ÇOCUKLARDA BAKTERİYEL MENENJİT

Prof. Dr. Ergin ÇİFTÇİ

Ankara Üniversitesi Tıp Fakültesi
Çocuk Enfeksiyon Hastalıkları Bilim Dalı

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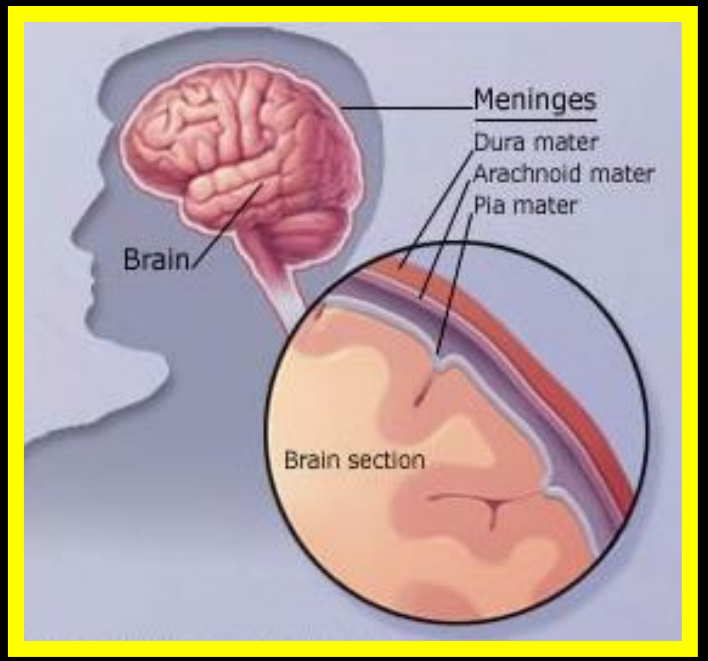
MENENJİT

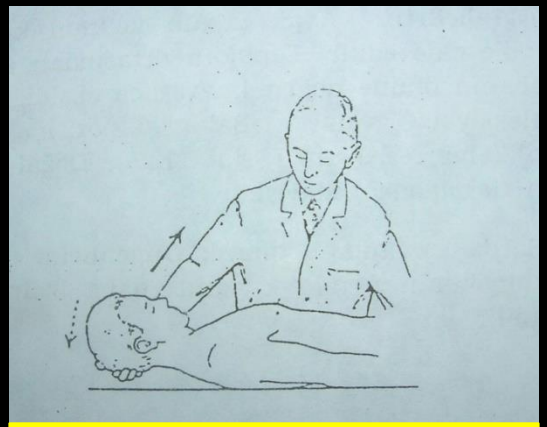
Tanım

- Menenjit, beyni ve omuriliği kaplayan meningeal zarların iltihaplanmasıdır.
- Çoğu zaman bakteri veya virüsler etkendir, mantar veya parazitler de menenjite neden olabilir.
- Virüs menenjiti daha sıktır ve genellikle daha hafif seyirlidir.
- Bakteriyel menenjit genellikle daha şiddetlidir ve uzun süreli komplikasyonlara veya ölüme neden olabilir.

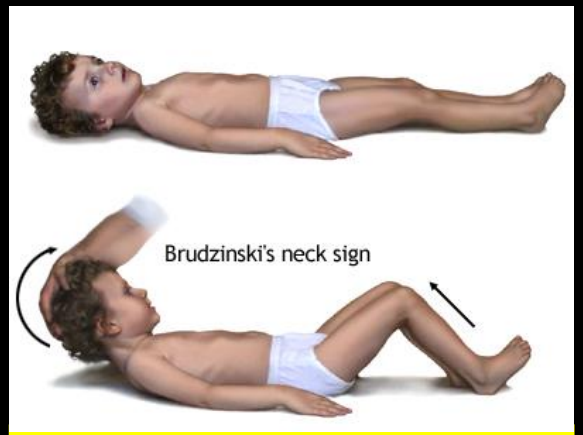


MENENJİT
Semptom ve Bulgular

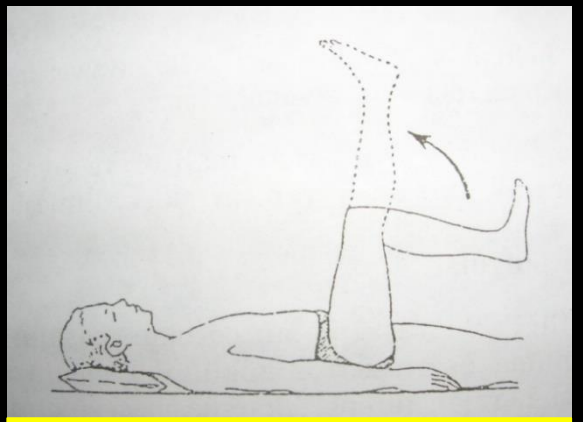
- Ense sertliği
- Kernig işareti pozitifliği
- Brudzinski işareti pozitifliği
- Fontanel şişkinliği
- Azalan bilinç seviyesi
- Konvülsif status epileptikus



Ense sertliği



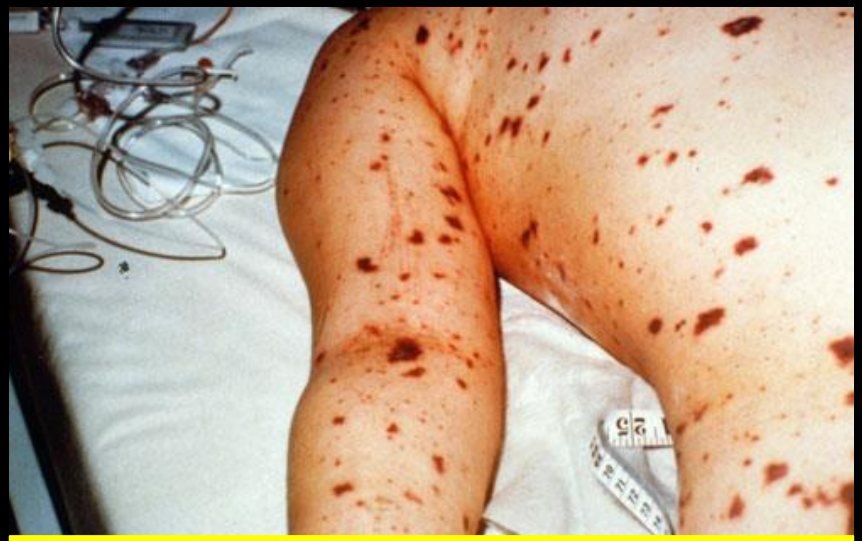
Brudzinski



Kernig

MENENJİT
Semptom ve Bulgular

- **Özellikle aşağıdaki özelliklerden herhangi biri mevcutsa, ateşi ve solmayan döküntüsü olan herhangi bir çocukta meningokok hastalığı düşünün:**
  - **Genel durumu kötü görünen bir çocuk**
  - **Çapı 2 mm'den büyük lezyonlar (purpura)**
  - **Kapiller dolum süresinin ≥3 saniye olması**



Meningococcal rash

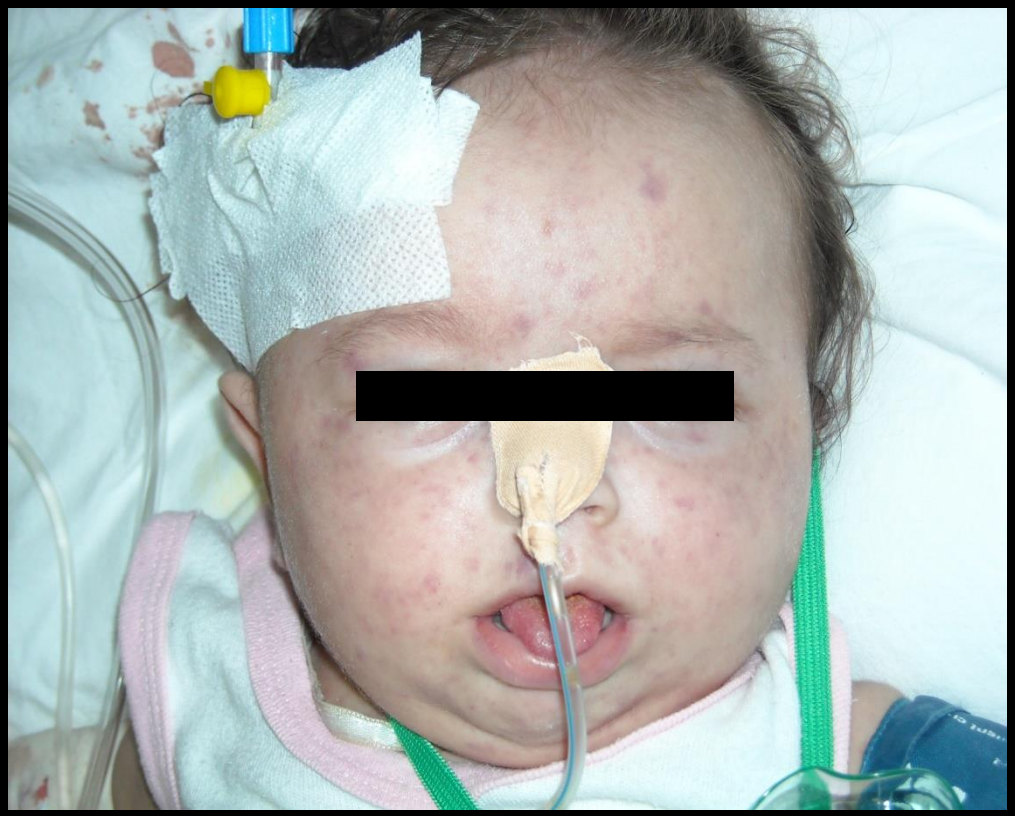
ÇOCUKLARDA MENENJİT

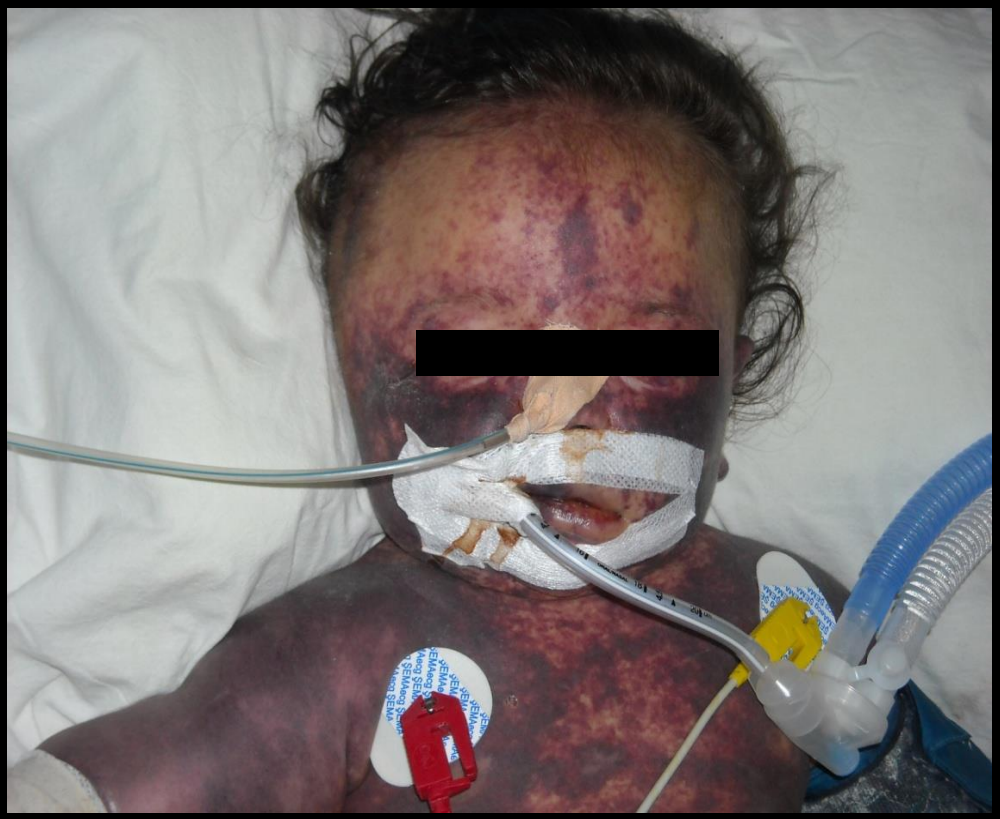
Hala Sorun

Purpura fulminans in a child due to *Neisseria meningitidis*

H. Özdemir · T. Kendirli · E. Çiftçi · E. İnce

Infection (2012) 40:717–718

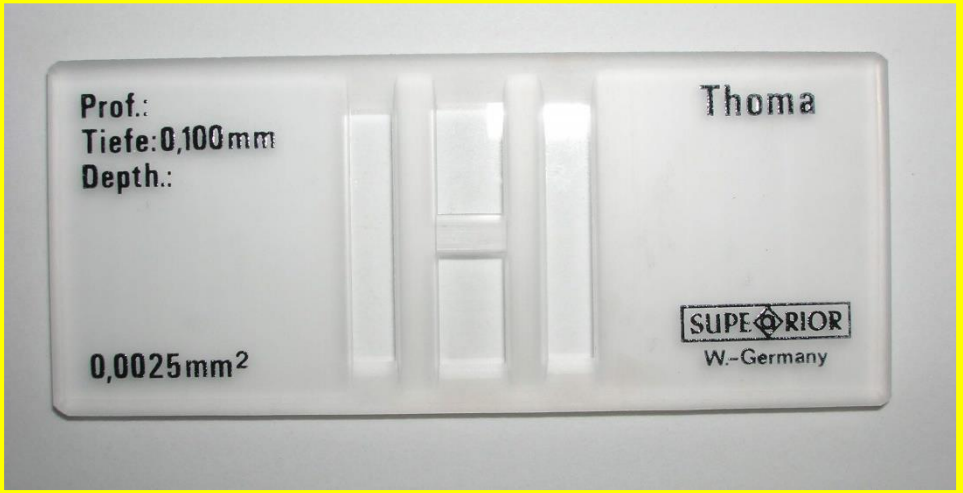




MENENJİT

Tanı

- **Menenjit tanısı lomber ponksiyon (spinal tap) ile alınan BOS incelemesi ile konulur.**



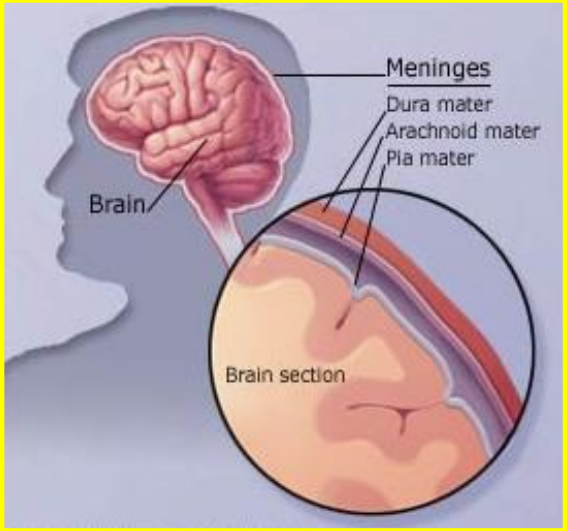
MENENJİT
BOS Bulguları

	Basınç (mmH_2O)	Lökosit sayısı (mm^3)	Protein (mg/dL)	Glukoz (mg/dL)
Normal	50-80	<5, >%75 lenfosit	20-45	>50 (serum glukozunun %75'i)
Akut bakteriyel menenjit	100-300	100-10,000 (genellikle 300-2,000) PNL	100-500	<40 (serum glukozunun %50'sinden az)
Viral menenjit meningoensefalit	80-150	<1,000, lenfosit	50-200	Genellikle N, <40
Tuberküloz menenjit	↑	10-500, başlangıçta PMN, sonra lenfosit	100-3,000	<50

BAKTERİYEL MENENJİT

Beyin Omurilik Sıvısı: Kurtarılmış Bölge!

1. **Antikordan yoksun**
2. **Kompleman aktivitesi yetersiz**



Tedavi edilmeyen bakteriyel menenjit ölümcül bir enfeksiyondur

BAKTERİYEL MENENJİT
Beyin Omurilik Sıvısı: Antibiyotik Geçişi Zor Bölge!

Antibiyotiklerin BOS'a geçişini kolaylaştıran özellikler

1. **Düşük moleküler ağırlık**
2. **Basit kimyasal yapı**
3. **Yağda çözünebilme**
4. **Proteine az bağlanma**
5. **Az iyonize olma**

BAKTERİYEL MENENJİT
Beyin Omurilik Sıvısı: Kan-Beyin Bariyeri Önemi

Beta laktam antibiyotiklerin BOS'na geçişi

Kan-Beyin Bariyeri normalse	%0.5-2
Kan-Beyin Bariyeri bozulmuşsa	%20-55

Bakterinin en etkili öldürülmesi için ulaşılması gereken BOS antibiyotik konsantrasyonu

Beta laktam antibiyotilerde	MBC'nun 10-30 katı
Vankomisin'de	MBC'nun 5-10 katı

ÇOCUKLARDA MENENJİT

Kılavuz

2004

IDSA GUIDELINE

Practice Guidelines for the Management of Bacterial Meningitis

Allan R. Tunkel,[1] Barry J. Hartman,[2] Sheldon L. Kaplan,[3] Bruce A. Kaufman,[4] Karen L. Roos,[5] W. Michael Scheld,[6] and Richard J. Whitley[7]

Clinical Infectious Diseases 2004; 39:1267–84

2014

CPS Position Statement

Guidelines for the management of suspected and confirmed bacterial meningitis in Canadian children older than one month of age

Nicole Le Saux; Canadian Paediatric Society, Infectious Diseases and Immunization Committee

Canadian Paediatric Society

Français en page 147

Paediatr Child Health Vol 19 No 3 March 2014

ÇOCUKLARDA MENENJİT
Kılavuz

2016

ORIGINAL ARTICLE

ESCMID guideline: diagnosis and treatment of acute bacterial meningitis

D. van de Beek[1], C. Cabellos[2], O. Dzupova[3], S. Esposito[4], M. Klein[5], A. T. Kloek[1], S. L. Leib[6], B. Mourvillier[7], C. Ostergaard[8], P. Pagliano[9], H. W. Pfister[5], R. C. Read[10], O. Resat Sipahi[11] and M. C. Brouwer[1], for the ESCMID Study Group for Infections of the Brain (ESGIB)

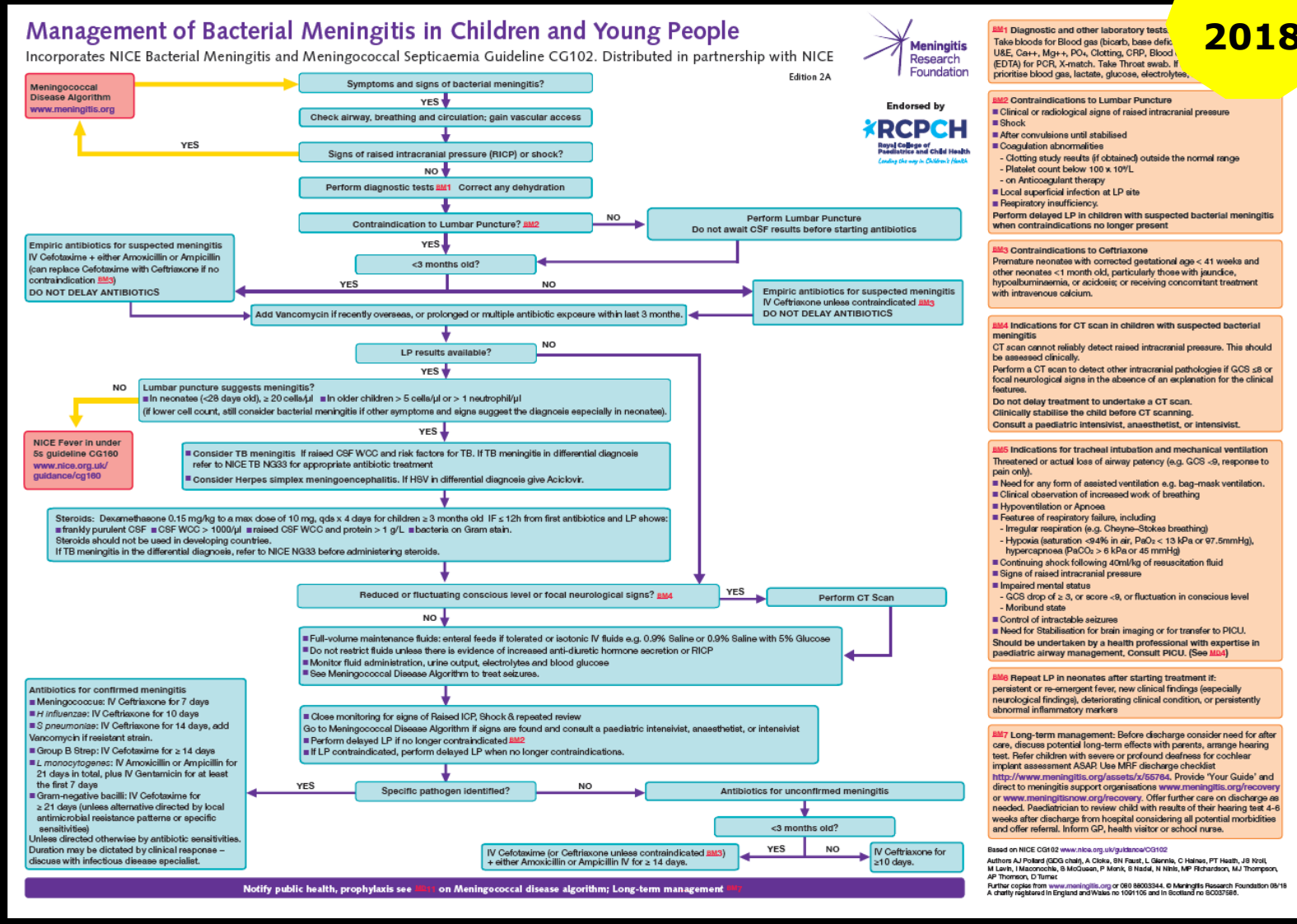
1) *Department of Neurology, Academic Medical Center, Amsterdam, The Netherlands,* 2) *Department of Infectious Diseases, Hospital Universitari de Bellvitge, Barcelona, Spain,* 3) *Department of Infectious Diseases, Charles University, Third Faculty of Medicine, Prague, Czech Republic,* 4) *Pediatric Highly Intensive Care Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Università degli Studi di Milano, Milan, Italy,* 5) *Department of Neurology, Klinikum Großhadern, Munich, Germany,* 6) *Institute for Infectious Diseases, University of Bern, Bern, Switzerland,* 7) *Department of Intensive Care Medicine, Groupe Hospitalier Bichat-Claude Bernard, Paris, France,* 8) *Department of Clinical Microbiology, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark,* 9) *Department of Infectious Diseases, "D. Cotugno" Hospital, Naples, Italy,* 10) *Department of Infectious Diseases, Southampton General Hospital, Southampton, United Kingdom and* 11) *Department of Infectious Diseases and Clinical Microbiology, Ege University, Izmir, Turkey*

Clin Microbiol Infect 2016; **22:** S37–S62

ÇOCUKLARDA MENENJİT

Kılavuz

2018



ÇOCUKLARDA MENENJİT

Kılavuz

2019

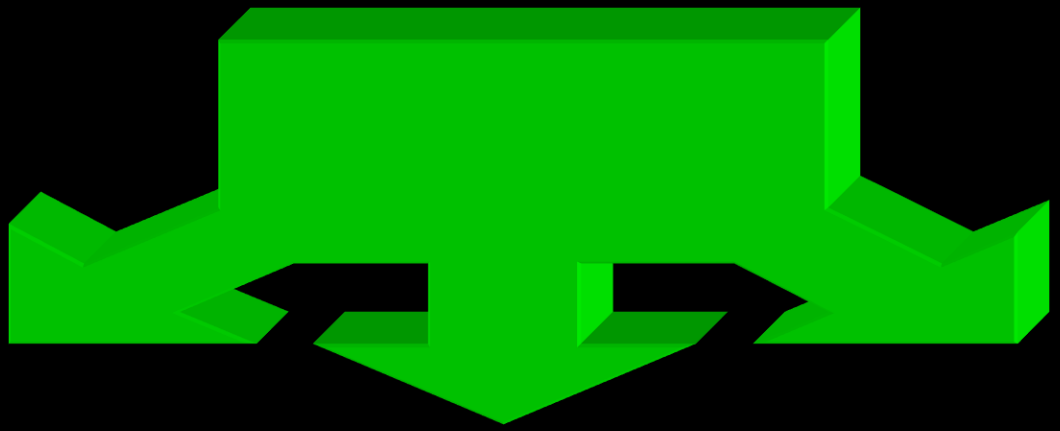
A systematic review of clinical guidelines on the management of acute, community-acquired CNS infections

Louise Sigfrid[1*†], Chelsea Perfect[2†], Amanda Rojek[1], Kajsa-Stina Longuere[3], Sam Lipworth[4], Eli Harriss[5], James Lee[1], Alex Salam[6], Gail Carson[1], Herman Goossens[7] and Peter Horby[1]

BMC Medicine (2019) 17:170

BAKTERİYEL MENENJİT

Tedavi



Antibiyotik tedavisi

Deksametazon tedavisi

Destek tedavisi ve izlem

BAKTERİYEL MENENJİT
Antibiyotik Tedavisi

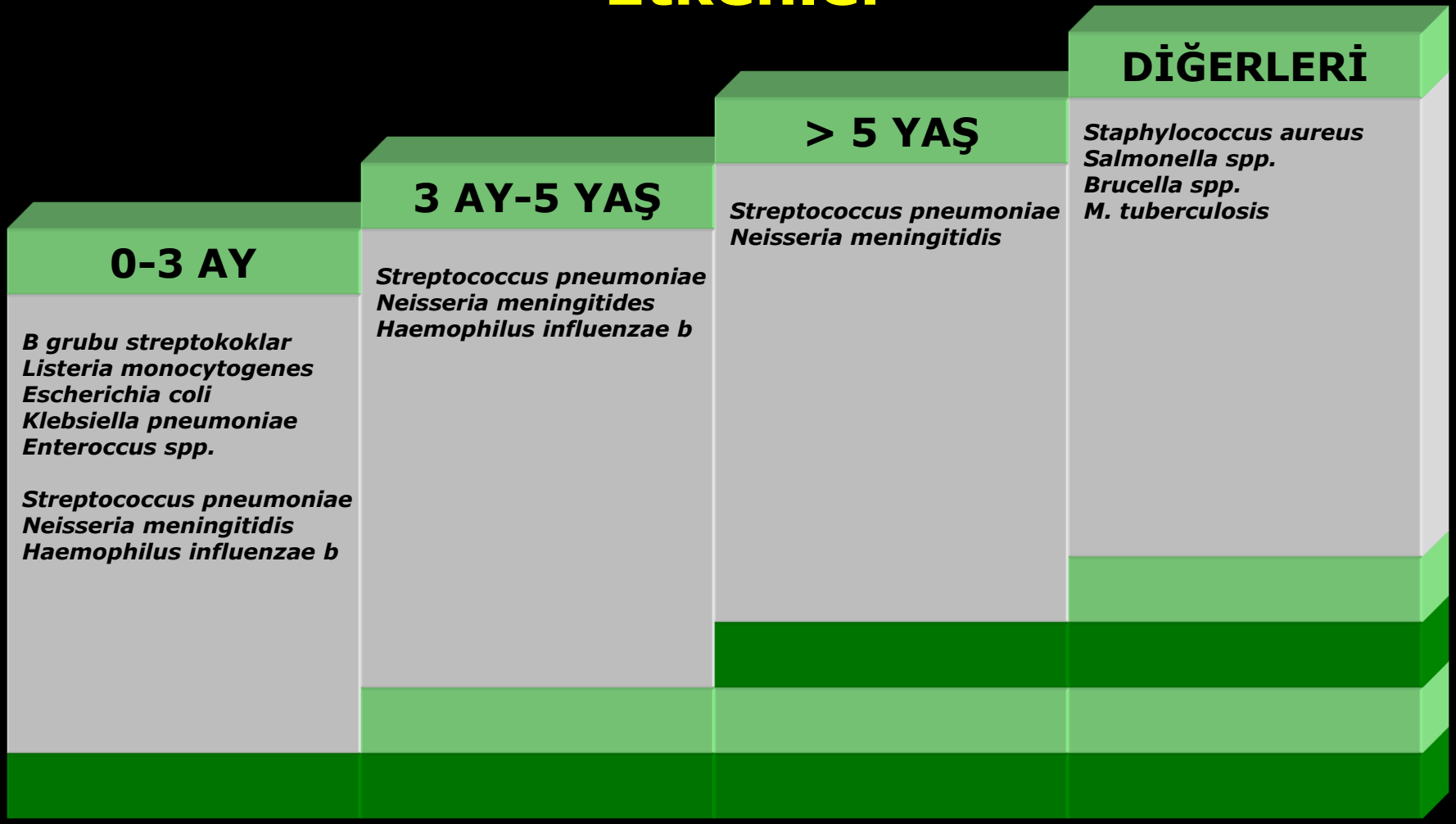
1. **Ampirik (Başlangıç) antibiyotik tedavisi**
2. **Etkene özgü tedavi**

BAKTERİYEL MENENJİT
Ampirik Antibiyotik Tedavisinde Genel İlkeler

1. **Yaş grubuna göre etkenleri bilmek**
2. **Tahmin edilen etkenin bölgesel direnç durumunu bilmek**

BAKTERİYEL MENENJİT

Etkenler



BAKTERİYEL MENENJİT

Etkenler

Çocuklarda Akut Bakteriyel Menenjit

Acute Bacterial Meningitis in Children

Halil Özdemir, Anıl Tapısız, Ergin Çiftçi, Erdal İnce, Ülker Doğru
Ankara Üniversitesi Tıp Fakültesi, Çocuk Enfeksiyon Hastalıkları Bilim Dalı, *Ankara, Türkiye*

Özet

Amaç: Bu çalışmada son 9 yıl içinde takip ettiğimiz akut bakteriyel menenjitli hastalarımızın klinik ve laboratuvar özellikleri ile etken dağılımlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Akut bakteriyel menenjit tanısı ile izlenen 44 hastanın bilgileri retrospektif olarak dosya taraması ile değerlendirildi.

Bulgular: Hastaların ortanca yaşı 11 ay (1 ay-13 yıl) ve erkek/kız oranı 2.38 idi. En sık başvuru yakınmaları ateş (%90,9), kusma (%61,4), uykuya meyil (%40,9), baş ağrısı (%38,6) ve konvülsiyondu (%25). Hastaların 25'inde (%56,8) etken saptandı. En sık saptanan etkenler *Streptococcus pneumoniae* (%27,3), *Haemophilus influenzae* tip b (%11,4) ve *Neisseria meningitidis* (%11,4) iken, 19 hastada (%43,2) etken saptanamadı. Hastaların 11'inde (%25) komplikasyon gelişti. Bu komplikasyonların 3'er tanesinin subdural efüzyon ve subdural ampiyem, 2'şer tanesinin hidrosefali ve işitme kaybı ve 1 tanesinin ise hidrosefali-epilepsi olduğu gözlendi. Hiçbir hasta kaybedilmedi.

Sonuç: *Streptococcus pneumoniae* en sık etkendir. Etkin antibiyotiklerin varlığına ve aşılara rağmen, bakteriyel menenjitler hala önemli bir morbidite nedenidir.

(Çocuk Enf Derg 2010; 4: 9-14)

Anahtar kelimeler: Bakteriyel menenjit, *Haemophilus influenzae, Neisseria meningitidis, Streptococcus pneumoniae*

Abstract

Objective: To evaluate the clinical and laboratory findings and etiological spectrum of the patients with acute bacterial meningitis in the last 9 years.

Material and methods: A retrospective chart review was conducted of 44 patients with acute bacterial meningitis.

Results: The median age of patients was 11 months (1 month-13 years) and the male/female ratio was 2.38. The most common symptoms were fever (90.9%), vomiting (61.4%), lethargy (40.9%), headache (38.6%) and convulsion (25%). The agents were detected in 25 patients (56.8%). The most frequently detected agents were *Streptococcus pneumoniae* (27.3%), *Haemophilus influenzae* type b (11.4%) and *Neisseria meningitidis* (11.4%), and in 19 patients (43.2%) no agents could be determined. In 11 patients (25%) complications developed, these being subdural effusion (3 patients), subdural empyema (3 patients), hydrocephalus (2 patients), hearing loss (2 patients), and hydrocephalus-epilepsy (1 patient). None of the patients died.

Conclusions: *Streptococcus pneumoniae* is the most common agent. Despite advances in vaccine development, chemoprophylaxis and treatment, acute bacterial meningitis remains a significant cause of substantial morbidity in children.

(J Pediatr Inf 2010; 4: 9-14)

Key words: Bacterial meningitis, *Haemophilus influenzae, Neisseria meningitidis, Streptococcus pneumoniae*

BAKTERİYEL MENENJİT

Etkenler

Multicenter Hospital-Based Prospective Surveillance Study of Bacterial Agents Causing Meningitis and Seroprevalence of Different Serogroups of *Neisseria meningitidis*, *Haemophilus influenzae* Type b, and *Streptococcus pneumoniae* during 2015 to 2018 in Turkey

Mehmet Ceyhan,[a] Yasemin Ozsurekci,[a] Sevgen Tanır Basaranoglu,[a] Nezahat Gurler,[b] Enes Sali,[c] Melike Keser Emiroglu,[d] Fatma Nur Oz,[e] Nursen Belet,[f] Murat Duman,[g] Emel Ulusoy,[h] Zafer Kurugol,[i] Hasan Tezer,[j] Aslinur Ozkaya Parlakay,[k] Ener Cagri Dinleyici,[l] Umit Celik,[m] Solmaz Celebi,[n] Ahmet Faik Oner,[o] Mehmet Ali Solmaz,[p] Adem Karbuz,[q] Nevin Hatipoglu,[r] Ilker Devrim,[s] Ilknur Caglar,[s] Sefika Elmas Bozdemir,[t] Emine Kocabas,[u] Ozlem Ozgur Gundeslioglu,[u] Murat Sutcu,[v] Ozge Metin Akcan,[v] Necdet Kuyucu,[w] Fesih Aktar,[x] Soner Sertan Kara,[y] Havva Ozlem Altay Akisoglu,[z] Nilden Tuygun,[aa] Zeynep Diyar Tamburaci Uslu,[bb] Eda Karadag Oncel,[cc] Cihangul Bayhan,[a] Ali Bulent Cengiz[a]

March/April 2020 Volume 5 Issue 2 e00060-20

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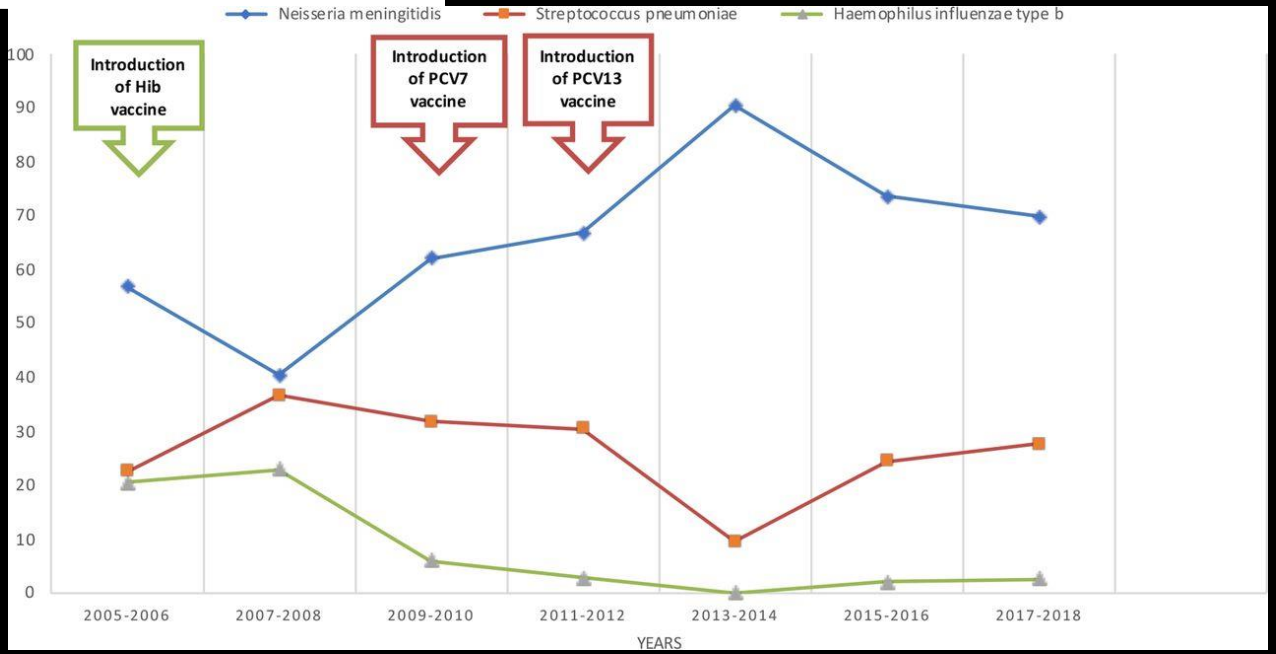
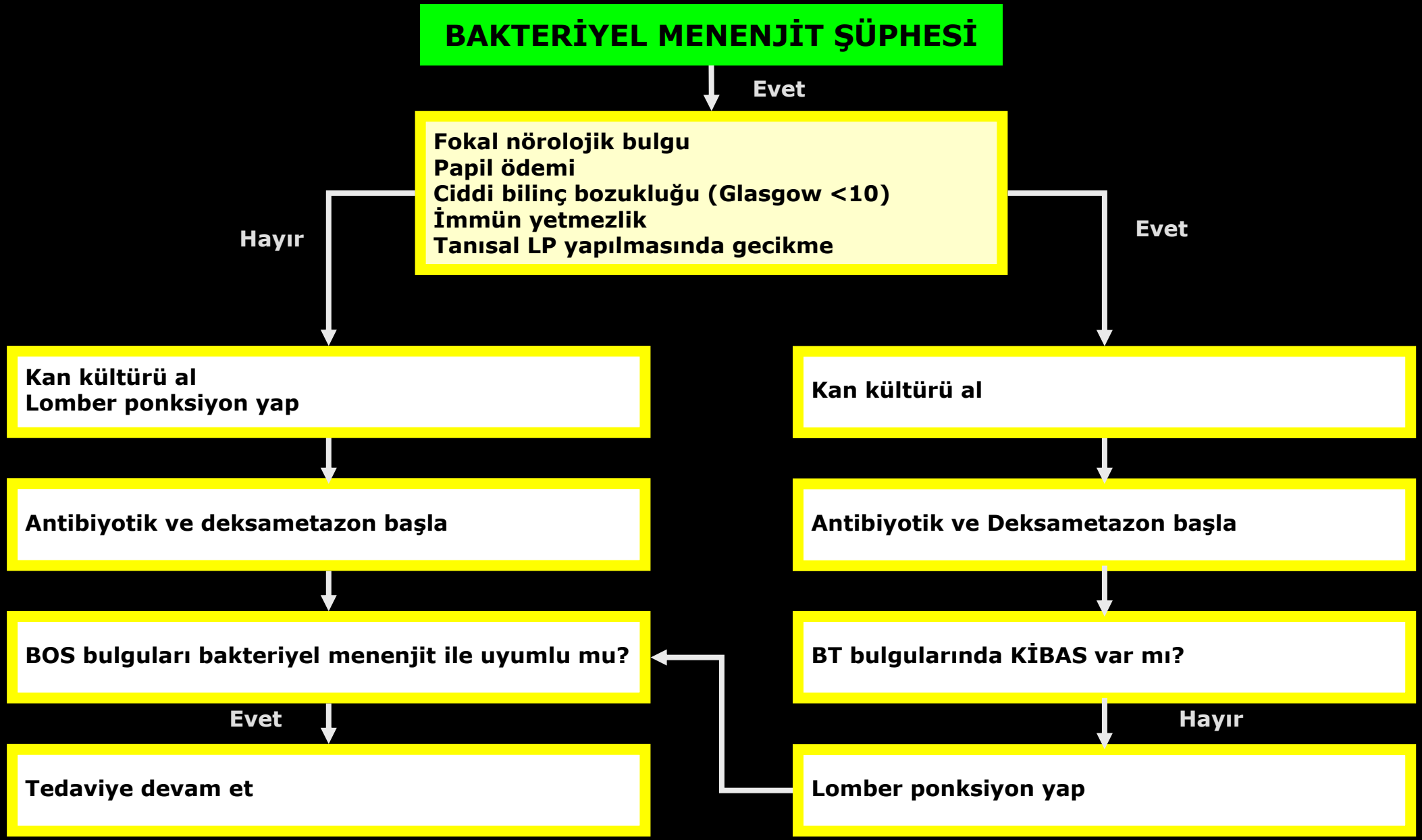


BAKTERİYEL MENENJİT
Erken Tanı ve Tedavinin Önemi

Semptomların süresinin uzun oluşu hastalık prognozunu olumsuz etkiler

BOS sterilizasyonunun gecikmesi hastalık prognozunu olumsuz etkiler

Antibiyotik tedavisi mümkün olan en kısa sürede başlanmalıdır

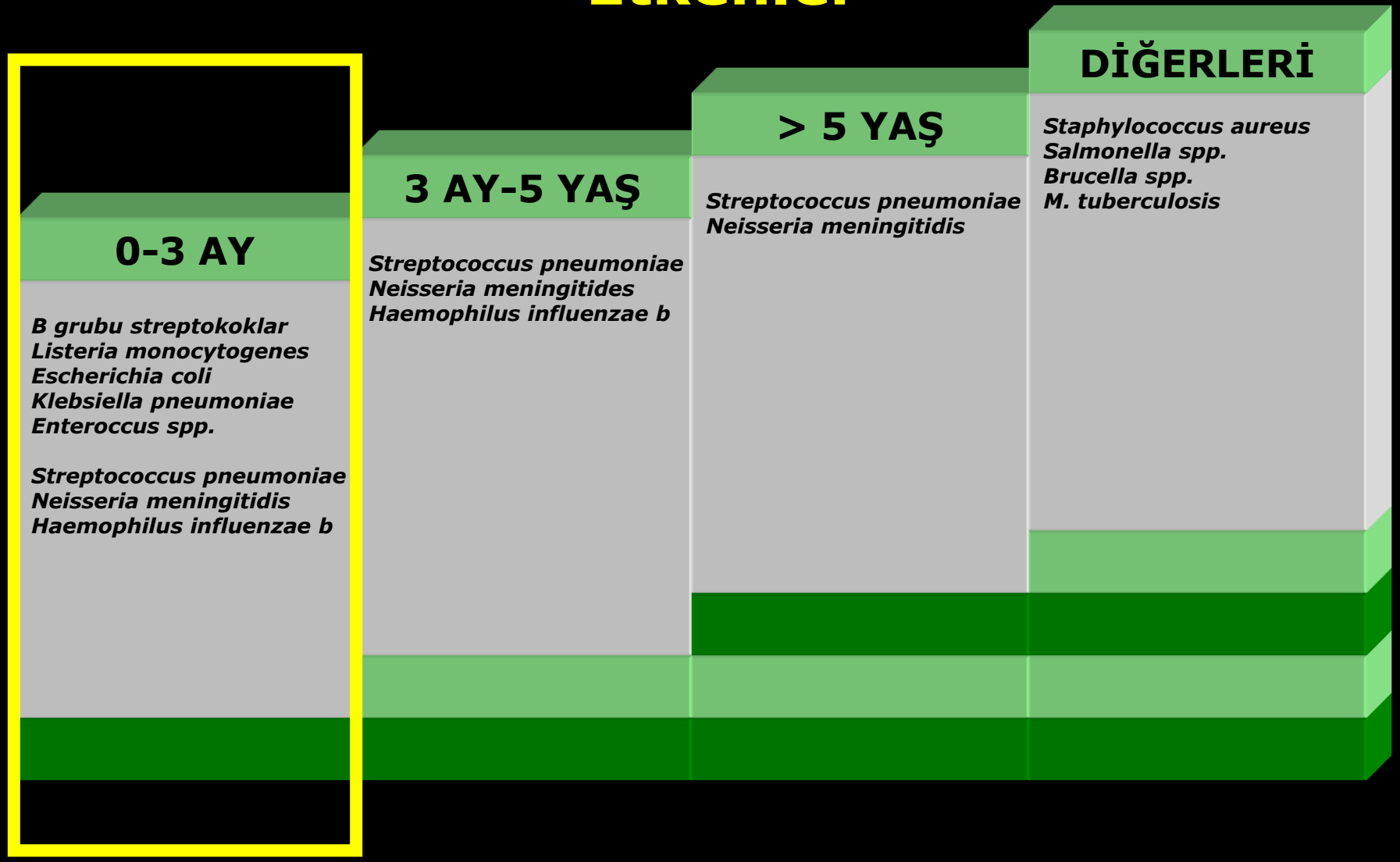

BAKTERİYEL MENENJİT ŞÜPHESİ
Evet
Fokal nörolojik bulgu
Papil ödemi
Ciddi bilinç bozukluğu (Glasgow <10)
İmmün yetmezlik
Tanısal LP yapılmasında gecikme
Hayır
Evet
Kan kültürü al
Lomber ponksiyon yap
Kan kültürü al
Antibiyotik ve deksametazon başla
Antibiyotik ve Deksametazon başla
BOS bulguları bakteriyel menenjit ile uyumlu mu?
BT bulgularında KİBAS var mı?
Evet
Hayır
Tedaviye devam et
Lomber ponksiyon yap

BAKTERİYEL MENENJİT
Antibiyotik Dozları

ANTİBİYOTİK	TOPLAM GÜNLÜK DOZ mg/kg (doz sayısı)		
	0-7 GÜN	8-28 GÜN	> 28 GÜN
Ampisilin	150 (3)	200 (3-4)	300 (4)
Sefotaksim	100-150 (2-3)	150-200 (3-4)	225-300 (3-4)
Seftriakson	-	-	100 (1-2)
Kloramfenikol	25 (1)	25-50 (1-2)	75-100 (4)
Vankomisin	20-30 (2-3)	30-45 (3-4)	60 (4)
Rifampin	-	10-20 (2)	10-20 (1-2)
Penisilin G	150 000 Ü (2-3)	200 000 Ü (3-4)	300 000 Ü (4-6)
Meropenem	-	-	120 (3)
Sefepim	-	-	150 (3)
Amikasin	15-20 (2)	30 (3)	20-30 (3)

BAKTERİYEL MENENJİT

Etkenler



BAKTERİYEL MENENJİT
0-3 Ayda Antibiyotik Tedavisi

1 **Ampisilin + Aminoglikozid**

2 **Ampisilin + Sefotaksim/Seftriakson**

TABLE 4.1. Empiric antibiotic in-hospital treatment for community-acquired bacterial meningitis [3]

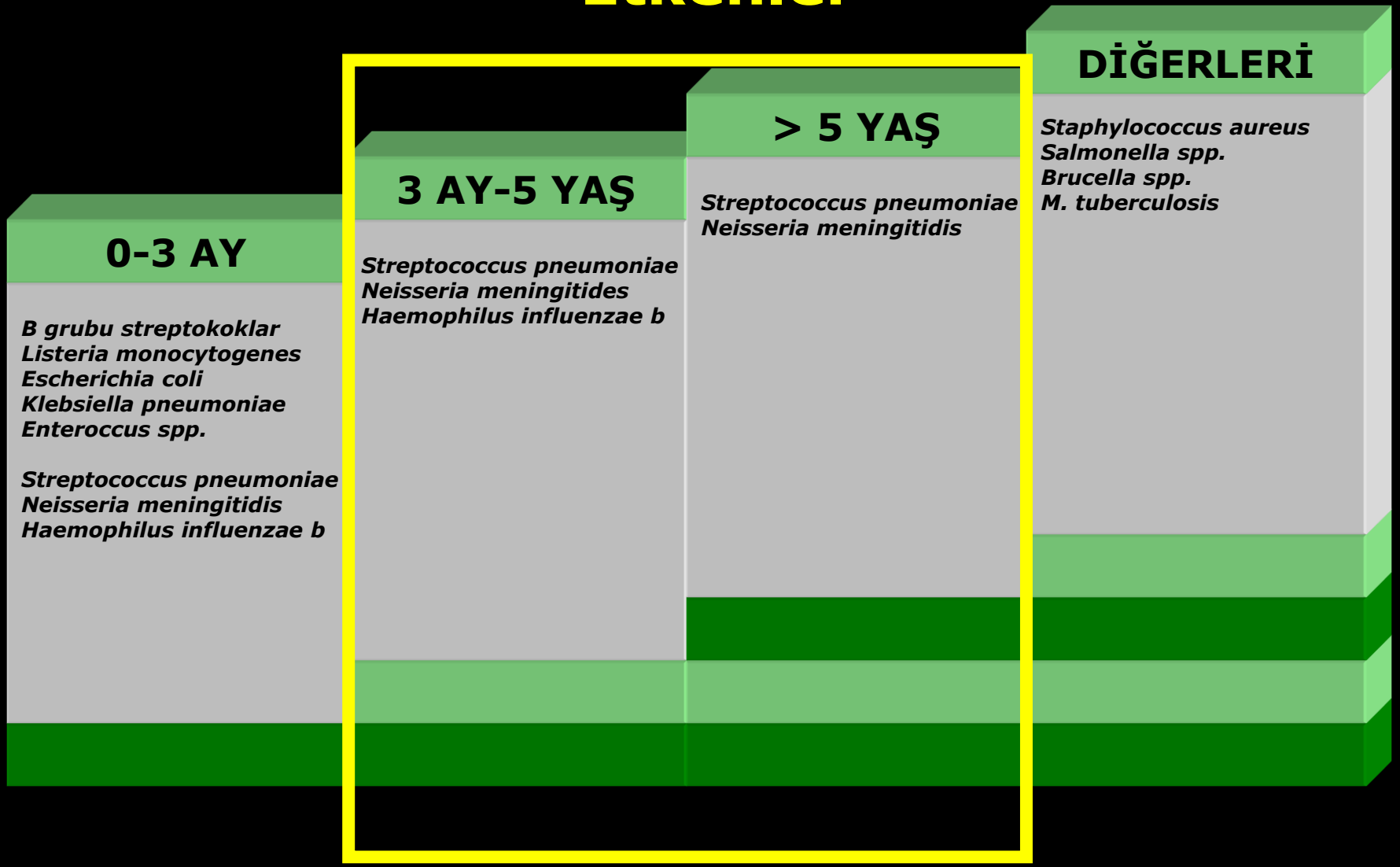
Patient group	Standard treatment: Reduced *Streptococcus pneumoniae* antimicrobial sensitivity to penicillin	Standard treatment: *S. pneumoniae* susceptible to penicillin	Intravenous dose[a]
Neonates <1 month old	Amoxicillin/ampicillin/penicillin plus cefotaxime, or amoxicillin/ampicillin plus an aminoglycoside		Age <1 week: cefotaxime 50 mg/kg q8h; ampicillin/amoxicillin 50 mg/kg q8h; gentamicin 2.5 mg/kg q12h Age 1–4 weeks: ampicillin 50 mg/kg q6h; cefotaxime 50mg/kg q6–8h; gentamicin 2.5 mg/kg q8h; tobramycin 2.5 mg/kg q8h; amikacin 10 mg/kg q8h
Age 1 month to 18 years	Cefotaxime or ceftriaxone plus vancomycin or rifampicin	Cefotaxime or ceftriaxone	Vancomycin 10–15 mg/kg q6h to achieve serum trough concentrations of 15–20 μg/mL; rifampicin 10 mg/kg q12h up to 600 mg/day; cefotaxime 75 mg/kg q6–8h; ceftriaxone 50 mg/kg q12h (maximum 2 g q12h)

Table 7 Empirical treatment recommendations for suspected bacterial meningitis

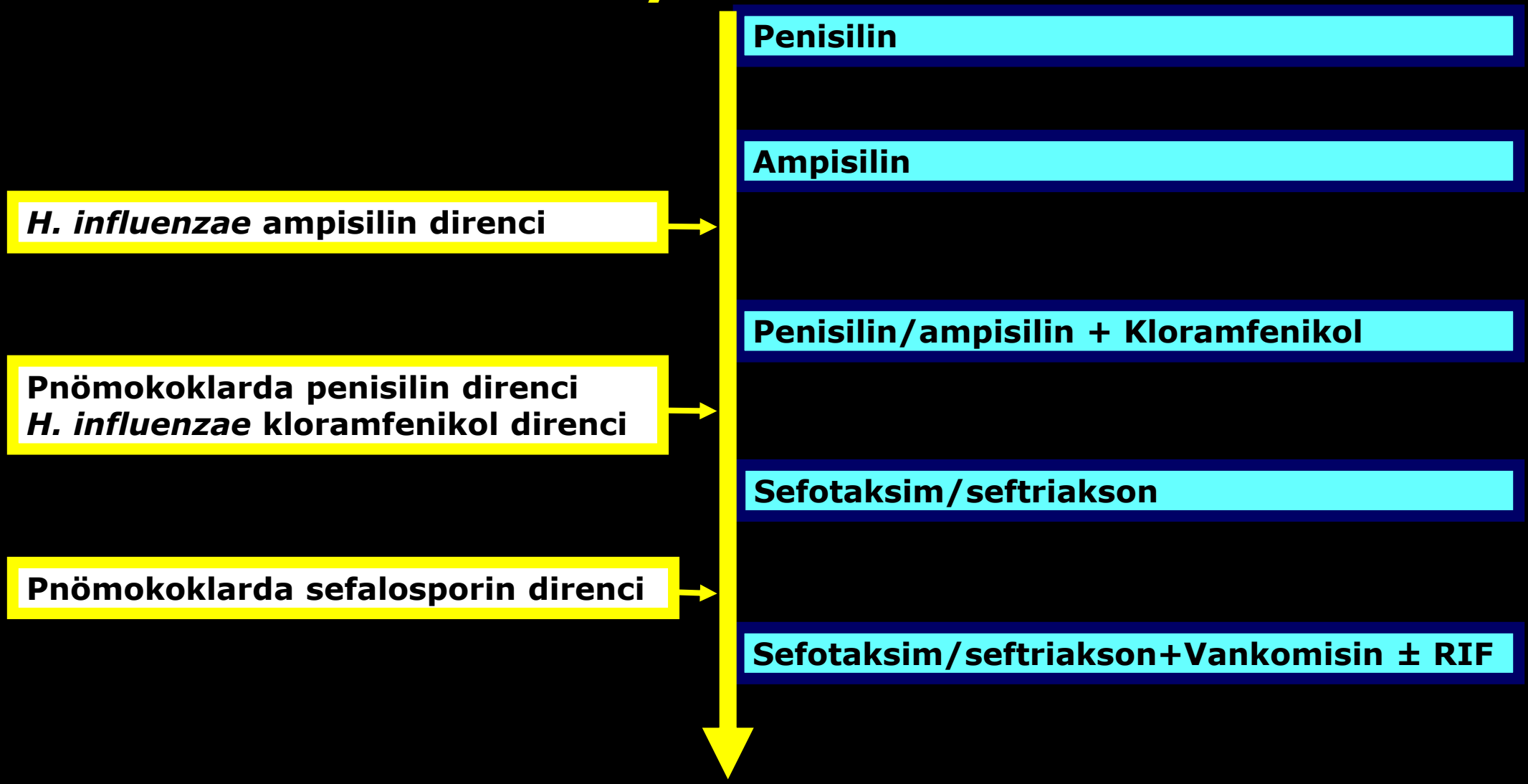
Initial treatment recommendations*					
CMG	3rd-generation cephalosporin (ceftriaxone^ or cefotaxime)	3rd generation-cephalosporin (ceftriaxone^ or cefotaxime) plus a penicillin (amoxicillin, ampicillin or penicillin)	Aminoglycoside (gentamicin) plus a penicillin (amoxicillin or ampicillin)	Add: glycopeptide (vancomycin)	Add: corticosteroids (before or with first dose of antibiotics)
EFNS Europe	P, A	E		Older children and adults**	Yes
ESCMID Europe	P, A	N, A > 50 years, or if risk factor for *L. monocytogenes*	N	**,^	Yes^ up to 4 h post-antibiotics
DSI Denmark	A	A if risk of *L. monocytogenes*			Yes
SPILF France	P, A	P, A if suspected L. monocytogenes°		If S. pneumoniae	Yes"
DGN: BM Germany	A	A		A**	Yes
HPSC Ireland	P > 2 m, A	N, P < 2 months	N, P < 2 months	**,^	Yes up to 24 h post-antibiotics
NVN Netherlands	P, A	N, A			Yes
MHSSE# Spain	P				Yes
NICE UK	P > 3 m	N, P < 3 months		If travel outside of the UK	Yes^^ up to 12 h post-antibiotics
UKJSS UK	A	A > 60 years		Pending travel history	Yes up to 12 h post-antibiotics
SIGN# Scotland	P > 3 m	N, P ≤ 3 months			Yes up to 24 h post-antibiotics
IDSA USA/ Global	P, A	N, A > 50 years	N	P, A	P^, infants if Hib, A
AEPED Spain	P	N, P ≤ 3 months		**,^	Yes
MSF Global	P > 3 m, A	N, P ≤ 3 months	N, P ≤ 3 months		Yes^
NNF Norway	NS	NS			Yes

BAKTERİYEL MENENJİT

Etkenler



BAKTERİYEL MENENJİT
Antibiyotik Tedavisi



BAKTERİYEL MENENJİT

Antibiyotik Duyarlılığı: *S. pneumoniae*

Tüm dünyada pnömokoklarda penisilin ve sefalosporin direnci giderek artıyor

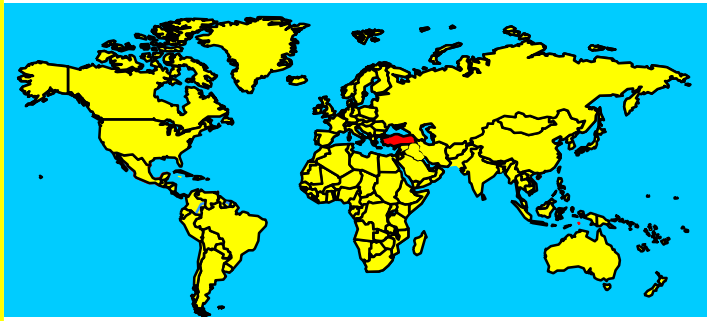
MIC değerlerine göre direnç durumu

	Duyarlı	Dirençli
Penisilin	**≤0.06 μg/mL**	**≥0.12 μg/mL**
Sefalosporin	**≤0.5 μg/mL**	**≥2.0 μg/mL**

BAKTERİYEL MENENJİT
Antibiyotik Duyarlılığı: *S. pneumoniae*

İnvaziv *S. pneumoniae* izolatlarında antibiyotik direnci

Toplam 93 *S. pneumoniae* izolatı incelenmiş



TÜRKİYE

	Orta Direnç	Yüksek Direnç	Toplam
Penisilin	**%31**	**%8**	**%39**
Sefotaksim	**%10**	**%4**	**%14**

Yalçın I, Gürler N, Alhan E, et al.
Serotype distribution and antibiotic susceptibility of invasive Streptococcus pneumoniae disease isolates from children in Turkey, 2001–2004
Eur J Pediatr 2006; 165: 654-657

BAKTERİYEL MENENJİT
Antibiyotik Duyarlılığı: *S. pneumoniae*

Antimicrobial Original Research Paper

Invasive pneumococci before the introduction of pneumococcal conjugate vaccine in Turkey: antimicrobial susceptibility, serotype distribution, and molecular identification of macrolide resistance

Hatice Uludag Altun[1,2], Gülsen Hascelik[1], Deniz Gür[1], Özgen Köseoglu Eser[1]

Journal of Chemotherapy 2015 VOL. 27 NO. 2

Table 1 MIC_{50}, MIC_{90}, MIC range, and resistance percentage of invasive pneumococcal isolates (n=182).

Antibiotics	MIC_{50} (mg/l)	MIC_{90} (mg/l)	MIC range (mg/l)	Intermediate resistance (%)	Resistance (%)
Penicillin (PEN) (CSF), *n*=32	≤0.06	1	≤0.06–2	0	16 (50)
PEN (non-CSF) *n*=150	≤0.06	0.5	≤0.06–2	0	0
Erythromycin (ERY)	≤0.25	1	≤0.25–8+	1 (0.5)	22 (12.1)
Clindamycin (CD)	≤0.25	<0.25	≤0.25–8+	0	14 (7.7)
Ceftriaxone (CRO)	≤0.25	0.5	≤0.25–1	9 (4)	0
Levofloxacin (LEV)	1	1	≤0.25–8+	–	2 (1.1)
Vancomycin (VAN)	≤0.25	0.25	≤0.25	0	0

MIC: minimal inhibitory concentration.

BAKTERİYEL MENENJİT
Antibiyotik Duyarlılığı: *S. pneumoniae*

Nasopharyngeal carriage of *Streptococcus pneumoniae* in healthy Turkish children after the addition of PCV7 to the national vaccine schedule

Halil Özdemir · Ergin Çiftçi · Rıza Durmaz · Haluk Güriz · Ahmet Derya Aysev · Adem Karbuz · Refik Gökdemir · Bülent Acar · Selin Nar Ötgün · Mustafa Ertek · Serdal Kenan Köse · Erdal İnce

Eur J Pediatr (2014) 173:313–320

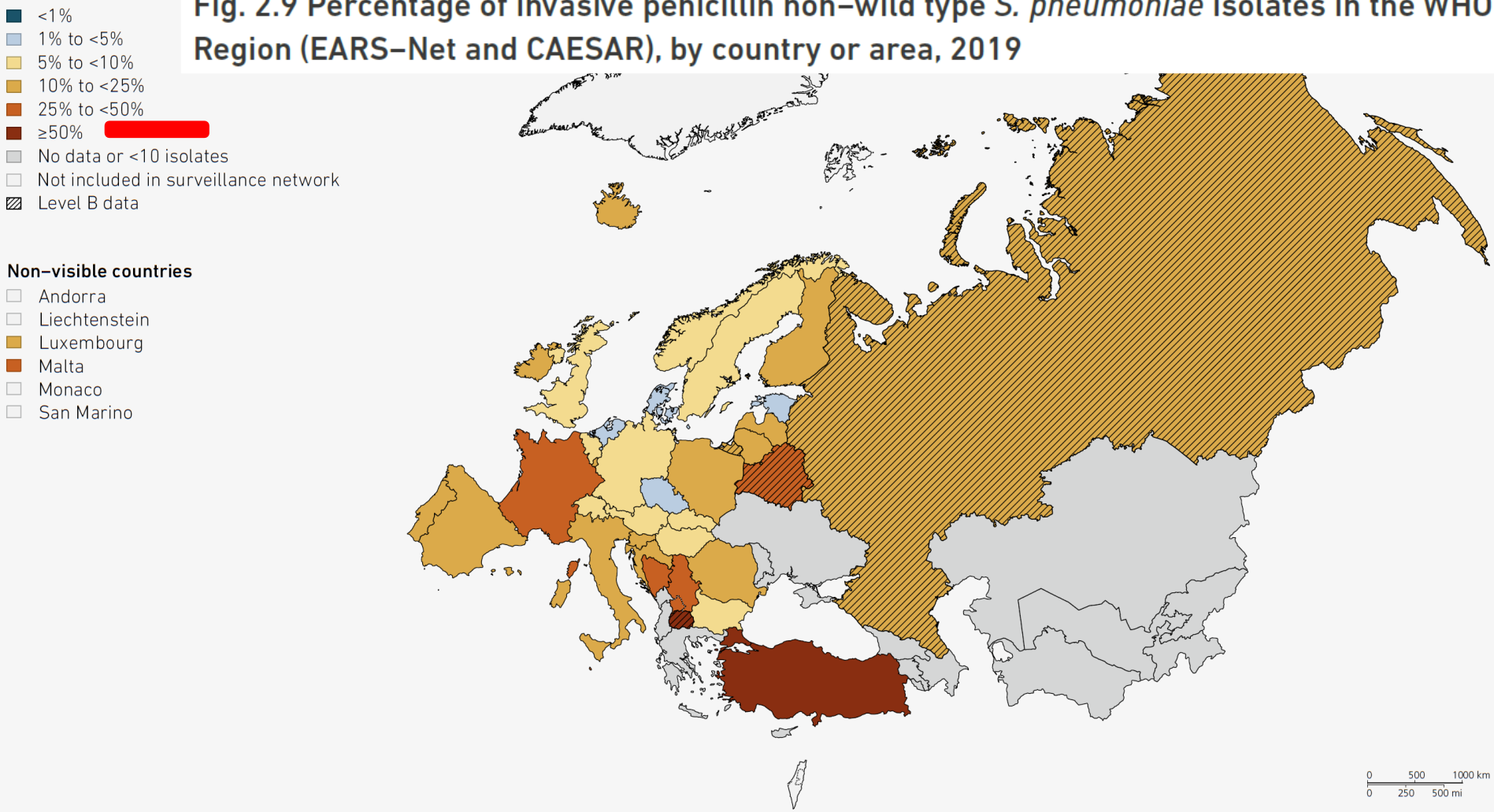
Antibiotics	Administration route	S (%)	LLR (%)	HLR (%)	NS (%)
Penicillin	Oral	27	50.6	22.4	73
	Parenteral	94.2	4.6	1.2	5.8
	Parenteral for meningitis	27	–	73	73
Ceftriaxone	Parenteral	82.2	14.5	3.3	17.8
	Parenteral for meningitis	52.3	29.9	17.8	47.7

BAKTERİYEL MENENJİT
Antibiyotik Duyarlılığı: *S. pneumoniae*

2.2.6 *Streptococcus pneumoniae*

S. pneumoniae causes a wide range of infections, from mild, self-limiting infections such as otitis media to more serious infections such as community-acquired pneumonia and meningitis, with high mortality in vulnerable patient groups. In the WHO European Region, large differences are seen in the percentage of penicillin non-wild type (Fig. 2.9). Czechia, Denmark, Estonia and the Netherlands report proportions lower than 5%, whereas proportions >25% were found in Belarus,[2] Bosnia and Herzegovina, France, Malta, North Macedonia,[2] Serbia and Turkey.

Fig. 2.9 Percentage of invasive penicillin non–wild type *S. pneumoniae* isolates in the WHO European Region (EARS–Net and CAESAR), by country or area, 2019



Level B data: the data provide an indication of the resistance patterns present in clinical settings in the country or area, but the proportion of resistance should be interpreted with care. Improvements are needed to attain a more valid assessment of the magnitude and trends of AMR in the country or area. See section 5.2 for more information about levels of evidence, which are only provided for CAESAR countries and areas.

EARS–Net countries: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.
CAESAR countries and areas: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, North Macedonia, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, Turkey, Turkmenistan, Ukraine, Uzbekistan and Kosovo[1]. Data for Serbia and Kosovo[1] were combined for this map.
[1] All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).

Data sources: 2019 data from the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2020) and 2019 data from the European Antimicrobial Resistance Surveillance Network (EARS–Net, ©ECDC 2020). Data for Slovenia were obtained from the Slovenian National Institute of Public Health.
Map production: Public Health Information and Geographic Information Systems (GIS), World Health Organization.

Table 6.74 Resistance levels for *S. pneumoniae* among blood and CSF isolates in Turkey in 2019

Antibiotic (group)	*S. pneumoniae*			
	N	%R	%I	%IR
Penicillin[a]	212	NA	NA	51
Cefotaxime/ceftriaxone	158	8**	15**	NA
Levofloxacin/moxifloxacin	189	4	0	NA
Erythromycin/clarithromycin/azithromycin	211	37	3	NA
Multidrug resistance[b]	200	NA	NA	33

NA = not applicable.

** Less than 70% of isolates were tested for this antibiotic (group), and the percentage resistance should be interpreted with caution.

[a] The percentage IR to penicillin is based on penicillin or, if not available, on oxacillin. For meningitis, the percentage IR should be interpreted as the percentage R. For non-meningitis indications, the percentage IR should be interpreted as the percentage of penicillin non-wild type. For this report, the term penicillin non-wild type refers to *S. pneumoniae* isolates reported by the local laboratories as I or R to penicillin, assuming MICs to penicillin above those of the wild-type, i.e. > 0.06 mg/L. The analysis is based on the qualitative susceptibility categories S, I and R as quantitative susceptibility information was missing for a large proportion of the data. For laboratories using EUCAST, this approach correctly defines all penicillin non-wild type (i.e. I/R) *S. pneumoniae* isolates. However, for laboratories using the CLSI methodology, isolates within the S category for benzylpenicillin might be non-wild type since the penicillin susceptibility breakpoint for non-meningitis cases is set as ≤ 2 mg/L. Due to this limitation, the actual percentage of penicillin non-wild type *S. pneumoniae* might be higher than reported in this table.

[b] Multidrug resistance is defined as combined penicillin non-wild type and resistance (R) to macrolides (erythromycin, clarithromycin and/or azithromycin). Isolates with missing data on one or more of the groups are excluded from the analysis of multidrug resistance.

BAKTERİYEL MENENJİT
Antibiyotik Tedavisi

Microorganism	Standard treatment	Alternatives	Duration
Streptococcus pneumoniae			
Penicillin susceptible (MIC <0.1 µg/mL)	Penicillin or amoxicillin/ampicillin	ment should include vancomycin or rifampicin. However, some	
Penicillin resistant (MIC >0.1 µg/mL), third-generation cephalosporin susceptible (MIC <2 µg/mL)	Ceftriaxone or cefotaxime	experts advise the use of ceftriaxone or cefotaxime as empiric	
Cephalosporin resistant (MIC ≥2 µg/mL)	Vancomycin *plus* rifampicin, or vancomycin *plus* ceftriaxone or cefotaxime, or rifampicin *plus* ceftriaxone or cefotaxime[c]	treatment instead of vancomycin or rifampicin when true resistance to third-generation cephalosporin (minimum inhibitory concentration (MIC) >2 mg/L) is not to be expected. When risk	
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

BAKTERİYEL MENENJİT
Vankomisin veya Rifampisin Tedavisi

There is uncertainty regarding the benefit of adding vancomycin or rifampicin to a third-generation cephalosporin in pneumococcal meningitis patients in the setting of decreased susceptibility rates of pneumococci. We systematically evaluated the literature for studies of the efficacy of vancomycin and rifampicin in infections caused by pneumococci resistant to third-generation cephalosporins, but only animal studies were identified [86–88]. These showed that ceftriaxone combined with either vancomycin or rifampicin resulted in a higher rate of CSF sterilization after 24 hours compared to monotherapy with ceftriaxone. Another animal study showed the superiority of ceftriaxone combined with either rifampicin or rifampicin and vancomycin compared to ceftriaxone combined with vancomycin. Although there is no clinical evidence for adding vancomycin or rifampicin in the setting of lower pneumococcal susceptibility rates, the committee advises addition of vancomycin or rifampicin to third-generation cephalosporins based on *in vitro* susceptibility patterns [89]. The advised duration of treatment is 10–14 days [3,40,90].

BAKTERİYEL MENENJİT
Vankomisin veya Rifampisin Tedavisi

Neler kazandırır?

a. Sefalosporin dirençli pnömokok menenjitinde tedavinin etkinliği artar

Neler kaybettirir?

a. Gereksiz ilaç verilmesi

b. Ekonomik yük

c. Direnç sorunu

Erken vankomisin verilenlerde işitme kaybı daha sık!

Vankomisin sefalosporinden en az 2 saat sonra verilmeli

Buckingham SC, et al.
Early vancomycin therapy and adverse outcome in children with pneumococcal meningitis
Pediatrics 2006; 117: 1688-1694

BAKTERİYEL MENENJİT
≥ 3 Aylık Çocuklarda Antibiyotik Tedavisi

Bakteriyel Menenjit Şüphesi

↓

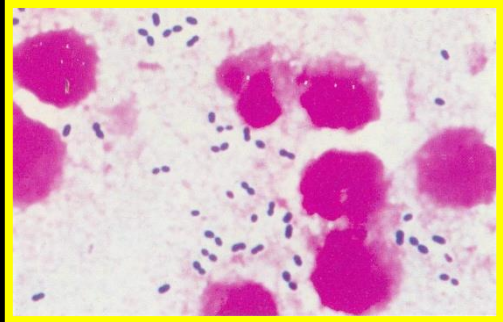
Lomber Ponksiyon

↓

Seftriakson/Sefotaksim + Deksametazon

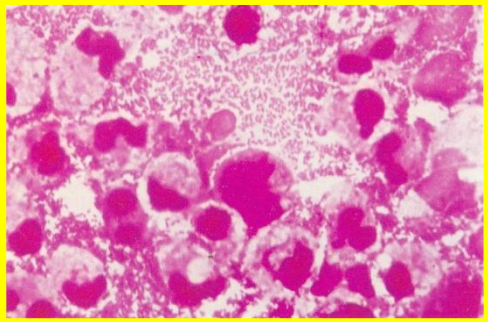
↓

GRAM BOYAMA

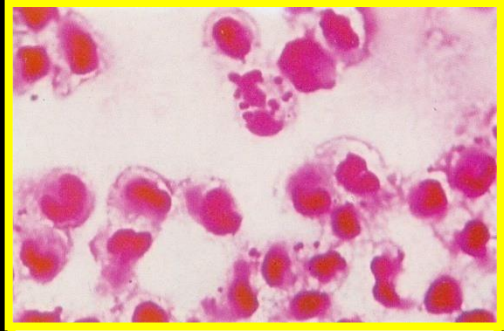


Gram (+) diplokok
Sefalosporin + Vankomisin
Deksametazon

Etken yok
Sefalosporin + Vankomisin
Deksametazon



Gram (-) kokobasil
Sefalosporin
Deksametazon



Gram (-) diplokok
Sefalosporin

BAKTERİYEL MENENJİT
≥ 3 Aylık Çocuklarda Antibiyotik Tedavisi

Bakteriyel Menenjit Şüphesi

↓

Lomber Ponksiyon

↓

Seftriakson/Sefotaksim + Deksametazon

↓

GRAM BOYAMA

↓

KÜLTÜR

S. pneumoniae	Etken yok	*H. influenzae*	*N. meningitidis*
Penisilin duyarlı Penisilin/sefalosporin Deksametazon Vankomisin kesilir Penisilin dirençli, SS MIC'i SS duyarlı: Sefalosporin SS dirençli: SS + Vankomisin Özel durumlarda Rifampin	Sefalosporin+ Vankomisin Deksametazon	Sefalosporin Deksametazon Vankomisin kesilir	Penisilin Ampisilin Sefalosporin Vankomisin kesilir

BAKTERİYEL MENENJİT
Etkene Özgü Tedavi: *S. pneumoniae*

Sefalosporin dirençli pnömokok menenjitinde rifampin kullanımı

A. 24-48 saatte klinik kötüleşme

B. 24-48 saat sonra BOS'da bakteri görülmesi veya kültürde üreme

C. Sefalosporin MIC ≥ 2 μg/mL

Seftriakson/sefotaksim + Vankomisin + Rifampin

Deksametazon kullanılıyorsa Vankomisin yerine Rifampin kullanılabilir

Vankomisin	**tek başına kullanılmamalıdır**
Rifampin	**tek başına kullanılmamalıdır**

Pediatr Infect Dis J. 2016 Dec 23. doi: 10.1097/INF.0000000000001513. [Epub ahead of print]

Role of Rifampin in Reducing Inflammation and Neuronal Damage in Childhood Bacterial Meningitis: A Pilot Randomized Controlled Trial.

Uppal L[1], Singhi S, Singhi P, Aggarwal R.

Author information

Abstract

BACKGROUND: Treatment of acute bacterial meningitis in children with bactericidal antibiotics causes cell wall lysis and a surge in inflammatory cascade, which in turn contributes to neuronal damage and morbidity. Pretreament with a non-bacteriolytic antibiotic, such as rifampin, has been shown to attenuate the inflammatory response in experimental models of bacterial meningitis. In a pilot study in children with bacterial meningitis we have studied markers of inflammatory response and neuronal damage in two groups of children with bacterial meningitis, one group received rifampin pretreatment with ceftriaxone, other group received ceftriaxone alone.

PATIENTS AND METHODS: Forty children with bacterial meningitis who were 3 months to 12 years of age were randomly assigned to receive either a single dose rifampin (20 mg/kg) thirty minutes before ceftriaxone or ceftriaxone alone was given. The primary outcome variables were cerebrospinal fluid (CSF)concentrations of tumor necrosis factor alpha (TNFα), S100B and neuron-specific enolase (NSE) on day 1 and day 5, secondary outcome variables were the values of TNFα and interleukin 6 (IL6) in serum on day 1 and day 5; and hearing and neurologic sequelae at 3 months after recovery from the illness.

RESULTS: Children in rifampin pretreatment group had significantly lower CSF TNFα concentrations [Median(IQR):15.5 (7.2-22.0) pg/ml versus 53.0 (9.0- 87.5) pg/ml ; p= 0.019] and S100B [Median (IQR) : 145.0 (54.7 - 450.0) pg/ml versus 447.5 (221.0- 804.6) pg/ml; p= 0.033] on day 1, and S100B [Median(IQR) : 109.7 (64.0-287.0) pg/ml versus 322 (106.7-578.0) pg/ml ; p =0.048] and NSE [Median(IQR) : 8.6 (5-14.75) ng/ml versus 18.2 (7.0-28.75) ng/ml ; p= 0.035] on day 5 when compared with ceftriaxone alone group. The rifampin treated group also had reduced morbidity and neurologic sequelae: however, these were not statistically significant.

CONCLUSIONS: Pretreatment with single dose rifampin 30 minutes before ceftriaxone administration reduced the CSF concentrations of markers of inflammation and neuronal damage in children with bacterial meningitis.

BAKTERİYEL MENENJİT
Tedavi Etkinliğinin İzlemi

LOMBER PONKSİYON KONTROLÜ

1. **24-48 saat içinde klinik durumda kötüleşme varsa**
2. **Deksametazon kullanılıyor ise**
3. **Penisilin/Sefalosporin dirençli pnömokok menenjiti varsa**
4. **Altta yatan bir risk faktörü varsa**

Patojenin eradike olup olmadığını denetlemek için LP düşünülmeli

BAKTERİYEL MENENJİT
Antibiyotik Tedavi Süresi

N. meningitidis	**: 7 gün**
H. influenzae **tip b**	**: 7-10 gün**
S. pneumoniae	**: 10-14 gün**
S. agalactiae **(GBS)**	**: 14-21 gün**
Gram (-) basil	**: En az 21 gün veya ilk negatif kültür sonrası 2 hafta (hangisi uzunsa)**
L. monocytogenes	**: En az 21 gün**
S. aureus (MRSA dahil)	**: En az 14 gün**

BAKTERİYEL MENENJİT
Alternatif Tedavi Yaklaşımları

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

BAKTERİYEL MENENJİT
Tedavinin Sonlandırılması

Komplike olmayan *H. influenzae* tip b, *N. meningitidis* ve *S. pneumoniae* menenjitlerinde tedavi sonunda lomber ponksiyon kontrolü yapmak gerekli değildir.

Tedavi sonunda lomber ponksiyon tekrarlanması gerekenler:

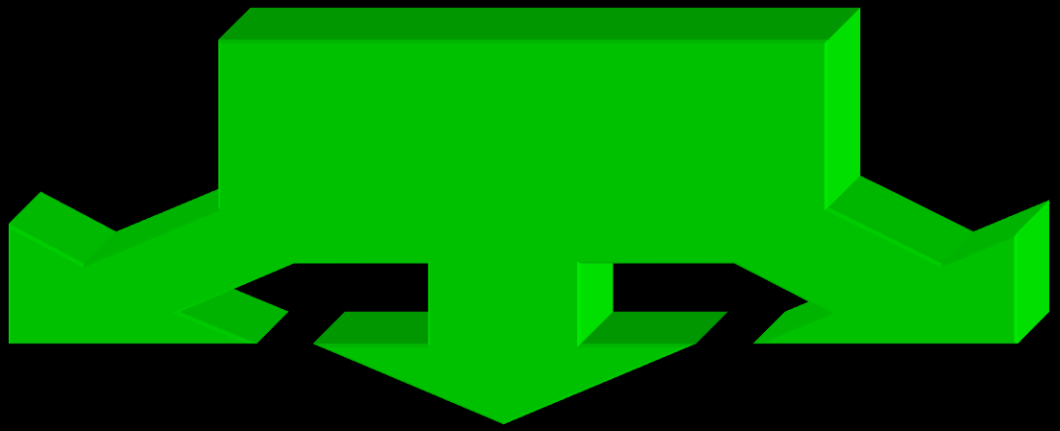
- **Yenidoğan bebekler**
- **Gram negatif basil menenjitleri**
- **48-72 saat sonunda uygulanan tedaviye yanıt vermemiş hastalar**

Tedavinin sonlandırılma kriterleri:

- **BOS glukozunun normale dönmesi**
- **Polimorfonükleer lökositlerin görülmemesi**
- **BOS kültüründe üreme olmaması**

BAKTERİYEL MENENJİT

Tedavi



Antibiyotik tedavisi

Deksametazon tedavisi

Destek tedavisi ve izlem

BAKTERİYEL MENENJİT
Deksametazon Tedavisi

Faydaları

a. İşitme kaybını azaltmak
b. Nörolojik sekeli azaltmak
c. Mortaliteyi azaltmak

Zararları

a. BOS antibiyotik geçişini azaltabilir
b. Klinik izlemi güçleştirir, yalancı iyilik hali yaratır

Antibiyotik tedavisinden önce veya eş zamanlı verilir
Antibiyotik tedavisi sonrası ilk 4 saat içinde başlanabilir.

DOZ

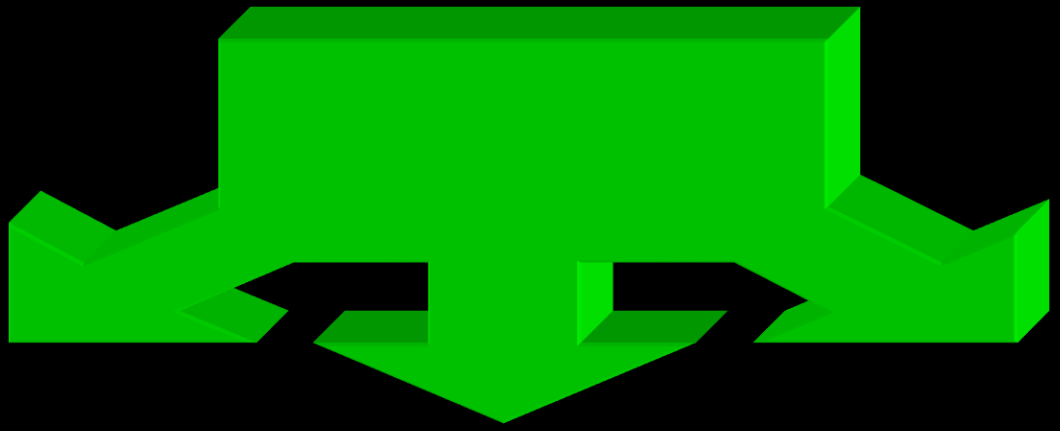
0.15 mg/kg/doz, günde 4 doz, 2 veya 4 gün

Table 7 Empirical treatment recommendations for suspected bacterial meningitis

Initial treatment recommendations*					
CMG	3rd-generation cephalosporin (ceftriaxone^ or cefotaxime)	3rd generation-cephalosporin (ceftriaxone^ or cefotaxime) plus a penicillin (amoxicillin, ampicillin or penicillin)	Aminoglycoside (gentamicin) plus a penicillin (amoxicillin or ampicillin)	Add: glycopeptide (vancomycin)	Add: corticosteroids (before or with first dose of antibiotics)
EFNS Europe	P, A	E		Older children and adults**	Yes
ESCMID Europe	P, A	N, A > 50 years, or if risk factor for *L. monocytogenes*	N	**,^	Yes^ up to 4 h post-antibiotics
DSI Denmark	A	A if risk of *L. monocytogenes*			Yes
SPILF France	P, A	P, A if suspected L. monocytogenes°		If S. pneumoniae	Yes"
DGN: BM Germany	A	A		A**	Yes
HPSC Ireland	P > 2 m, A	N, P < 2 months	N, P < 2 months	**,^	Yes up to 24 h post-antibiotics
NVN Netherlands	P, A	N, A			Yes
MHSSE# Spain	P				Yes
NICE UK	P > 3 m	N, P < 3 months		If travel outside of the UK	Yes^^ up to 12 h post-antibiotics
UKJSS UK	A	A > 60 years		Pending travel history	Yes up to 12 h post-antibiotics
SIGN# Scotland	P > 3 m	N, P ≤ 3 months			Yes up to 24 h post-antibiotics
IDSA USA/ Global	P, A	N, A > 50 years	N	P, A	P^, infants if Hib, A
AEPED Spain	P	N, P ≤ 3 months		**,^	Yes
MSF Global	P > 3 m, A	N, P ≤ 3 months	N, P ≤ 3 months		Yes^
NNF Norway	NS	NS			Yes

BAKTERİYEL MENENJİT

Tedavi



Antibiyotik tedavisi

Deksametazon tedavisi

Destek tedavisi ve izlem

BAKTERİYEL MENENJİT
Hastanın İzlenmesi

Kan basıncı

Nabız sayısı

Solunum sayısı

Vücut sıcaklığı

Baş çevresi ölçümü

Nörolojik muayene

BAKTERİYEL MENENJİT

Sıvı Tedavisi

Başlangıçta ağızdan beslenmemelidir

Dolaşım yetmezliğinin düzeltilmesi

Sıvı kaybı olan hastalarda sıvı açığının düzeltilmesi

İlk gün 800-1000 mL/m^2/gün

Ardından 1500-1700 mL/m^2/gün

(Uygunsuz ADH salınımı bulgusu olmayan hastalarda)

Pediatr Clin N Am 2005; 52: 795-810

Cochrane Database Syst Rev 2005; 3: CD004786

BAKTERİYEL MENENJİT
Kafa İçi Basınç Artışı Tedavisi

Sıvı kısıtlaması

Baş 30 derecelik açı yapacak şekilde kaldırılması

Mannitol (0.1-1 mg/kg)

Furosemid (1 mg/kg)

Mekanik ventilasyon ile solunumsal alkaloz oluşturulması

Pediatr Clin N Am 2005; 52: 795-810

BAKTERİYEL MENENJİT
Yaygın Damar İçi Pıhtılaşması Tedavisi

Taze donmuş plazma

Taze tam kan

Trombosit

Tromboz bulgusu varsa heparin

BAKTERİYEL MENENJİT
Konvülzyon Tedavisi

Diazepam (0.1-0.2 mg/kg/doz)

Fenitoin (15-20 mg/kg yükleme, 5 mg/kg/gün idame)

Fenobarbital

Midazolam

Pediatr Clin N Am 2005; 52: 795-810

BAKTERİYEL MENENJİT
Kafa İçi Komplikasyonların Tedavisi

Subdural effüzyon

Epidural apse

Beyin apsesi

Hidrosefali

Venöz sinüs trombozu

Serebral veya serebellar herniasyon

BAKTERİYEL MENENJİT
Tedavinin Sonlandırılması

Komplike olmayan *H. influenzae* tip b, *N. meningitidis* ve *S. pneumoniae* menenjitlerinde tedavi sonunda lomber ponksiyon kontrolü yapmak gerekli değildir.

Tedavi sonunda lomber ponksiyon tekrarlanması gerekenler:

- **Yenidoğan bebekler**
- **Gram negatif basil menenjitleri**
- **48-72 saat sonunda uygulanan tedaviye yanıt vermemiş hastalar**

Tedavinin sonlandırılma kriterleri:

- **BOS glukozunun normale dönmesi**
- **Polimorfonükleer lökositlerin görülmemesi**
- **BOS kültüründe üreme olmaması**

Pediatr Clin N Am 2005; 52: 795-810

BAKTERİYEL MENENJİT
Sekeller ve İzlem

İşitme kaybı

S. pneumoniae	**%30**
H. influenzae	**%5-20**
N. meningitidis	**%10**

Mental retardasyon
Epilepsi
Görme kaybı
Davranış problemleri
Motor işlev bozuklukları
Hidrosefali

BAKTERİYEL MENENJİT

Temas Edenlerin Korunması *H. influenzae* tip b

Ailede 48 aydan küçük çocuk yoksa profilaksi gerekli değildir.

Ailede 48 aydan küçük ve yaşına göre *H. influenzae* tip b aşı şemasını tamamlamamış çocuk varsa, bütün aile üyeleri

Hastaya tanı konulmasından önceki 5-7 gün içinde hasta ile günde en az 4 saat zaman geçiren kişiler

Son iki ayda ≥2 invaziv *H. influenzae* tip b hastalığı görülen kreş/anaokulu temaslıları

Ampisilin veya kloramfenikol ile tedavi edilmiş ise hasta da hastaneden çıkmadan önce kemoprofilaksi almalıdır.

Rifampin 20 mg/kg/gün (en fazla 600 mg), günde bir kez, 4 gün

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BAKTERİYEL MENENJİT
Temas Edenlerin Korunması *N. meningitidis*

Hasta ile yakın teması olan tüm kişilere yaşından ve aşılama durumundan bağımsız olarak kemoprofilaksi önerilmektedir.

- **Aynı evde yaşayanlar**
- **Aynı kreş/anaokuluna gidenler (son 7 gün içinde)**
- **Hastanın solunum salgıları ile doğrudan temas eden (ağızdan ağıza solunum, solunum salgılarını aspire etme, entubasyon yapma gibi) sağlık çalışanları**

Penisilin ile tedavi edilen menenjitli hasta da hastaneden çıkmadan önce profilaksi almalıdır.

Rifampin 10 mg/kg/doz, her 12 saatte bir, 2 gün
Seftriakson 125 (≤ 15 yaş) 250 mg (> 15 yaş) IM tek doz
Siprofloksasin 500 mg (> 18 yaş) tek doz

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