycin[f]	Trimethoprim/sulfamethoxazole, linezolid, rifampicin,[e] fosfomycin,[e] daptomycin	At least 14 days
Vancomycin resistant (MIC >2.0 µg/mL)	Linezolid[f]	Rifampicin,[e] fosfomycin,[e] daptomycin[b]	At least 14 days

[a]Recommendations must be in accordance with the results of the susceptibility testing.
[b]Based on case reports.
[c]Ceftriaxone dose 2 g q12h and cefotaxime 2–3g q6h.
[d]Adding an aminoglycoside can be considered.
[e]Must not be used in monotherapy.
[f]Addition of rifampicin can be considered.

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Meningitis updates

I. Healthcare associated meningitis/ventriculitis guidelines (Tunkel CID 2017):

Table 1. Recommended Antimicrobial Therapy in Patients With Healthcare-Associated Ventriculitis and Meningitis Based on Isolated Pathogen and In Vitro Susceptibility Testing

Microorganism	Standard Therapy	Alternative Therapies
Staphylococci[a]		
Methicillin sensitive	Nafcillin or oxacillin	Vancomycin
Methicillin resistant	Vancomycin	Daptomycin, trimethoprim-sulfamethoxazole, or linezolid
Propionibacterium acnes	Penicillin G	Third-generation cephalosporin,[b] vancomycin, daptomycin, or linezolid
Streptococcus pneumoniae		
Penicillin MIC ≤0.06 μg/mL	Penicillin G	Third-generation cephalosporin[b]
Penicillin MIC ≥0.12 μg/mL		
Cefotaxime or ceftriaxone MIC <1.0 μg/mL	Third-generation cephalosporin[b]	Cefepime or meropenem
Cefotaxime or ceftriaxone MIC ≥1.0 μg/mL	Vancomycin plus a third-generation cephalosporin[b,c]	Moxifloxacin[d]
Pseudomonas aeruginosa	Cefepime, ceftazidime, or meropenem	Aztreonam or ciprofloxacin
Haemophilus influenzae		
β-lactamase negative	Ampicillin	Third-generation cephalosporin,[b] cefepime, or a fluoroquinolone
β-lactamase positive	Third-generation cephalosporin[b]	Cefepime, aztreonam, or a fluoroquinolone
Extended spectrum β-lactamase-producing gram-negative bacilli	Meropenem	Cefepime or a fluoroquinolone
Acinetobacter baumannii	Meropenem	Colistin (usually formulated as colistimethate sodium)[e] or polymyxin B[e]
Other Enterobacteriaceae[f]	Third-generation cephalosporin[b]	Meropenem, aztreonam, trimethoprim-sulfamethoxazole, or ciprofloxacin
Candida species[g]	Lipid formulation of amphotericin B ± flucytosine	Fluconazole or voriconazole
Aspergillus species	Voriconazole	Lipid formulation of amphotericin B or posaconazole

II. *N. meningitidis* serogroup B outbreaks
   A. 2016 Santa Clara University (7 cases)
   B. 2015 University of Oregon (7 cases, 1 death) and Providence College (2 cases)
   C. 2013-2014 Princeton University (9 cases, 1 death)
   D. 2013 UC Santa Barbara (4 cases)

III. Meningitis B vaccine (approved 2015, https://www.cdc.gov/vaccines/hcp/vis/vis-statements/mening-serogroup.html)

Serogroup B Meningococcal Vaccines

Two serogroup B meningococcal vaccines — Bexsero® and Trumenba® — have been licensed by the Food and Drug Administration (FDA).

These vaccines are recommended routinely for people 10 years or older who are at increased risk for serogroup B meningococcal infections, including:

- People at risk because of a serogroup B meningococcal disease outbreak
- Anyone whose spleen is damaged or has been removed
- Anyone with a rare immune system condition called "persistent complement component deficiency"
- Anyone taking a drug called eculizumab (also called Soliris®)
- Microbiologists who routinely work with isolates of *N. meningitidis*

These vaccines may also be given to anyone 16 through 23 years old to provide short term protection against most strains of serogroup B meningococcal disease; 16 through 18 years are the preferred ages for vaccination.

For best protection, more than 1 dose of a serogroup B meningococcal vaccine is needed. The same vaccine must be used for all doses. Ask your health care provider about the number and timing of doses.

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IV. Multiplex PCR assay for meningitis (Leber *JCM* 2016)

A. CSF diagnostic test for *H. influenzae, L. monocytogenes, N. meningitidis, S. agalactiae, S. pneumoniae, E. coli*, CMV, EV, HSV-1, HSV-2, VZV, HHV-6, HPeV, and *C. neoformans/gattii.*

B. Uses only 200uL CSF and takes about 1 hr

C. Performance compared to culture as standard found to have high sensitivity (86-99%) but with several caveats

1. False positives found for *S. pneumoniae*, *S. agalactiae*, HHV-6
2. False negative for *S. agalactiae*
3. *L. monocytogenes* and *N. meningitidis* weren't encountered in study

Multicenter Evaluation of BioFire FilmArray Meningitis/Encephalitis Panel for Detection of Bacteria, Viruses, and Yeast in Cerebrospinal Fluid Specimens

TABLE 3

Performance summary and characteristics of the FilmArray ME Panel versus those of the comparator assays[a]

Analyte	Sensitivity/PPA[b]			Specificity/NPA[b]		
	TP/(TP + FN)[c]	%	95% CI	TN/(TN + FP)[c]	%	95% CI
Bacteria						
E. coli K1	2/2	100	34.2–100	1,557/1,558	99.9	99.6–100
H. influenzae	1/1	100		1,558/1,559	99.9	99.6–100
L. monocytogenes	0/0			1,560/1,560	100	99.8–100
N. meningitidis	0/0			1,560/1,560	100	99.8–100
S. agalactiae	0/1	0.0		1,558/1,559	99.9	99.6–100
S. pneumoniae	4/4	100	51.0–100	1,544/1,556	99.2	98.7–99.6
Viruses						
CMV	3/3	100	43.9–100	1,554/1,557	99.8	99.4–99.9
EV	44/46	95.7	85.5–98.8	1,507/1,514	99.5	99.0–99.8
HSV-1	2/2	100	34.2–100	1,556/1,558	99.9	99.5–100
HSV-2	10/10	100	72.2–100	1,548/1,550	99.9	99.5–100
HHV-6	18/21	85.7	65.4–95.0	1,532/1,536	99.7	99.3–99.9
HPeV	9/9	100	70.1–100	1,548/1,551	99.8	99.4–99.9
VZV	4/4	100	51.0–100	1,553/1,556	99.8	99.4–99.9
Yeast						
C. neoformans/C. gattii	1/1	100		1,555/1,559	99.7	99.3–99.9

V. Arbovirus meningitis (Krow-Lucal MMWR 2017)

A. Case numbers out for 2015: WNV (2175), La Crosse (55), SLEV (23), JaC (11), POWV (7), EEE (6)

B. Meningitis is rare as a manifestation but can occur without encephalitis

TABLE 1. Number and percentage of reported cases of West Nile virus and other arboviral diseases, by virus type and selected patient characteristics — United States, 2015*

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	Virus type					
	West Nile (N = 2,175)	La Crosse (N = 55)	St. Louis encephalitis (N = 23)	Jamestown Canyon (N = 11)	Powassan (N = 7)	Eastern equine encephalitis (N = 6)
Characteristic	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**	**No. (%)**
Age group (yrs)						
<18	54 (2)	51 (93)	0 (0)	1 (9)	0 (0)	1 (17)
18–59	1,108 (51)	1 (2)	9 (39)	6 (55)	1 (14)	2 (33)
≥60	1,013 (47)	3 (5)	14 (61)	4 (36)	6 (86)	3 (50)
Sex						
Male	1,289 (59)	31 (56)	15 (65)	6 (55)	5 (71)	6 (100)
Female	886 (41)	24 (44)	8 (35)	5 (45)	2 (29)	0 (0)
Period of illness onset						
January–March	2 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
April–June	60 (3)	7 (13)	3 (13)	5 (45)	4 (57)	1 (17)
July–September	1,804 (83)	47 (85)	19 (83)	5 (45)	1 (14)	5 (83)
October–December	309 (14)	1 (2)	1 (4)	1 (9)	2 (29)	0 (0)
Clinical syndrome						
Nonneuroinvasive	720 (33)	4 (7)	4 (17)	5 (45)	1 (14)	0 (0)
Neuroinvasive	1,455 (67)	51 (93)	19 (83)	6 (55)	6 (86)	6 (100)
Encephalitis	753 (35)	40 (73)	12 (52)	4 (36)	6 (86)	2 (33)
Meningitis	637 (29)	10 (18)	7 (30)	1 (9)	0 (0)	2 (33)
Acute flaccid p[illegible]	118 (5)	2 (4)	1 (4)	1 (9)	0 (0)	0 (0)
Other	[illegible]	0 (0)	1 (4)	1 (9)	1 (14)	0 (0)
Outcome						
Hospitalization	1,616 (74)	52 (95)	19 (83)	9 (82)	7 (100)	6 (100)
Death	146 (7)	0 (0)	2 (9)	0 (0)	1 (14)	4 (67)

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