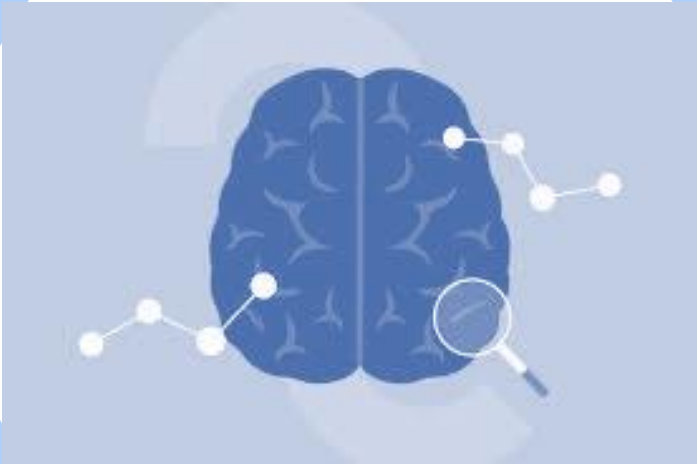
Farmakoterapi Populasi Khusus



Chotijatun Nasriyah

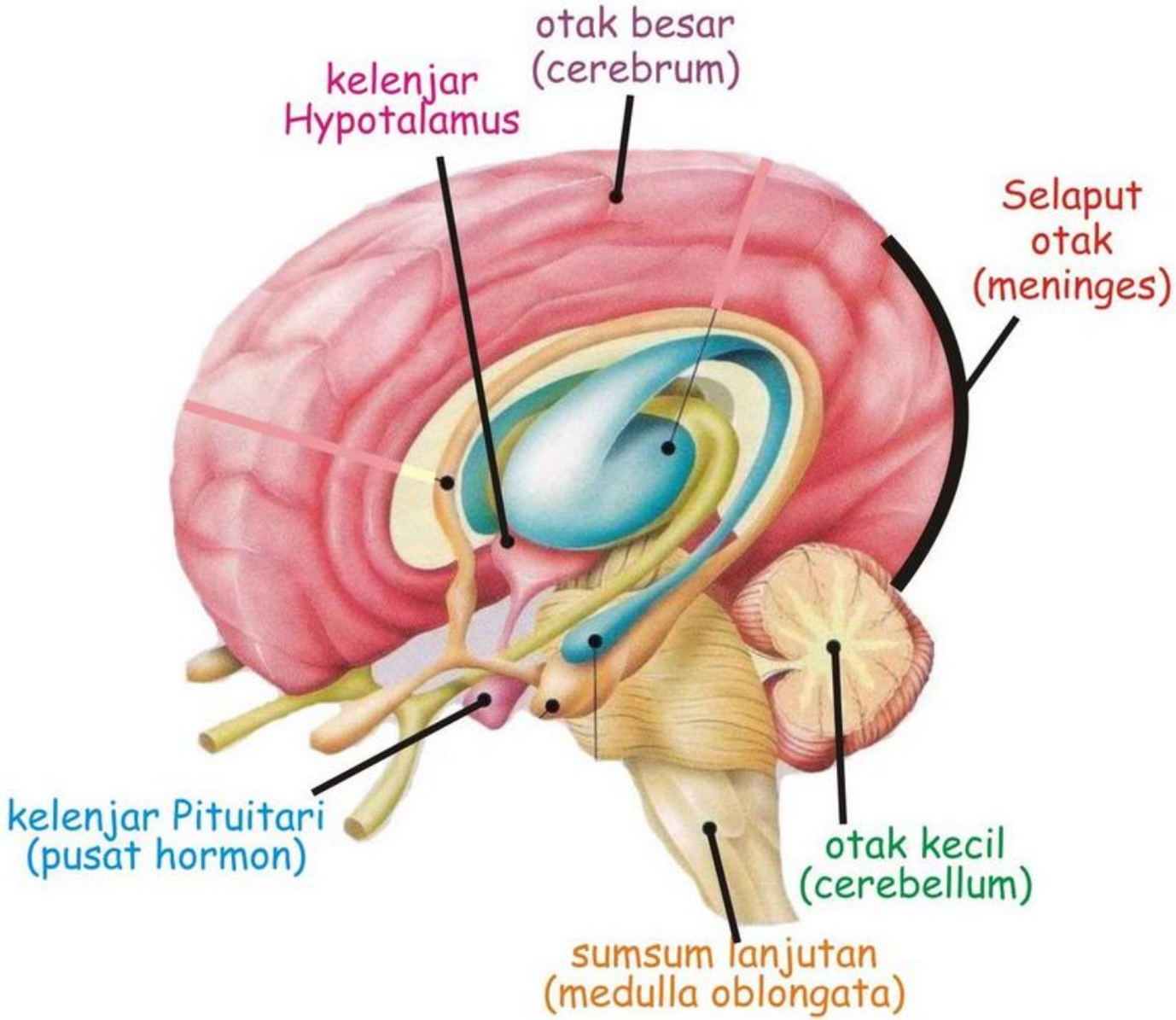
by: CH

Meningitis

- merupakan penyakit peradangan akibat infeksi pada meninges atau selaput membran otak
- Etiologi : bakteri dan virus
- *Streptococcus pneumoniae* dan *Neisseria meningitidis* (80%) penyebab pd bayi imunokompeten (> 4 mggu), anak dan dewasa
- *Listeria monocytogenes* dan *Stafilokokus*
- *E. coli*, *Klebsiella*, *Enterobacter* dan *Pseudomonas aeruginosa* (< 10%)

by: CH

Anatomi Otak



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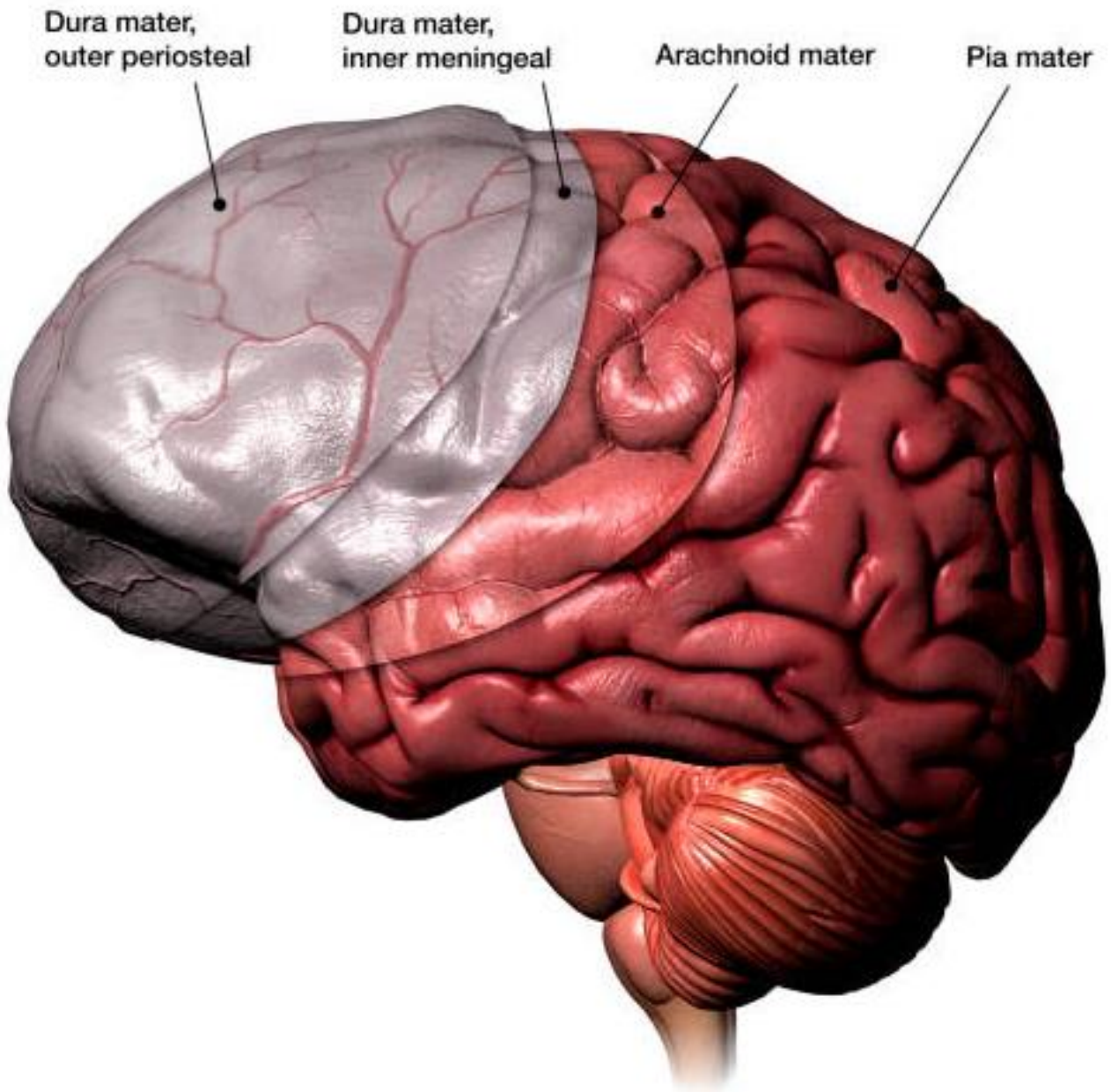
Selaput Meninges



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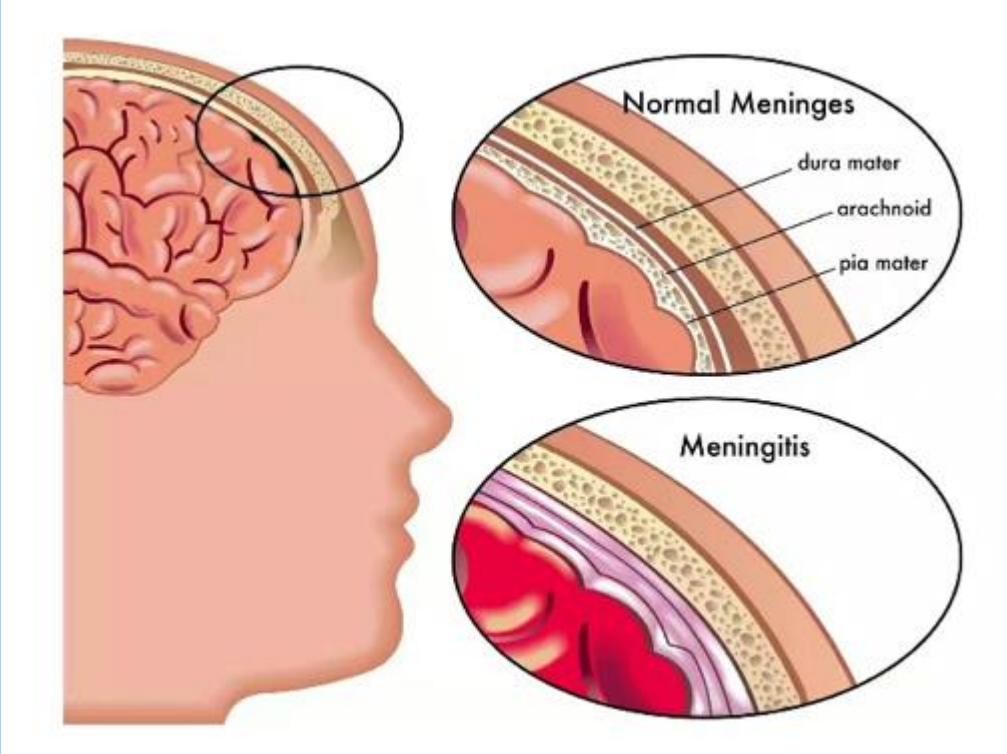
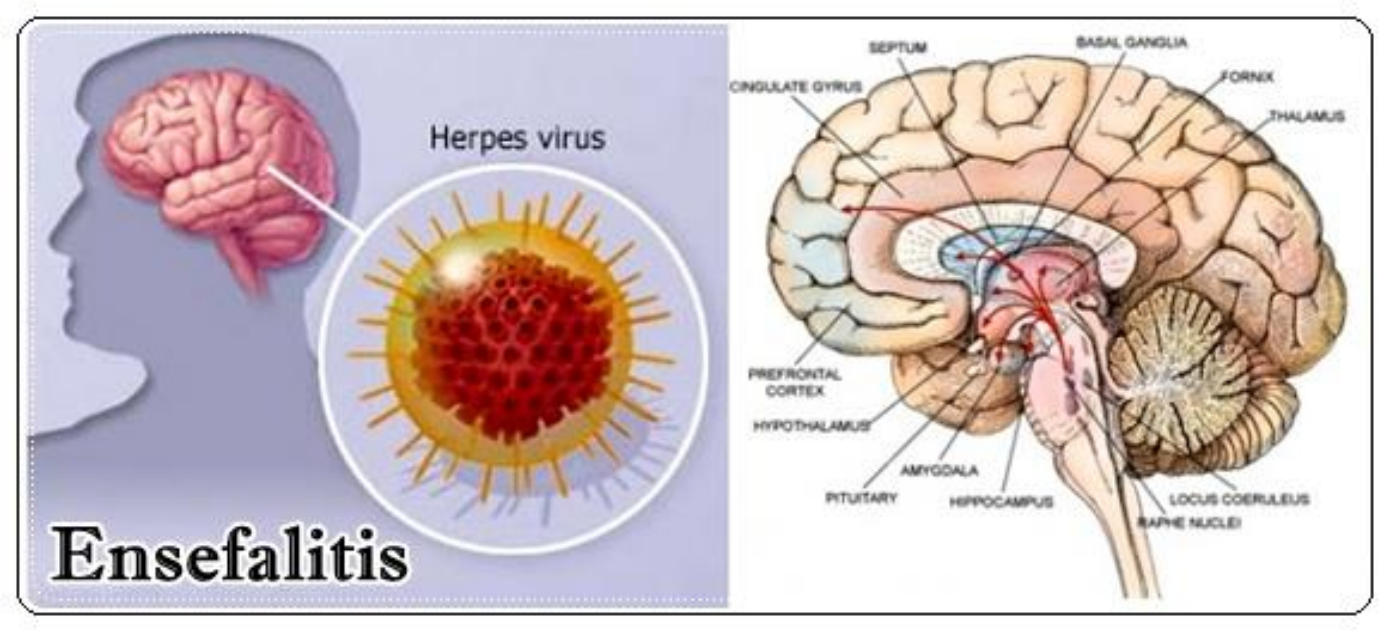
Ensefalitis vs Meningitis





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Pemeriksaan Lab

Spesimen	Jenis pemeriksaan
Darah	Kultur
	Hitung sel
	C-reaktif protein
	Tekanan (*opening pressure*)
	Warna
	Hitung sel

Pemeriksaan Lab

	Biokimia: Glukosa dan rasio dengan glukosa darah Protein Lain-lain seperti feritin, *chlorida*, laktat dehidrogenase (LDH) Mikrobiologi Pewarnaan Gram dan kultur Pemeriksaan lainnya: *counterimmunoelectrophoresis* (CIE), radioimmunoassay (RIA), *latex particle agglutination* (LPA), *enzyme-linked immunosorbent assay* (ELISA), *polymerase chain reaction* (PCR)
Cairan tubuh lainnya seperti cairan *petechial*, sputum, sekresi dari orofaringeal, hidung dan telinga.	Kultur

TABLE 36-1 Mean Values of the Components of Normal and Abnormal Cerebrospinal Fluid

Type	Normal	Bacterial	Viral	Fungal	Tuberculosis
WBC (cells/mm^3 or 10^6/L)	<5 (<30 in newborns)	1000–5000	50–1000	20–500	25–500
Differential[a]	Monocytes	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes
Protein (mg/dL)	<50 (<500 mg/L)	Elevated	Mild elevation	Elevated	Elevated
Glucose (mg/dL)	45–80 (2.5–4.4 mmol/L)	Low	Normal	Low	Low
CSF/blood glucose ratio	50%–60%	Decreased	Normal	Decreased	Decreased

Gejala klinik

Usia 5 – 12 tahun:

Demam (92%)

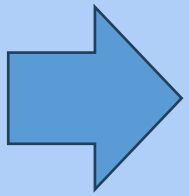
Kaku kuduk (77%)

Sakit kepala hebat

Mual/muntah (82%)

Fotofobia

Kejang (40%)



2 atau lebih gejala tersebut

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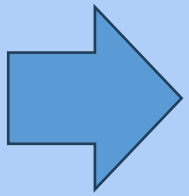
Gejala klinik anak

Anak dengan :

- Panas
- Muntah
- Kaku kuduk
- Gangguan kesadaran

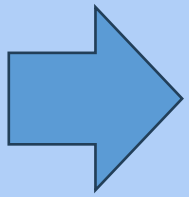


meningitis bakteri

by: CH

Gejala klinik dewasa

- Infeksi saluran nafas atas
- Kelemahan umum
- Mialgia
- Nyeri punggung bbr jam / hari



tanda meningitis

Streptococcus pneumonia lebih berat lebih cepat kesadaran menurun ----- precoma ----- koma

Patogenesis

Kolonisasi Kuman nasofarings

↓

Invasi lokal (I : Mucosal infasion)

↓

Bakteriemia (II : intravascular survival)

↓

Melekat pada endotel pleksus khoroid / endotel vascular otak

↓

Kerusakan sel endotel

↓

Invasi selaput otak (III: crossing BBB)

↓

Replikasi bakterial di LCS + inflamasi LCS (IV Survival in CSF)

↓

Meningitis

by: CH

Kuman Mencapai leptomening dan subarachnoid melalui

1. Luka terbuka di kepala
2. Penyebaran langsung dari :
   - ✓ Infeksi telinga bag. Tengah (OM)
   - ✓ Sinus paranasalis
   - ✓ Kulit kepala – muka
   - ✓ Benda asing terinfeksi (shunting)
3. Sepsis
4. Thromboplebitis cortical
5. Abses sub/ekstra dural ke otak

by: CH

Penanganan

- Secepatnya dan tepat ------ mencegah kecacatan dan kematian
- Pemeriksaan LCS dalam 30 menit → AB sesuai : gram, antigen
- Sebelum hasil kultur ----- AB empiris sesuai umur

Bakteri Penyebab

Umur	Kuman
• Bayi < 8 minggu	E. Coli; Gr (--) entero bacter; Group B streptococcus; S. Aurius
• Anak 2 bln -15 tahun	H. Influinzae (< 5 th); Neisseria Meningitides; Streptococcus Pneumonae; S. Aurius (sangat ganas sukar diatasi)

Bakteri Penyebab

Umur	Kuman
• Anak > tua dewasa muda	Neisseria Meningitides; Streptococcus Pneumonae; H. Influinzae; S. Aurius
• > 40 Th	Streptococcus Pneumonae; Neisseria Meningitides; S. Aurius

Penyebab

Penularan	Kuman
○ Luka tembus kepala	S. Aurius; Group β Haemoliticus Streptococ
○ Cedera kepala tertutup	Streptococcus Pneumonae; H.Influinzae; Anaerobic & Mikroaerophilic Strepococcus; S. Aurius

Penyebab

Penularan

- Infeksi pericranial: Sinusitis, Otitis, Inf. Muka / Mulut
- Neurosurgery

Kuman

Streptococcus Pneumonae; H. Influinzae; s.d.a

S. Aurius; Gr (--) Enteric Bact; Gr (--) Anaerobic Bact

Tatalaksana

Sifat Antibiotika ideal :

- Larut dalam lemak ----- menembus BBB
- Gol beta lactam (penicillin dan sefalosphorin gen II/III sukar menembus BBB
- Aktif dalam LCS purulen dan asam
- AB dosis tinggi IV

by: CH

Tatalaksana

Lama pemberian :

- Pneumokok : 10 14 hari
- H. Influenza : 10 hari
- Meningokok : 7 hari
- Gram (--) : 21 hari

Kombinasi tidak boleh antagonistik misal Chloramphenicol & Gentamycin

AB

TABLE 36-2 Bacterial Meningitis: Most Likely Etiologies and Empiric Therapy by Age Group

Age	Most Likely Organisms	Empirical Therapy[a]
<1 month	*S. agalactiae* Gram-negative enterics[b] *L. monocytogenes*	Ampicillin + cefotaxime *or* ampicillin + aminoglycoside
1–23 months	*S. pneumoniae* *N. meningitidis* *H. influenzae* *S. agalactiae*	Vancomycin[c] + 3rd generation cephalosporin (cefotaxime *or* ceftriaxone)
2–50 years	*N. meningitidis* *S. pneumoniae*	Vancomycin[c] + 3rd generation cephalosporin (cefotaxime *or* ceftriaxone)
>50 years	*S. pneumoniae* *N. meningitidis* Gram-negative enterics[b] *L. monocytogenes*	Vancomycin[c] + ampicillin + 3rd generation cephalosporin (cefotaxime *or* ceftriaxone)

by: CH

TABLE 36-3 Penetration of Anti-infective Agents into the CSF[a]

Therapeutic Levels in CSF With or Without Inflammation of Meninges	
Acyclovir	Levofloxacin
Chloramphenicol	Linezolid
Ciprofloxacin	Metronidazole
Fluconazole	Moxifloxacin
Flucytosine	Pyrazinamide
Foscarnet	Rifampin
Fosfomycin	Sulfonamides
Ganciclovir	Trimethoprim
Isoniazid	Voriconazole
Therapeutic Levels in CSF With Inflammation of Meninges	
Ampicillin ± sulbactam	Imipenem
Aztreonam	Meropenem
Cefepime	Nafcillin
Cefotaxime	Ofloxacin
Ceftazidime	Penicillin G
Ceftriaxone	Piperacillin/Tazobactam[b]
Cefuroxime	Pyrimethamine
Colistin	Quinupristin/Dalfopristin
Daptomycin	Ticarcillin ± clavulanic acid[b]
Ethambutol	Vancomycin
Nontherapeutic Levels in CSF With or Without Inflammation of Meninges	
Aminoglycosides	Cephalosporins (second generation)[d]
Amphotericin B	Doxycycline[e]
β-Lactamase inhibitors[c]	Itraconazole[f]
Cephalosporins (first generation)	

by: CH

Terapi

TABLE 36-4 Antimicrobial Agents of First Choice and Alternative Choice for Treating Meningitis Caused by Gram-Positive and Gram-Negative Microorganisms

Organism	Antibiotics of First Choice	Alternative Antibiotics	Recommended Duration of Therapy
Gram-Positive Organisms			
Streptococcus pneumoniae[a]			10–14 days
Penicillin susceptible MIC ≤0.06 mcg/mL (mg/L)	Penicillin G or ampicillin (A-III)	Cefotaxime (A-III), ceftriaxone (A-III), cefepime (B-II), or meropenem (B-II)	
Penicillin resistant MIC >0.06 mcg/mL (mg/L)	Vancomycin[b,c] + cefotaxime or ceftriaxone (A-III)	Moxifloxacin (B-II)	
Ceftriaxone resistant MIC >0.5 mcg/mL (mg/L)	Vancomycin[b,c] + cefotaxime or ceftriaxone (A-III)	Moxifloxacin (B-II)	
Staphylococcus aureus			14–21 days
Methicillin susceptible	Nafcillin or oxacillin (A-III)	Vancomycin (A-III) or meropenem (B-III)	
Methicillin resistant	Vancomycin[b,c] (A-III)	Trimethoprim-sulfamethoxazole or linezolid (B-III)	
Group B *Streptococcus*	Penicillin G or ampicillin (A-III) ± gentamicin[b,c]	Ceftriaxone or cefotaxime (B-III)	14–21 days
S. epidermidis	Vancomycin[b,c] (A-III)	Linezolid (B-III)	14–21 days[g]
L. monocytogenes	Penicillin G or ampicillin ± gentamicin[b,c,e] (A-III)	Trimethoprim-sulfamethoxazole (A-III), meropenem (B-III)	≥21 days
Gram-Negative Organisms			
Neisseria meningitis			7–10 days
Penicillin susceptible	Penicillin G or ampicillin (A-III)	Cefotaxime or ceftriaxone (A-III)	
Penicillin resistant	Cefotaxime or ceftriaxone (A-III)	Meropenem or moxifloxacin (A-III)	
Haemophilus influenzae			7–10 days
β-lactamase negative	Ampicillin (A-III)	Cefotaxime (A-III), ceftriaxone (A-III), cefepime (A-III) or moxifloxacin (A-III)	

by: CH

Lanjutan ....

TABLE 36-4 Antimicrobial Agents of First Choice and Alternative Choice for Treating Meningitis Caused by Gram-Positive and Gram-Negative Microorganisms (*Continued*

Organism	Antibiotics of First Choice	Alternative Antibiotics	Recommended Duration of Therapy
β-lactamase positive	Cefotaxime or ceftriaxone (A-I)	Cefepime (A-I) or moxifloxacin (A-III)	
Enterobacteriaceae[f]	Cefotaxime or ceftriaxone (A-II)	Cefepime (A-III), moxifloxacin (A-III), meropenem (A-III) or aztreonam (A-III)	21 days
Pseudomonas aeruginosa	Cefepime or ceftazidime (A-II) ± tobramycin[b,c] (A-III)	Ciprofloxacin (A-III), meropenem (A-III), piperacillin plus tobramycin[a,b] (A-III), colistin sulfomethate[g] (B-III), aztreonam (A-III)	21 days

by: CH

Terapi tambahan

Dexamethasone :

- ✓ menghambat inflamasi dalam subarachnoid
- ✓ IDSA ------ deksametason tambahan pada bayi dan anak (usia 6 minggu ke atas) ----- dg meningitis *H. influenzae*
- ✓ Recommended i.v dose is 0,15 mg/kg every 6 hours for 2–4 days; initiated 10–20 minutes prior to or concomitant with the first dose of antibiotics

by: CH

Terapi tambahan

Dexamethasone :

- ✓ If pneumococcal meningitis is suspected or proven, adults should receive dexamethasone 0.15 mg/kg (up to 10 mg) every 6 hours for 2–4 days with the first dose administered 10–20 minutes prior to first dose of antibiotics

by: CH

Indikasi dexamethasone

- ✓ penderita resiko tinggi
- ✓ Status mental terganggu
- ✓ edema otak/TIK ↑

by: CH

Penyulit

- ✓ ggn serebrovaskuler (15,1%)
- ✓ edema otak (14%)
- ✓ Hidrosefalus (11,6%)
- ✓ perdarahan otak (2,3%)

by: CH

Penyulit

Pada anak :

- efusi subdural
- kerusakan system saraf yang berat
- tuli (20%)
- ggn bicara/penglihatan
- ataxia, kejang, retardasi mental

by: CH

Penyulit

- Perhatikan balance cairan & elektrolit pd kasus muntah ---- dehidrasi ----- hemokonsentrasi ------ hipotensi/thrombosis serebri
- Over hidrasi ---- edema serebri >

Cari guide/jurnal management meningitis in pregnancy, child and elderly

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THANK YOU