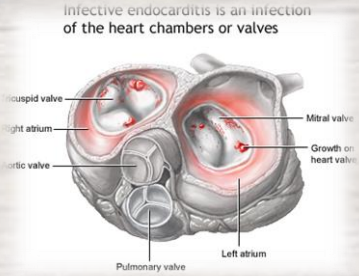


İnfektif Endokarditin Antibiyotik Tedavisinde Antimikrobiyal Direnç Bir Sorun mu? Penisilin

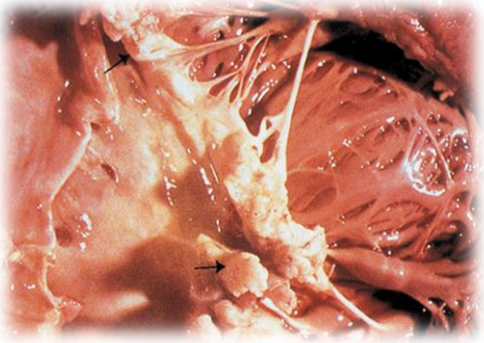
Dr Emel YILMAZ

UÜTF-Enf Hast ve Kl Mikrob AD

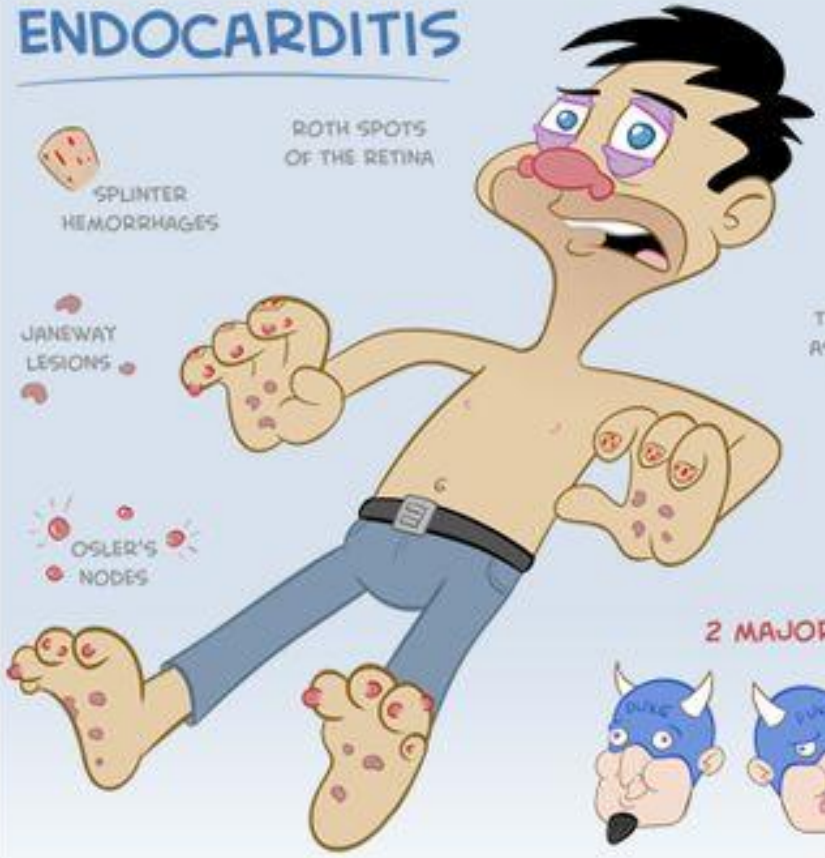
İEÇG-KLİMİK 21.10.2017

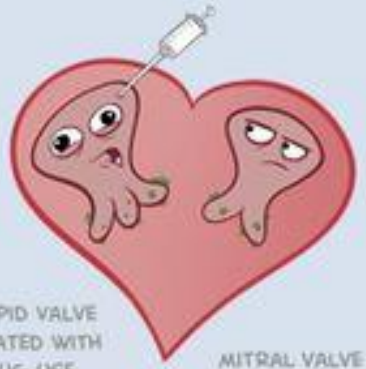
İnfektif Endokardit

- Koruyucu uygulamalara rağmen insidansı değişmedi
  - 30-100 epizod/1 milyon hasta yılı
  - 3-9/100.000 kişi (gelişmiş ülkelerde)
- Tanı ve tedavideki gelişmelere rağmen halen mortalite yüksek
  - Hastane mortalitesi %15-22
  - İlk bir yılda mortalite %30
  - Beş yıllık mortalite %40



ENDOCARDITIS





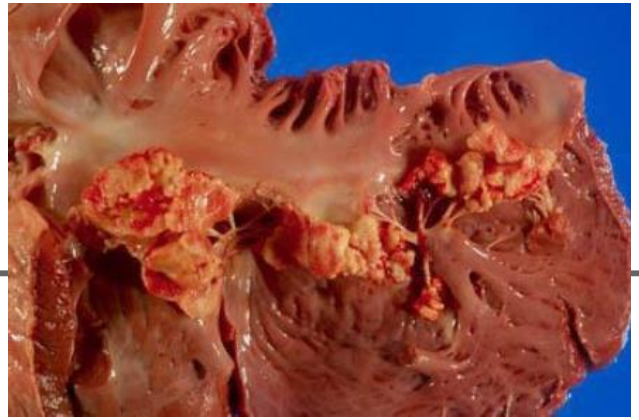
DUKE MAJOR CRITERIA

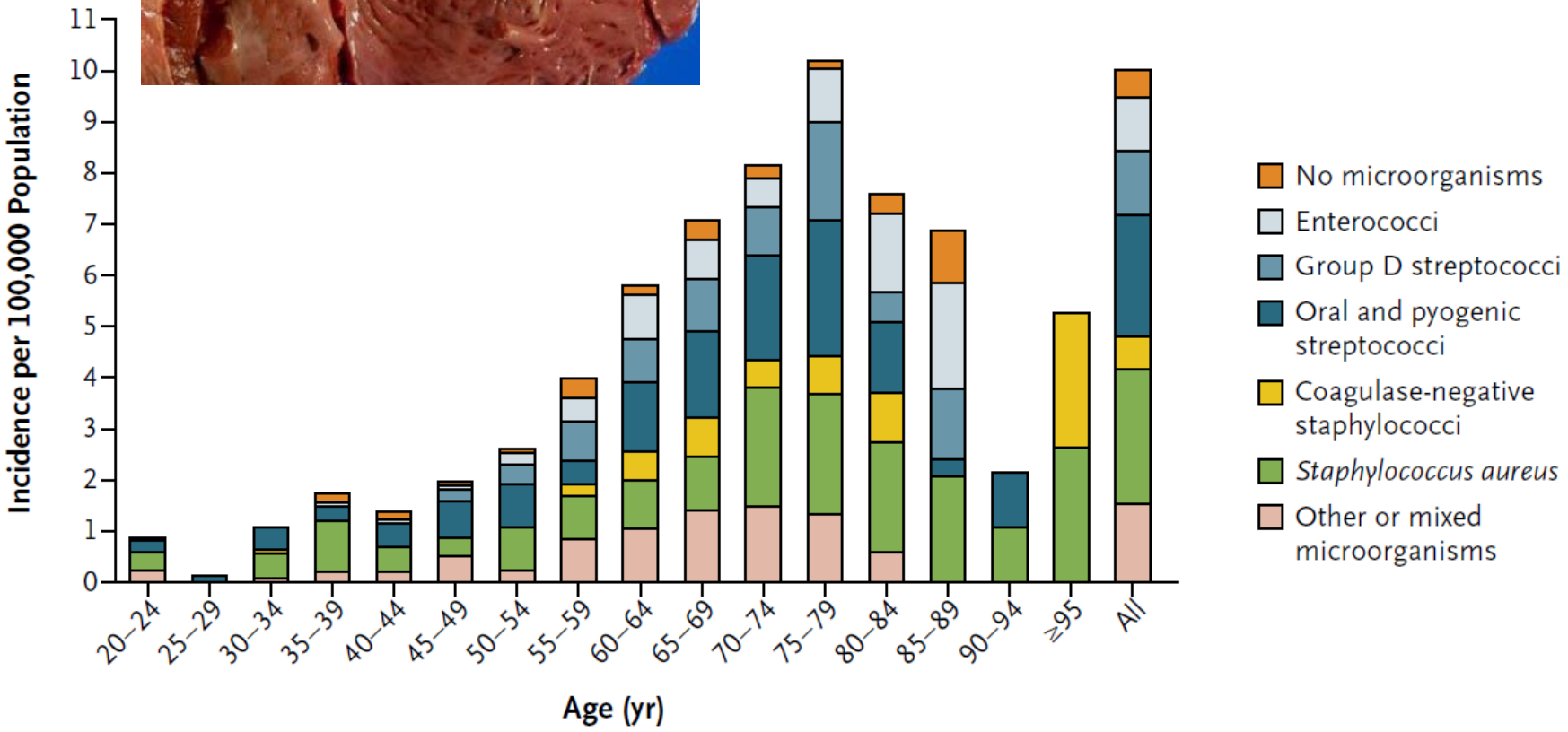
- TWO POSITIVE BLOOD CULTURES
- POSITIVE ECHO
- NEW REGURGITANT MURMUR

DUKE MINOR CRITERIA

- PREDISPOSING CONDITION
- FEVER
- IMMUNOLOGIC SIGNS
- ONE POSITIVE BLOOD CULTURE
- POSITIVE ECHO NOT MEETING MAJOR CRITERIA

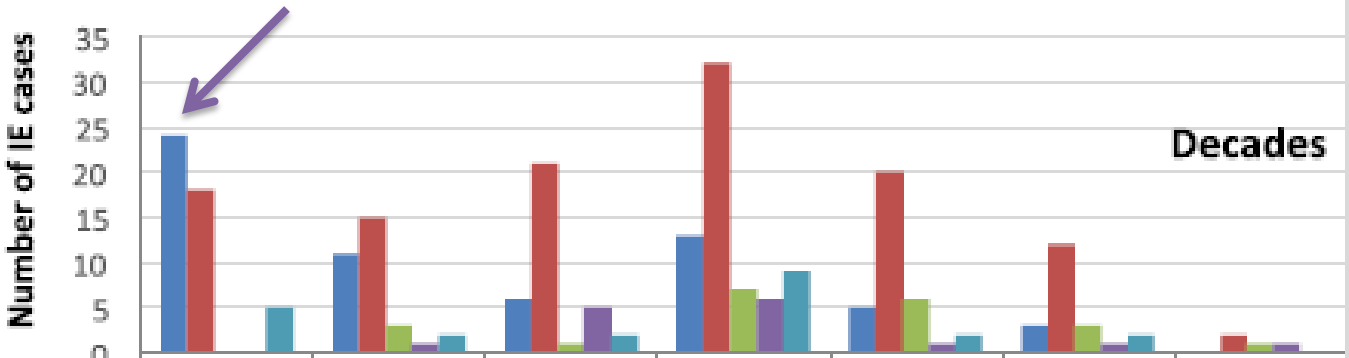
DUKE CRITERIA FOR DIAGNOSIS





Bruno Hoen, M.D., Ph.D.

N Engl J Med 2013;368:1425-33.
DOI: 10.1056/NEJMcp1206782



	18-29	30-39	40-49	50-59	60-69	70-79	80-90
Streptococcus spp.	24	11	6	13	5	3	0
Staphylococcus spp.	18	15	21	32	20	12	2
Enterococcus spp.	0	3	1	7	6	3	1
Brucella spp.	0	1	5	6	1	1	1
Gram-negative rods	5	2	2	9	2	2	0

Figure 1. Distribution of the most frequent five causative agents of infective endocarditis according to decades.

Şimşek S et al Int J Infect Dis 2015; 31: 30: 106

Contents lists available at ScienceDirect

Journal of Cardiology 63 (2014) 145–148

Original article

Clinical features of infective endocarditis: Comparison between the 1990s and 2000s

Tom Nakagawa (MD), Hiroshi Wada (MD)*, Kenichi Sakakura (MD), Yoko Yamada (MD), Kohki Ishida (MD), Tatsuro Ibe (MD), Nahoko Ikeda (MD), Yoshitaka Sugawara (MD), Junya Ako (MD), Shin-ichi Momomura (MD, FJCC)

Nakagawa T et al. J Cardiol 2014; 63: 145-8.

Table 3
Causative microorganisms.

	1990s ($n=37$)	2000s ($n=75$)	p-Value
Streptococcus viridans	16 (43.2%)	29 (38.7%)	NS
Streptococcus bovis	1 (2.7%)	3 (4%)	NS
Other streptococci	1 (2.7%)	5 (6.7%)	NS
HACEK group	0 (0%)	0 (0%)	NS
S. aureus	6 (16.2%)	8 (10.7%)	NS
MRSA	2 (5.4%)	3 (4%)	NS
Staphylococcus epidermidis	0 (0%)	3 (4%)	NS
MRSE	0 (0%)	2 (2.7%)	NS
Enterococcus species	4 (10.8%)	10 (13.3%)	NS
Fungi	1 (2.7%)	0 (0%)	NS
Others	1 (2.7%)	4 (5.3%)	NS
Unknown	7 (18.9%)	13 (17.3%)	NS

2005 **AHA Scientific Statement**

Infective Endocarditis

Di
A Sta
F
Dise

2007 **AHA Guideline**

Prevention of Infective Endocarditis

Guidelines From the American Heart Association

A Guideline From the American Heart Association Rheumatic Fever,

Endocar
Disease
Card

2010 **AHA Scientific Statement**

Update on Cardiovascular Implantable Electronic Device

2014 **AHA/ACC Guideline**

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the management of infective endocarditis

The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC)

Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM)

Authors/Task Force Members: Gilbert Habib* (Chairperson) (France), Patrizio Lancellotti* (co-Chairperson) (Belgium), Manuel J. Antunes (Portugal), Maria Grazia Bongiorni (Italy), Jean-Paul Casalta (France), Francesco Del Zotti (Italy), Raluca Dulgheru (Belgium), Gebrine El Khoury (Belgium), Paola Anna Erba[a] (Italy), Bernard Iung (France), Jose M. Miro[b] (Spain), Barbara J. Mulder (The Netherlands), Edyta Plonska-Gosciniak (Poland), Susanna Price (UK), Jolien Roos-Hesselink (The Netherlands), Ulrika Snygg-Martin (Sweden), Franck Thuny (France), Pilar Tornos Mas (Spain), Isidre Vilacosta (Spain), and Jose Luis Zamorano (Spain)

Tedavi

- Doğal kapak, geç protez kapak İE
  - Stafilokoklar ileri yaşlarda ve girişim yapılanlarda, gelişmiş ülkelerde….
  - Streptokoklar genç yaşlarda, gelişmekte olan ülkelerde, konjenital kalp hastalığı vs
  - Enterokoklar: yaşlılarda ve protez kapakta daha sık
- Protez kapak İE
  - Stafilokoklar (MR), enterokoklar, HACEK dışı gram negatif basiller

Tedavi

- Erken tedavi ağır sepsis, MODS, ani ölümü önlüyor
- Antibiyoterapi başlandıktan bir hafta sonra inme riski %65 azalıyor

Tedavi

- Genelde ampirik başlanır

- Parenteral

- Bakterisidal antibiyotik

- Penisilin İE’de;

Streptokoklar

Enterokoklar

Tedavi

- Tür düzeyinde tanımlama önemli
- MİK değeri önemli (antibiyotik seçimi, doz, tedavi süresi)
- Konak savunması yetersiz (10^8-10^{10} CFU/1 gr)
- Direnç olmasa da tolerans (yavaş üreyen veya durağan fazdaki bakteriler) sorunu
  - Uzun süreli tedavi
  - Uygun antibiyotik dozu

Tür düzeyinde tanımlama gerekli

- *S milleri*, *S anginosus* grup (*S anginosus*, *S intermedius*, *S constellatus*)
  - Büyük vejetasyonlar
  - Metastatik apse

Uzun tedavi olmalı

- *Abiotrophia spp*
- *Granulicatella spp*

Nutrisyonel varyant streptokoklar

Büyük vejetasyonlar (>10 mm)
Komplikasyon daha sık görülür
Kapak replasmanı daha fazla

Antimikrobiyal duyarlılık güvenilir değil

Penisiline tolerans gösterir

- Tedavi kesildikten sonra üremeye devam eden, yavaş üreyen ve dorman bakteriler antibiyotiğe karşı toleranstan bahsedilir

Penisiline Tolerans

- Minimal bakterisid konsantrasyon minimal inhibitör konsantrasyondan çok yüksektir
- MBK/MİK ≥ 32 ‘dir
- Streptokoklar arasında %11’dir (%4-90)
- Penisilin dozu değişir (MİK yüksek gibi düşünülmeli)
- Uzun süreli tedavi gereklidir (6 hafta)
- Aminoglikozid ile kombinasyon düşünülmeli

Hanslık et al CMI. 2003; 9: 852-7

Table 1 Comparison of characteristics of endocarditis patients infected with non-tolerant and tolerant strains of streptococci

Characteristic	Non-tolerant $n = 14$	Tolerant $n = 10$	P
Median age (range)	66 (41–87)	69 (42–92)	NS
Gender (female)	8	4	NS
Valves infected			
Aortic	7	3	NS
Mitral	2	7	NS
Aortic and mitral	3	0	NS
Undetermined	2	0	NS
Prosthetic valve	2	0	NS
Patients evaluated by transesophageal echocardiogram	12	8	NS
Duke's classification			
Definite infective endocarditis	10	7	NS
Possible infective endocarditis	4	3	NS
Severity criteria at presentation			
Major arterial emboli	6	3	NS
Vegetation size ≥10 mm	5	2	NS
Severe heart failure	4	2	NS
Intracardiac extension of the infection	0	0	NS
Heart block	0	1	NS
Antibiotic treatment before the diagnosis of endocarditis	3	1	NS
Streptococcal species			
Streptococcus bovis	9	5	NS
Streptococcus mitis	2	0	NS
Group B β-hemolytic *Streptococcus*	1	0	NS
Streptococcus sanguis	1	3	NS
Streptococcus oralis	1	1	NS
Streptococcus milleri	0	1	NS
MIC, mg/L (amoxicillin, median range)	0.060 (0.032–1)	0.16 (0.032–1)	NS
MBC, mg/L (amoxicillin, median range)	0.188 (0.032–4)	32 (4–256)	<0.0001
MBC/MIC, (median range)	2 (1–15)	250 (32–533)	<0.0001
Streptococci with natural resistance to aminoglycosides	14	10	NS

MBC, minimum bactericidal concentration; MIC, minimum inhibitory concentration; NS, not significant.

Hanslık T et al. CMI 2003; 9: 852-7

Table 2 Comparison of outcome of endocarditis patients infected with non-tolerant and tolerant strains of streptococci

Characteristic	Non-tolerant $n = 14$	Tolerant $n = 10$	P
Serum bactericidal titers[a]			
Peak ≥1/64 and trough ≥1/32	7/9	0/8	0.003
Peak ≥1/16 and trough ≥1/8	9/9	3/8	0.009
Peak ≥1/8 and trough ≥1/2	9/9	7/8	–
Initial antibiotic treatment failure	1	5[b]	0.050
Mean number of days to apyrexia (range)	3 (1–12)	7 (1–30)	NS
Median number of weeks required for treatment completion (range)	5 (4–6)	6 (4–15)	0.012
Surgical treatment			
Patients with severity criteria at admission[c]	5	1	NS
Patients without severity criteria at admission[a]	0	2	NS
Death (consecutive to infective endocarditis)	2 (0)	1 (1)	NS

[a]Determined for nine patients infected with non-tolerant streptococcal strains and eight infected with tolerant strains.
[b]See Table 3.
[c]Vegetation size ≥10 mm, major arterial emboli and/or severe heart failure.
MBC, minimum bactericidal concentration; MIC, minimum inhibitory concentration; NS, not significant.

Table 3 Treatment of patients with endocarditis infected with tolerant strains of streptococci

	First-line treatment				Second-line treatment				
Patient	Antibiotic	MIC (mg/L)	MBC/MIC	SBT peak–trough	Reason for change	Antibiotic	Vancomycin MBC/MIC	SBT peak–trough	Outcome
1	Amox (12 g) + Genta	1	>128	1/2–1/2	Treatment failure: persistent fever on the 9th day of treatment	Vanco + Genta	1	1/16–1/8	On the 30th day, mitral valve perforation appeared on cardiac echography. Surgery was performed. Cured
2	Pen G (40 million units) + Genta	0.250	512	1/8–1/2	Unsatisfactory SBT	Vanco + Genta	256	ND	Surgery was performed Cured
3	Amox (12 g) + Netil	1	256	1/8–1/2	–	–	–	–	Admitted to hospital with severe hemodynamic failure. Died on the 18th day
4	Amox (8 g) + Netil	0.06	>533	1/8–1/2	Treatment failure: persistent fever on the 13th day of treatment	Vanco + Rifam	4	1/2–1/2	Cured
5	Amox (6 g) + Netil	0.06	533	1/16–1/4	Treatment failure: recurrence of fever on the 20th day of treatment	Teico	ND	ND	Cured
6[a]	Vanco (2 g) + Genta	0.5	256	1/16–1/8	–	–	–	–	Cured
7	Amox (12 g) + Genta	0.25	128	1/32–1/8	–	–	–	–	Cured
8	Pen G (40 million units) + Genta	0.032	125	1/32–1/16	–	–	–	–	Cured
9	Amox (6 g) + Genta	0.06	533	ND	Treatment failure: on the 26th day, mitral abscess appeared on cardiac echography	Vanco + Genta	ND	ND	Surgery was performed Cured
10	Amox (12 g) + Genta	0.06	>32	ND	Treatment failure: persistent fever	Vanco + Netil	ND	ND	Cured

[a]Patient 6 had penicillin allergy and was treated with vanco

Amox, amoxicillin; Netil, netilmycin; Pen G, penicillin G; Rifam, rifampi

concentration; MBC, minimal bactericidal concentration; SBT

Penisilin G
Amoksisilin

+

Aminoglikozid

MİK değeri önemli

- Streptokokların etken olduğu İE'lerde MİK arttıkça
  - ↑doz penisilin
  - Seftriakson

+ AG

Holland TL. Nature Rev. 2016; 2: 10-4.

Streptokoklarda (VGS) Penisilin Direnci

- CLSI

S	**≤0,12 µg/mL**	**İE'de uygun değil**
I	0,25-2 µg/mL	
R	≥4 µg/mL	

- İE'de

S	**≤0,12 µg/mL**
Rölatif R	>0,12-≤0,5 µg/mL
R	>0,5 µg/mL

Fujitani S et al. CID 2008; 46: 1064-66

	E testi	Mikrodilüsyon	
	MİK	MİK	MBK
Pen G	4	2	2
Seftriakson	1,5	1	4
Gentamisin	1,5	1	4
Vankomisin	1	1	64
Sinerji testi			
PenG+Gentamisin		≤0,03	1
Seftriakson+Gentamisin		1	2

Fujitani S et al. CID 2008; 46: 1064-66

Oral streptokoklar, *S bovis* grup

Penisilin MİK≤0,125 mg/L

Tedavi süresi 4 hafta (PVE varsa 6 hafta)

Penisilin G 12-18 mU/gün
veya
Amoksisilin 100-200 mg/kg/gün
veya
Seftriakson 1x2 g

>65 yaş, KRY, 8. sinir hasarı olanlar

Tedavi süresi 2 hafta

Ateş <7 gün
HIV (+) CD4 >200
vejetasyon<1 cm

Penisilin G 12-18 mU/gün
veya
Amoksisilin 100-200 mg/kg/gün
veya
Seftriakson 1x2 g
+
Gentamisin 3mg/kg/gün 1x

Doğal kapak İE
Normal renal fonksiyon

Beta laktam alerjisi

Vankomisin 30 mg/kg/gün (2X)

PVE 6 hafta

Oral streptokoklar, *S bovis* grup

Penisilin MİK 0,250-2 mg/L

Penisilin G 24 mU/gün
veya
Amoksisilin 200 mg/kg/gün
veya
Seftriakson 1x2 g
+
Gentamisin 3mg/kg/gün 2 hafta 1x

>65 yaş, KRY, 8. sinir hasarı olanlar

4 hafta

PVE 6 hafta

Beta laktam alerjisi

Vankomisin 30 mg/kg/gün (2X)
Gentamisin 3mg/kg/gün 2 hafta 1x

Doğal kapak İE
Normal renal fonksiyon

PVE 6 hafta

MİK >2 mg/L ise enterokok İE gibi tedavi

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Nov. 2004, p. 4463–4465 Vol. 48, No. 11
0066-4804/04/$08.00+0 DOI: 10.1128/AAC.48.11.4463–4465.2004

Antimicrobial Susceptibility Patterns among Viridans Group Streptococcal Isolates from Infective Endocarditis Patients from 1971 to 1986 and 1994 to 2002

Rajesh M. Prabhu,[1] Kerryl E. Piper,[1] Larry M. Baddour,[1] James M. Steckelberg,[1] Walter R. Wilson,[1] and Robin Patel[1,2]*

Division of Infectious Diseases, Department of Internal Medicine,[1] and Division of Clinical Microbiology, Department of Laboratory Medicine and Pathology,[2] Mayo Clinic College of Medicine, Rochester, Minnesota

TA Received 4 April 2004/Returned for modification 6 June 2004/Accepted 23 July 2004 to

1986 and 1994 to 2002[a]

Antimicrobic	1971–1986 (n = 27)			1994–2002 (n = 23)			
	MIC_{90} (range)	% not S	% R	MIC_{90} (range)	% not S	% R	P^b
Penicillin[c]	0.125 (0.125–0.125)	0	0	0.5 (0.125–4)	13	4	0.09
Clindamycin[a]	0.125 (0.125–0.25)	0	0	0.125 (0.125–128)	4	4	0.46
Erythromycin[d]	4 (0.125–8)	11	11	16 (0.125–128)	26	26	0.27
Azithromycin[e]	8 (0.125–32)	11	11	16 (0.125–128)	26	26	0.27
Vancomycin[f]	1 (0.5–2)	4	4	2 (0.5–2)	9	9	0.59
Levofloxacin[g]	4 (0.125–4)	11	0	8 (0.25–32)	22	9	0.44
Moxifloxacin	0.25 (0.125–2)	NA	NA	0.25 (0.125–4)	NA	NA	
Gatifloxacin	0.5 (0.125–0.5)	NA	NA	0.5 (0.125–8)	NA	NA	
Ciprofloxacin	8 (0.5–16)	NA	NA	8 (0.5–64)	NA	NA	
Garenoxacin	0.25 (0.125–1)	NA	NA	0.25 (0.125–1)	NA	NA	

[a] Abbreviations: S, susceptible; I, intermediate; R, resistant; NA, not applicable.
[b] Fisher's exact test for percent not susceptible, 1971 to 1986 compared to 1994 to 2002 period.
[c] NCCLS breakpoints: S, ≤0.12 μg/ml; I, 0.25–2 μg/ml; R, ≥4 μg/ml.
[d] NCCLS breakpoints: S, ≤0.25 μg/ml; I, 0.5 μg/ml; R, ≥1 μg/ml.
[e] NCCLS breakpoints: S, ≤0.5 μg/ml; I, 1 μg/ml; R, ≥2 μg/ml.
[f] NCCLS breakpoints: S, ≤1 μg/ml.
[g] NCCLS breakpoints: S, ≤2 μg/ml; I, 4 μg/ml; R, ≥8 μg/ml.

Available online at www.scholarsresearchlibrary.com

Scholars Research Library

Annals of Biological Research, 2010, 1 (1) : 130-133
(http://scholarsresearchlibrary.com/archive.html)

Antimicrobial Susceptibility Trends among Viridan Streptococci Isolates from Cases of Endocarditis from 2007– 2009

Prabhu N *et al*

Table 2: Susceptibility pattern of viridans group of streptococci isolated from clinical samples

Antibiotics	$MIC_{90}S$ range	No. of isolates included	Sensitive	Resistant
Azithromycin	8 (0.125 – 32)	30	28 (93.3)	2 (6.7)
Ciprofloxacin	8 (0.5 – 16)	30	28 (93.3)	2 (6.7)
Clindamycin	0.125 (0.125 – 128)	30	28 (93.3)	2 (6.7)
Erythromycin	4 (0.125 – 8)	30	25 (83.3)	5 (16.7)
Levofloxacin	4 (0.125 – 8)	30	29 (96.7)	1 (3.3)
Penicillin	0.125 (0.125 – 4)	30	28 (93.3)	2 (6.7)
Vancomycin	0.125 (0.125 – 4)	30	26 (86.6)	4 (13.4)

Figures in parentheses indicate percentages

Table 1
Clinical profile of seven infective endocarditis patients infected with high-level penicillin-resistant *Streptococcus oralis*

Case number	Age (years/sex)	TTE	MIC (μg/mL)		Treatment
			Penicillin	Ceftriaxone	
CPE 12	11/F	Vegetation attached to septal leaflet of anterior TV	4	1	Ceftriaxone 600 mg i.v. tds; ampicillin 1.8 g i.v. tds
CPE 13	45/M	Vegetation attached to TV	4	2	Ampicillin 3 g q4h i.v.; ciprofloxacin 200 mg i.v. bd
CPE 14	7/M	Vegetation attached to PV	16	0.5	Ceftriaxone 600 mg i.v. tds; ampicillin 300 mg/kg i.v. tds
CPE 16	34/M	Vegetation attached to RCC of AV	8	1	Ampicillin 3 g q6h i.v.; ceftriaxone 1 g q4h i.v.
CPE 17	17/M	Vegetation attached to RVOT and PA	8	1	The patient received 20 Lakh units of Penicillin G every 4 hours i.v.; ciprofloxacin 200 mg q4h i.v.
CPE 18	30/F	Vegetation attached to NCC of AV	4	0.0625	Ceftriaxone 2 g i.v. bd; gentamicin 80 mg i.v. bd
CPE 19	21/M	Vegetation attached to AML	4	0.5	Ceftriaxone 1 g i.v. tds; gentamicin 80 mg i.v. bd

Seftriakson+AG
Yüksek doz penisilin+AG
Mortalite yok
Tedavi süresi 4 hafta

Vazquez MF et al. Antimicrob Agents 2008; 32: 538-47

MAJOR ARTICLE

Infective Endocarditis Due to Penicillin-Resistant Viridans Group Streptococci

Bettina Knoll,[1] Imad M. Tleyjeh,[3] James M. Steckelberg,[1,2] Walter R. Wilson,[1,2] and Larry M. Baddour[1,2]

[1]Department of Medicine and [2]Division of Infectious Diseases, Mayo Clinic College of Medicine, Rochester, Minnesota; and [3]Division of Infectious Diseases, Department of Medicine, King Fahd Medical City, Riyadh, Saudi Arabia

Background. The emergence of viridans group streptococci that are relatively or fully resistant to penicillin is increasingly being recognized worldwide, but only a scant number of penicillin-resistant isolates have been described

Clinical Infectious Diseases 2007; 44:1585–92

Table 2. Treatment of 19 patients with native-valve endocarditis due to penicillin-resistant viridans group streptococci.

Patient	Year	Antibiotic (MIC, μg/mL)	Species	Valve	Treatment (duration in weeks)	Outcome
1	1967	Pen (0.5)	*Streptococcus mitis*	MV	Procaine pen, 1.2 MU im tid (1); pen G, 40–60 MU iv inf qd (2); pen G, 25 MU iv inf qd (2); Stm, 500 mg im tid (2)	Cured 14 years
2	1970	Pen (0.5)	ND	AV	Pen G, 20 MU iv inf qd (1); pen G, 40 MU iv inf qd (2); Stm, 500 mg im bid (3)	Cured 35 years
3	1970	Pen (0.5)	ND	MV	Procaine pen, 1.2 MU im tid (2); Stm, 0.5 g im tid (2)	Cured 13 years
4	1970	Pen (0.5)	ND	MV	Pen G, 20 MU iv inf qd (2); pen G, 40 MU iv inf qd (1); Stm, 500 mg im bid (3)	Cured 3 years
5	1971	Pen (0.5)	ND	MV	Stm, 0.5 gm im bid (2); pen G, 40 MU iv inf qd (1); pen G, 20 MU iv inf qd (1)	Cured 10 years
6	1971	Pen (0.5)	ND	MV	Procaine pen, 1.2 MU im tid (2); Stm, 0.5 g im tid (2); probenecid, 0.5 g tid (2)	Cured 3 years
7	1973	Pen (1.0)	ND	MV	Pen G, 20 MU iv inf qd (1); procaine pen G, 1.2 MU im qid (1); Stm, 0.5 gram im bid (1.5)	Cured 3 years
8	1975	Pen (0.5)	ND	MV	Clindamycin, 1.2 g iv tid (2); Stm, 500 mg im bid (2)	Cured 13 years
9	1977	Pen (1.0)	ND	MV	Procaine pen, 1.2 MU im qid (2); Stm, 500 mg im bid (2)	Cured 25 years
10	1978	Pen (4.0)	ND	AV	Pen G, 20 MU iv inf qd (3); Stm, 0.5 g im bid (2)	Relapse, deceased
11	1983	Pen (1.0)	*S. mitis*	MV	Pen G, 20 MU iv inf qd (2); Stm, 500 mg bid (2)	Cured 4 years
12	1986	Pen (0.5)	*Streptococcus sanguis*	AV	Vancomycin, 15 mg/kg iv bid (1); pen G, 20 MU iv inf qd (5); Gm, 120 mg iv load, 110 mg iv tid (4)	Cured 13 years
13	1992	Pen (1.0), cef (0.25)	*S. sanguis*	MV	Cef, 2 g iv qd (6); Gm, 90–100 mg iv tid (1.5)	Cured 14 years
14	1994	Pen (1.0), cef (8.0)	ND	AV	Cef, 2 g iv qd (4)	Cured 2 years
15	1995	Pen (1.0), cef (0.25)	ND	MV	Pen, 20 MU iv inf qd (4); Gm, 3 mg/kg iv qd (4)	Cured 10 years
16	1997	Pen (2.0)	*S. mitis*	MV/AV	Cephalexin, 500 mg (0.75); pen G 24 MU iv inf qd (0.75); vancomycin, 15 mg/kg iv bid (3); Gm, 3 mg/kg iv qd (1)	Deceased, intraoperative
17	2004	Pen (1.0), cef (1.0)	*Streptococcus salivarius*	MV	Pen G, 24 MU iv inf qd (3); Gm, 80 mg iv bid-tid (3); cef, 2 g iv qd (1.8)	Cured 4 months
18	2005	Pen (1.0), cef (0.5)	ND	AV	Cef, 2 g iv qd (4)	Cured 2 months
19	2006	Pen (1.0)	ND	AV	Gm, 80 mg iv tid (2); cef iv 2 g qd (2); vancomycin, 15 mg/kg iv bid (6)	Cured 4 months

NEW MICROBIOLOGICA, 34, 187-193, 2011

Erythromycin and penicillin resistance mechanisms among viridans group streptococci isolated from blood cultures of adult patients with underlying diseases

Alper Ergin[1], Özgen Köseoğlu Eser[2], Gülşen Hasçelik[2]

[1]Hacettepe University, School of Health Services, Medical Laboratory Programme, Ankara, Turkey;
[2]Hacettepe University, Faculty of Medicine, Department of Medical Microbiology, Ankara, Turkey

Malignitesi olan hastaların kan kültüründen izole edilen) 50 suşun (Viridans Grup Streptokok) VGS %50'sinde penisilin direnci tespit edilmiş

TABLE 2 - *The correlation between penicillin and erythromycin-resistant isolates according to species distribution, MIC, MLS and underlying diseases.*

S	Age	Species	Pen MIC	Ery MIC	Mls	Geno type	Underlying diseases	Clinical outcome
M	67	*S.mitis*	0.03	>256	cMLS	ermB	Squamous cell cancer	Exitus
M	39	*S.mitis*	1	>256	cMLS	ermB	Stomach cancer	Exitus
F	22	*S.mitis*	2	4	cMLS	ermB	Ewing sarcoma	Exitus
F	56	*S.mitis*	4	<0.016	-	-	Chronic myeloid leukemia	Exitus
M	78	*S.mitis*	4	32	cMLS	ermB	Brain abscess	Follow up
F	58	*S.mitis*	0.5	8	cMLS	ermB	Brain abscess	Cure
F	42	*S.mitis*	0.5	>256	cMLS	ermB	Chronic kidney failure	Follow up
M	33	*S.mitis*	4	0.5	-	-	Sinus vena thrombosis	Exitus
F	62	*S.mitis*	0.03	>256	cMLS	ermB	Chronic obstructive pulmonary disease	Cure
M	84	*S.mitis*	4	0.023	-	-	Lung cancer	Follow up
F	77	*S.oralis*	0.12	8	M	mef E	Acute myeloid leukemia	Exitus
M	46	*S.oralis*	4	>256	cMLS	ermB	Multiple myeloma	Cure
F	75	*S.oralis*	16	>256	cMLS	ermB	Sigmoid cancer	Cure
F	69	*S.oralis*	32	>256	cMLS	ermB	Burkitt lymphoma	Follow up
F	39	*S.oralis*	4	>256	cMLS	ermB	Brain abscess	Follow up
M	48	*S.oralis*	16	>256	cMLS	ermB	Chronic obstructive pulmonary disease	Cure
F	69	*S.parasanguinis*	4	>256	cMLS	ermB	Non-Hodgkin lymphoma	Follow up
F	33	*S.parasanguinis*	4	4	M	mef E	Acute myeloid leukemia	Exitus
F	71	*S.parasanguinis*	8	2	-	-	Vascular demans	Follow up
M	61	*S.parasanguinis*	1	>256	cMLS	ermB+ mef E	Chronic obstructive pulmonary disease	Cure
F	32	*S.sanguinis*	4	1	-	-	Fanconi anemia - bone marrow transplantation	Exitus
M	61	*S.sanguinis*	4	1	-	-	Intracardiak stenozis	Cure
F	65	*S.sanguinis*	1	>256	cMLS	ermB+ mef E	Acute myeloid leukemia	Exitus
F	62	*S.vestibularis*	4	>256	cMLS	ermB	Mitral valve operation	Cure

S, Sex; Pen, Penicillin; Ery, Erythromycin; MLS, Macrolide-Lincosamide-Streptogramin phenotype.

- Hematolojik malignitesi olan 75 hastanın orofarenks kültüründe VGS penisilin direnci %57,3 duyarlılık azalmış

Sayın Kutlu S et al KLİMİK Derg 2012; 25: 6-9

- İmmünsüprese hastalardan izole edilen VGS'lerde penisilin direnci >%50
- Diğer hastalardan izole edilen VGS'lerde penisilin direnci yok

Akova M. Virulance 2016: 7: 252-66.

- ARA tanısı olan ve Penisilin profilaksisi alanlarda oral streptokoklarda penisilin direnci düşünülmeli
  - *S mitis* MIC (2,7-4µg/mL) bulunmuş

Barillo JE et al NEJM 1979; 300: 296-300

Le Infezioni in Medicina, n. 3, 190-193, 2016

Antimicrobial susceptibility against penicillin, ampicillin and vancomycin of viridans group Streptococcus in oral microbiota of patients at risk of infective endocarditis

Serap Süzük[1], Banu Kaşkatepe[2], Mustafa Çetin[3]

[1]Public Health Institute of Turkey, National Antimicrobial Resistance Laboratory, Ankara, Turkey;
[2]Banu Kaşkatepe, University of Ankara, Faculty of Pharmacy, Department of Pharmaceutical Microbiology, Ankara, Turkey;
[3]Ankara Numune Training and Research Hospital, Department of Cardiology, Ankara, Turkey

ARA profilaksisi alanlarda VGS 'lerde penisilin direnci düşünülmeli

Table 1 - Number and antibiotic susceptibility rates of VGS.

Group name	*No. (%)*	*Penicillin*		*Ampicillin*	
		Not susceptible No. (%)*	*Susceptible No. (%)*	*Not susceptible* No. (%)*	*Susceptible No. (%)*
***S. mitis* Group**	16 (32.65%)	8 (50.00)	8 (50.00)	4 (25.00)	12 (75.00)
***S. anginosus* Group**	16 (32.65%)	9 (54.25)	7 (43.75)	11 (68.75)	5 (31,25)
***S. sanguinis* Group**	8 (16.33%)	6 (75.00)	2 (25.00)	6 (75.00)	2 (25.00)
***S. mutans* Group**	6 (12.24%)	4 (66.67)	2 (33.33)	3 (50.00)	3 (50.00)
***S. salivarius* Group**	3 (6.12%)	3 (100.00)	0 (0)	3 (100.00)	0 (0)

*resistant and reduced susceptibility.

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Infective endocarditis in Turkey: aetiology, clinical features, and analysis of risk factors for mortality in 325 cases

Serap Şimşek-Yavuz [a,*], Ayfer Şensoy [b], Hulya Kaşıkçıoğlu [c], Sabahat Çeken [b], Denef Deniz [b], Atilla Yavuz [d], Funda Koçak [e], Kenan Midilli [f], Mehmet Eren [c], İbrahim Yekeler [g]

[a] *Istanbul University, Istanbul Medical Faculty, Infectious Disease and Clinical Microbiology Department, Istanbul, Turkey*
[b] *Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Infectious Disease and Clinical Microbiology Department, Istanbul, Turkey*
[c] *Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Cardiology Department, Istanbul, Turkey*
[d] *Kartal Lutfi Kırdar Research and Education Hospital, Cardiology Department, Istanbul, Turkey*
[e] *Basaksehir State Hospital, Infectious Disease and Clinical Microbiology Department, Istanbul, Turkey*
[f] *Istanbul University, Cerrahpasa Medical Faculty, Microbiology Department, Istanbul, Turkey*
[g] *Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Cardiovascular Surgery Department, Istanbul, Turkey*

- 325 İE
- 253 etkene ulaşılmış
- 63 streptokok hepsi penisilin duyarlı

International Journal of Infectious Diseases 30 (2015) 106–114

Enterokok İE

Beta laktam ve aminoglikozid duyarlı

Amoksisilin/ampisilin 200 mg/kg/gün (4-6X)
+
Gentamisin 3 mg/kg/gün tek doz

4-6 hafta

2-6 hafta??

veya

Ampisilin 200 mg/kg/gün (4-6 X)
+
Seftriakson 4 g/gün (2X)

veya

Vankomisin 30 mg/kg/gün (2X)
+
Gentamisin 3 mg/kg/gün tek doz

±HLAR
E faecalis için uygun

Pen G 24 MU+Gentamisin

Semptomlar 3 aydan fazla ya da PVE ise 6 hafta

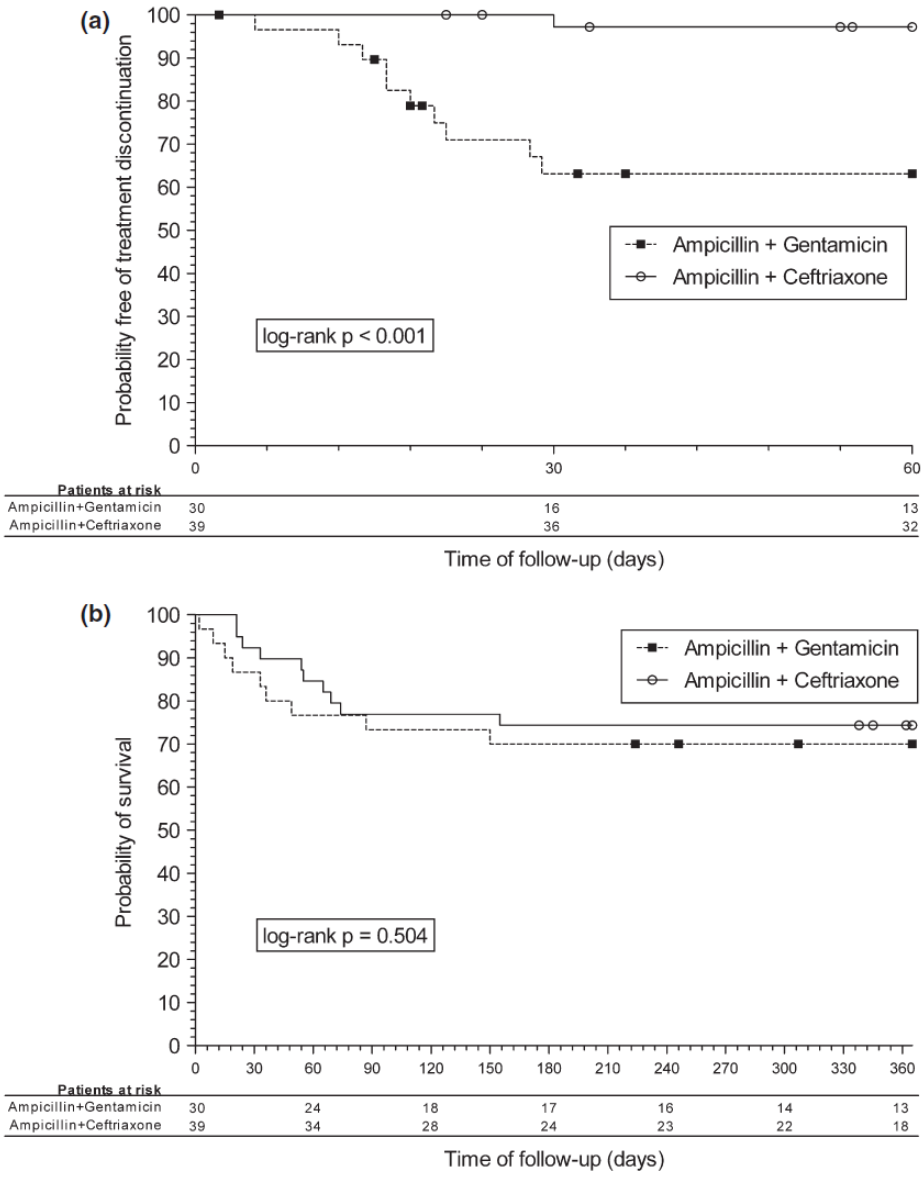
6 hafta

Changes in the treatment of *Enterococcus faecalis* infective endocarditis in Spain in the last 15 years: from ampicillin plus gentamicin to ampicillin plus ceftriaxone

J. M. Pericas[1], C. Cervera[1], A. del Rio[1], A. Moreno[1], C. Garcia de la Maria[1], M. Almela[2], C. Falces[3], S. Ninot[4], X. Castañeda[1], Y. Armero[1], D. Soy[5], J. M. Gatell[1], F. Marco[2], C. A. Mestres[4], J. M. Miro[1] and The Hospital Clinic Endocarditis Study Group[†]

1) *Infectious Diseases Service, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer,* 2) *Microbiology Service, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer,* 3) *Cardiology Service, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer,* 4) *Department of Cardiovascular Surgery, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer and* 5) *Pharmacy Service, Hospital Clínic, Institut d'Investigacions Biomèdiques August Pi i Sunyer, University of Barcelona, Barcelona, Spain*

- 1997-2011 yılları arasında
- 30 olgu (7'si HLAR) Ampisilin (8 g/gün)+Gentamisin (3 mg/kg/gün)
- 39 olgu (18'i HLAR) Ampisilin + Seftriakson



Yan etki daha az

Tedavi başarısı benzer

FIG. 2. Kaplan–Meier survival analysis curves. (a) Treatment discontinuation at 60 days. (b) 1-year mortality.

MAJOR ARTICLE

Ampicillin Plus Ceftriaxone Is as Effective as Ampicillin Plus Gentamicin for Treating *Enterococcus faecalis* Infective Endocarditis

Nuria Fernández-Hidalgo,[1] Benito Almirante,[1] Joan Gavaldà,[1] Mercè Gurgui,[2] Carmen Peña,[3] Arístides de Alarcón,[4] Josefa Ruiz,[5] Isidre Vilacosta,[6] Miguel Montejo,[7] Nuria Vallejo,[8] Francisco López-Medrano,[9] Antonio Plata,[10] Javier López,[11] Carmen Hidalgo-Tenorio,[12] Juan Gálvez,[13] Carmen Sáez,[14] José Manuel Lomas,[15] Marco Falcone,[18] Javier de la Torre,[16] Xavier Martínez-Lacasa,[17] and Albert Pahissa[1]

[1]Servei de Malalties Infeccioses, Hospital Universitari Vall d'Hebron, and [2]Unitat de Malalties Infeccioses, Hospital de la Santa Creu i Sant Pau, Universitat Autònoma de Barcelona, Department of Medicine, [3]Servei de Malalties Infeccioses, Hospital Universitari de Bellvitge, Barcelona, [4]Servicio de Enfermedades Infecciosas y Medicina Interna, Hospital Universitario Virgen del Rocío, Seville, [5]Unidad de Gestión Clínica de Enfermedades Infecciosas, Hospital Universitario Virgen de la Victoria, Málaga, [6]Instituto Cardiovascular, Servicio de Cardiología, Hospital Clínico San Carlos, Madrid, [7]Unidad de Enfermedades Infecciosas, Hospital Universitario de Cruces, Bizkaia, [8]Servicio de Cardiología, Hospital Germans Trias i Pujol, Barcelona, [9]Unidad de Enfermedades Infecciosas, Hospital Universitario 12 de Octubre, Madrid, [10]Servicio de Enfermedades Infecciosas, Hospital

Table 3. Outcomes of 246 Episodes of *Enterococcus faecalis* Infective Endocarditis Treated With Ampicillin Plus Ceftriaxone or Ampicillin Plus Gentamicin

Variable	Ampicillin + Ceftriaxone (n = 159)	Ampicillin + Gentamicin (n = 87)	*P* Value
Failures			
Death during treatment	35 (22%)	18 (21%)	0.81
Death during 3-mo follow-up	13 (8%)	6 (7%)	0.72
Adverse effects requiring treatment withdrawal	2 (1%)	22 (25%)	<0.001
Treatment failure requiring change of antimicrobials	2 (1%)	2 (2%)	0.54
Relapse	3/124 (3%)	3/69[a] (4%)	0.67

[a] These patients had received 28, 36, and 42 days of ampicillin plus gentamicin, respectively.

Enterokok İE

- Beta laktam direnci varsa
  - Beta laktamaz
    - Ampisilin/sulbaktam
    - Amoksisilin/klavunat
  - PBP5'de değişiklik
    - Vankomisin
- HLAR gentamisin MİK >500 mg/L
  - Streptomisin 15 mg/kg (2X) IM

- Enterokoklardan *E faecium*'da en sık direnç var
- Aminopenisilin direnci
  - *E faecalis* direnci <%1-%25
  - *E faecium* %90 (çoğunlukla hastane kökenli)
- Beta laktamaz nadir

Akova M. Virulance 2016: 7: 252-66.

World Health Organization
Europe

Annual report

Table 6.70 Percentage of resistance for *E. faecalis* and *E. faecium* among blood and CSF isolates in Turkey in 2014

	E. faecalis		*E. faecium*	
	n	Resistance (%)	*n*	Resistance (%)
Aminopenicillins (I+R)	746	8	655	82
High-level gentamicin (R)	450	22	391	43
Vancomycin (R)	860	3	780	16
Linezolid (I+R)	806	3	721	4

The aminopenicillins group comprises amoxicillin and ampicillin.

Table 6.76 Percentage of resistance for *E. faecalis* and *E. faecium* among blood and CSF isolates in Turkey in 2015

	E. faecalis		*E. faecium*	
	n	Resistance (%)	*n*	Resistance (%)
Aminopenicillins (I+R)	1563	9	1405	87
High-level gentamicin (R)	805	54	851	69
Vancomycin (R)	1536	3	1435	16
Linezolid (I+R)	1465	2	1395	4

The aminopenicillins group comprises amoxicillin and ampicillin.

Table 33. Resistance levels for *E. faecium* and *E. faecalis* among blood and CSF isolates in Turkey

Antibiotic class	*E. faecalis*		*E. faecium*	
	N	Resistance (%)	N	Resistance (%)
Aminopenicillins (I+R)[a]	788	5	638	99
High-level gentamicin (R)	561	25	434	49
Vancomycin (R)	829	1	636	23
Teicoplanin (R)	538	0	411	18
Linezolid (I+R)	709	2	568	4

[a] The aminopenicillins group consists of amoxicillin and ampicillin.

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Infective endocarditis in Turkey: aetiology, clinical features, and analysis of risk factors for mortality in 325 cases

Serap Şimşek-Yavuz [a,*], Ayfer Şensoy [b], Hulya Kaşıkçıoğlu [c], Sabahat Çeken [b], Denef Deniz [b], Atilla Yavuz [d], Funda Koçak [e], Kenan Midilli [f], Mehmet Eren [c], İbrahim Yekeler [g]

[a] *Istanbul University, Istanbul Medical Faculty, Infectious Disease and Clinical Microbiology Department, Istanbul, Turkey*
[b] *Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Infectious Disease and Clinical Microbiology Department, Istanbul, Turkey*
[c] *Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Cardiology Department, Istanbul, Turkey*
[d] *Kartal Lutfi Kırdar Research and Education Hospital, Cardiology Department, Istanbul, Turkey*
[e] *Basaksehir State Hospital, Infectious Disease and Clinical Microbiology Department, Istanbul, Turkey*
[f] *Istanbul University, Cerrahpasa Medical Faculty, Microbiology Department, Istanbul, Turkey*
[g] *Siyami Ersek Thoracic and Cardiovascular Surgery Hospital, Cardiovascular Surgery Department, Istanbul, Turkey*

- 325 İE
- 253 etkene ulaşılmış
- 22 enterokok hepsi penisilin, vankomisin duyarlı ve HLAR yok

International Journal of Infectious Diseases 30 (2015) 106–114

Journal of Antimicrobial Chemotherapy (2006) **57**, 819–824
doi:10.1093/jac/dkl087
Advance Access publication 20 March 2006

JAC

Antimicrobial treatment of infective endocarditis caused by viridans streptococci highly susceptible to penicillin: historic overview and future considerations

D. W. M. Verhagen[1,2], A. C. Vedder[1], P. Speelman[1] and J. T. M. van der Meer[1]*

[1]*Department of Internal Medicine, Division of Infectious Diseases, Tropical Medicine & AIDS, Academic Medical Centre, Amsterdam, The Netherlands;* [2]*Department of Internal Medicine, Free University Medical Centre, Amsterdam, The Netherlands*

In this article we present the path that led to current concepts regarding antimicrobial treatment of

Table 1. Medical Research Council penicillin trials, 1945 and 1946

Penicillin (million units)	Duration of treatment (days)	Total number treated	Died with infection apparently controlled (no.)	Died with infection uncontrolled (no.)	Relapsed (no.)	Cure (no.)	Relapsed or died of infection [no. (%)]
First trial							
1	5	18	3	2	13	0	15 (83)
0.5	10	16	4	0	8	4	8 (50)
0.25	20	18	6	0	4	8	4 (22)
Second trial							
0.1	28	17	4	0	7	6	7 (41)
0.25	28	83	30	2	11	40	13 (16)
0.5	28	58	22	3	1	32	4 (7)

European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv319

ESC GUIDELINES

2015 ESC Guidelines for the of infective endocarditis

The Task Force for the Management of European Society of Cardiology (ESC)

Endorsed by: European Association for ((EACTS), the European Association

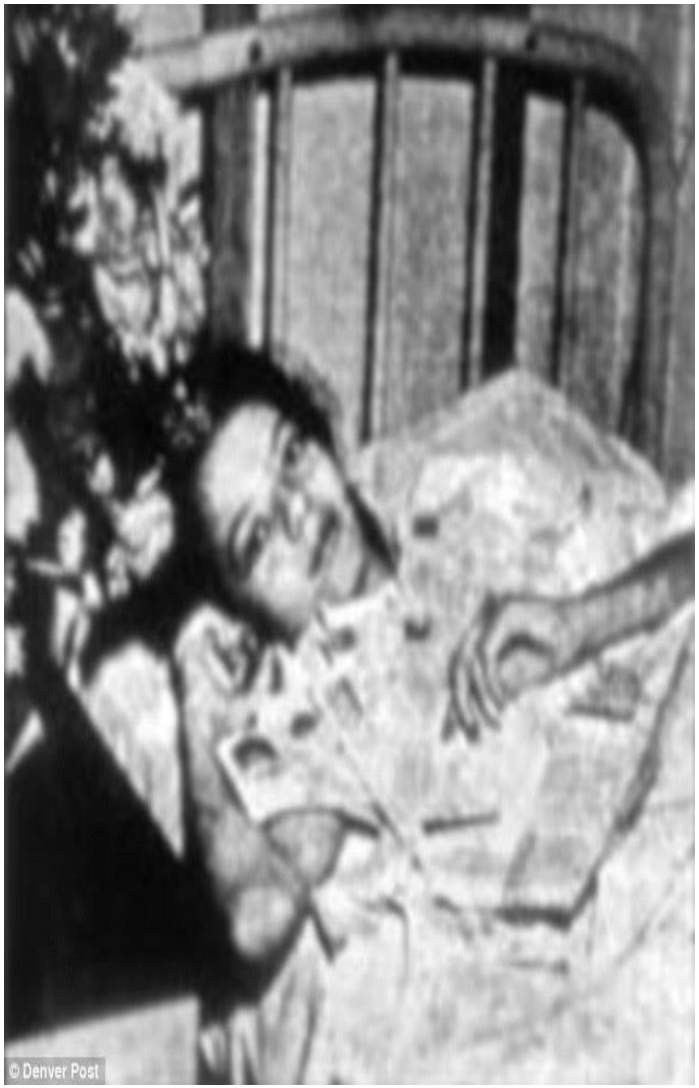
Authors/Task Force Members: Gilbert Habib
Patrizio Lancellotti* (co-Chairperson) (Belgi
Maria Grazia Bongiorni (Italy), Jean-Paul Casa
Raluca Dulgheru (Belgium), Gebrine El Khou
Bernard Iung (France), Jose M. Miro[b] (Spain)
Edyta Plonska-Gosciniak (Poland), Susanna F
(The Netherlands), Ulrika Snygg-Martin (Sw
Pilar Tornos Mas (Spain), Isidre Vilacosta (Sp

Table 16 Antibiotic treatment of infective endocarditis due to oral streptococci and *Streptococcus bovis* group[a]

Antibiotic	Dosage and route	Duration (weeks)	Class[b]	Level[c]	Ref.[d]	Comments
Strains penicillin-susceptible (MIC ≤ 0.125 mg/L) oral and digestive streptococci						
Standard treatment: 4-week duration						
Penicillin G	12–18 million U/day i.v. either in 4–6 doses or continuously	4	I	B	6,8, 135–139	Preferred in patients > 65 years or with impaired renal or VIII (vestibulocochlear) cranial nerve functions. 6-week therapy recommended for patients with PVE
or Amoxicillin[e]	100–200 mg/kg/day i.v. in 4–6 doses	4	I	B		
or Ceftriaxone[f]	2 g/day i.v. or i.m. in 1 dose	4	I	B		
	Paediatric doses:[g] Penicillin G 200,000 U/kg/day i.v. in 4–6 divided doses Amoxicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Ceftriaxone 100 mg/kg/day i.v. or i.m. in 1 dose					
Standard treatment: 2-week duration						
Penicillin G	12–18 million U/day i.v. either in 4–6 doses or continuously	2	I	B	6,8, 127, 135–138	Only recommended in patients with non-complicated NVE with normal renal function.
or Amoxicillin[e]	100–200 mg/kg/day i.v. in 4–6 doses	2	I	B		
or Ceftriaxone[f] combined with	2 g/day i.v. or i.m. in 1 dose	2	I	B		
Gentamicin[h]	3 mg/kg/day i.v. or i.m. in 1 dose	2	I	B		
or Netilmicin	4–5 mg/kg/day i.v. in 1 dose	2	I	B		Netilmicin is not available in all European countries.
	Paediatric doses:[g]					

Table 18 Antibiotic treatment of infective endocarditis due to *Enterococcus* spp.

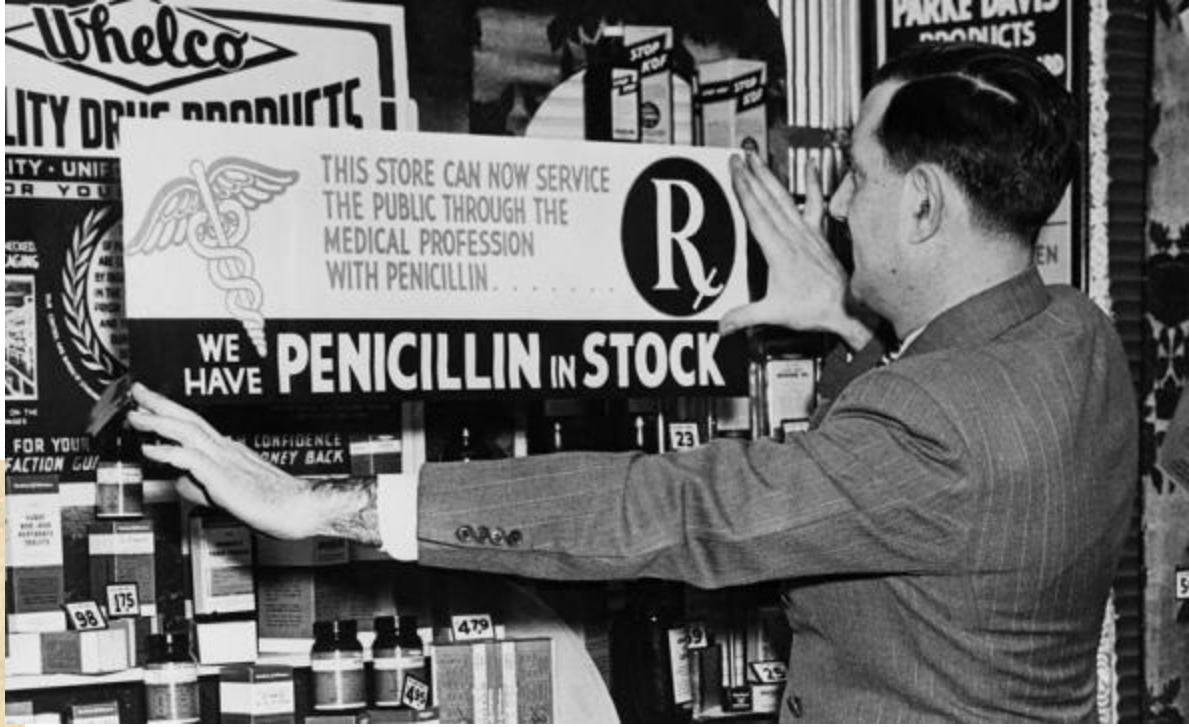
Antibiotic	Dosage and route	Duration, weeks	Class[g]	Level[h]	Ref.[i]	Comments
Beta-lactam and gentamicin-susceptible strains (for resistant isolates see [a,b,c])						
Amoxicillin* with	200 mg/kg/day i.v. in 4–6 doses	4–6	I	B	6,8, 129, 135, 136, 186	6-week therapy recommended for patients with >3 months symptoms or PVE
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose	2–6**	I	B		
	Paediatric doses:[e] Ampicillin 300 mg/kg/day i.v. in 4–6 equally divided doses Gentamicin 3 mg/kg/day i.v. or i.m. in 3 equally divided doses					
Ampicillin with Ceftriaxone	200 mg/kg/day i.v. in 4–6 doses	6	I	B	183–185	This combination is active against *Enterococcus faecalis* strains with and without HLAR, being the combination of choice in patients with HLAR *E. faecalis* endocarditis. This combination is not active against *E. faecium*
	4 g/day i.v. or i.m. in 2 doses	6	I	B		
	Paediatric doses:[e] Amoxicillin as above Ceftriaxone 100 mg/kg/12 h i.v. or i.m.					
Vancomycin[f] with	30 mg/kg/day i.v. in 2 doses	6	I	C		
Gentamicin[d]	3 mg/kg/day i.v. or i.m. in 1 dose	6	I	C		
	Paediatric doses:[e] Vancomycin 40 mg/kg/day i.v. in 2–3 equally divided doses. Gentamicin as above					


© Denver Post


PENICILLIN SQUIBB
Sodium Salt of Penicilli
Contains 10,000 Florey unit
No Preservative
KEEP BELOW 45° F.
Caution: New Drug--Limited
federal law to investigational u
E.R. Squibb & Sons, N.Y.
Biological Laboratories
New Brunswick, N.J.


© Denver Post

- Streptokoklarda ve toplum kökenli enterokoklarda penisilin direnci şimdilik sorun değil
- Özellikle İE riski olan ve penisilin profilaksisi yapılan ya da malignitesi olan kişilerde VGS'larda penisilin direnci olabilir
- İE tanısı olan hastalarda etiyolojik tanıya ulaşılmaya çalışılmalı
- Ulusal veri tabanı oluşturulmalı



Teşekkürler

Table 5. Summary of treatment recommendations for enterococcal endocarditis

Regimen	Antimicrobial	Dose and route	Duration (weeks)	
1.	amoxicillin OR	2 g q4h iv	4–6	for amoxicillin-suscepti ≤4 mg/L AND genta isolates
	penicillin AND	2.4 g q4h iv	4–6	duration 6 weeks for P
	gentamicin[a]	1 mg/kg q12h iv	4–6 (see Recommendation 9.3)	
2.	vancomycin[a] AND	1 g q12h iv or dosed according to local guidelines	4–6	for penicillin-allergic pa -resistant isolate; ensure vancomycin MI
	gentamicin[a]	1 mg/kg IBW q12h iv	4–6	duration 6 weeks for P
3.	teicoplanin[a] AND	10 mg/kg q24h iv	4–6	alternative to Regimen
	gentamicin[a]	1 mg/kg q12h iv	4–6	ensure teicoplanin M
4.	amoxicillin[a,b]	2 g q4h iv	≥6	for amoxicillin-suscepti gentamicin resistant

PVE, prosthetic valve endocarditis; IBW, ideal body weight; iv, intravenously; q4h, every 4 h; q12h, every 12 h;
[a]Amend dose according to renal function.
[b]Streptomycin 7.5 mg/kg every 12 h intramuscularly can be added if isolate is susceptible.

Gentamisin dirençli ise

Table 16. Antibiotics suggested as surveillance antibiotics for *Pseudomonas aeruginosa*

Surveillance antibiotic	Predictive for:	Main resistance mechanisms
Ticarcillin	Piperacillin	AmpC hyperproduction Penicillinase Efflux
Ceftazidime	Cefepime Aztreonam	AmpC hyperproduction Efflux
Imipenem	Meropenem	AmpC hyperproduction plus reduced permeability Carbapenemase
Meropenem	Imipenem	AmpC hyperproduction plus reduced permeability Efflux Carbapenemase
Ciprofloxacin	Fluoroquinolones	Topoisomerase mutations (and/or efflux)
Netilmicin[a]	Gentamicin	Aminoglycoside-modifying enzymes
Tobramycin[a] Amikacin	Gentamicin Tobramycin	Reduced permeability

[a]Predictor for resistance to gentamicin only in amikacin-susceptible strains.

Table 17. Antibiotics suggested as surveillance antibiotics for *Acinetobacter baumannii*

Surveillance antibiotic	Predictive for:	Main resistance mechanisms
Imipenem	Meropenem	Reduced permeability Carbapenemase Oxacillinase PBP modification
Ciprofloxacin	Fluoroquinolones	Topoisomerase mutation
Gentamicin		Aminoglycoside-modifying enzymes
Tobramycin[a] Amikacin	Gentamicin	Reduced permeability Efflux

[a]Predictor for resistance to gentamicin only in amikacin-susceptible strains.
PBP, penicillin-binding protein.

Table 18. Antibiotics suggested as surveillance antibiotics for *Staphylococcus aureus*

Surveillance antibiotic	Predictor for:	Main resistance mechanisms
Penicillin	Ampicillin	Penicillinase

Table 19. Antibiotics suggested as surveillan for *Streptococcus pneumoniae*

Surveillance antibiotic	Predictor for:	Main res
Penicillin Cefotaxime	Amoxycillin[a] Ceftriaxone Cefepime	Modified Modidife
Ciprofloxacin Erythromycin	Fluoroquinolones Azithromycin Clarithromycin Roxithromycin	Topoisom Ribosoma Efflux
Telithromycin		Ribosoma Efflux
Co-trimoxazole Tetracycline		Changes Efflux Ribosoma
Chloramphenicol Linezolid		Acetyltra Ribosoma

[a]MICs should be determined.
PBP, penicillin-binding protein.

Table 20. Antibiotics suggested as surveillan for *Enterococcus* spp.

Surveillance antibiotic	Predictor for:	Main resis
Ampicillin	Penicillin Piperacillin Carbapenem	PBP modif PBP overp
Gentamicin (HLR)	Amikacin[a] Tobramycin Netilmicin	Aminoglyc enzymes
Streptomycin (HLR)		Aminoglyc enzymes Ribosomal
Ciprofloxacin Vancomycin Erythromycin	Fluoroquinolones Teicoplanin	Topoisom VanA, Van Ribosomal Efflux
Quinupristin-dalfopristin[b]		Modifying Ribosomal (high-leve
Linezolid		Ribosomal

[a]Infrequent isolates may exhibit synergy with amikacin despite h to gentamicin.
[b]Only for *Ent. faecium*.
HLR, high-level resistance; PBP, penicillin-binding protein.