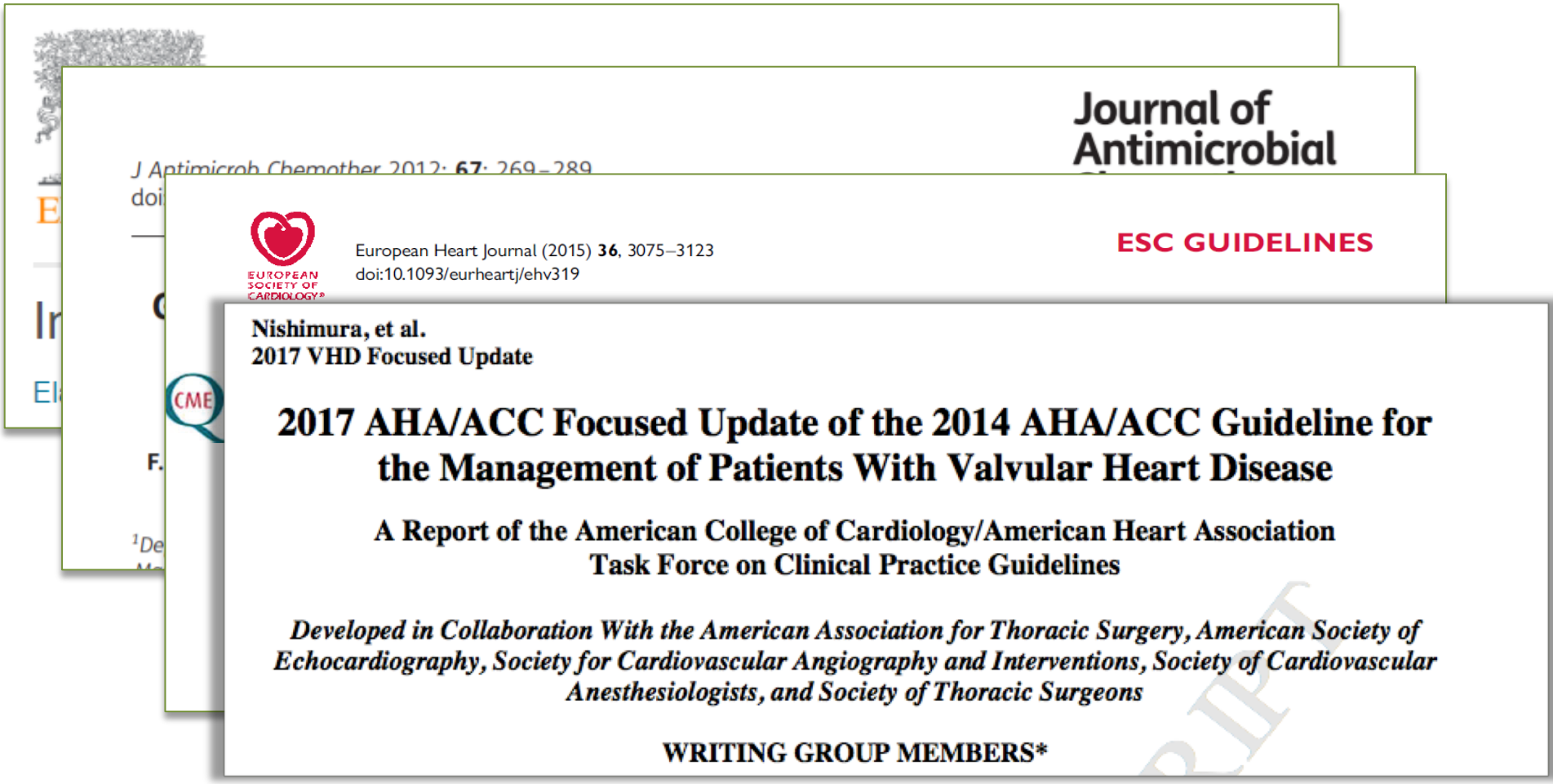
İnfektif Endokarditin Antibiyotik Tedavisinde Antimikrobiyal Direnç Bir Sorun Mu?

Dr Güle Çınar

Rehberler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ESC GUIDELINES
Nishimura, et al.
2017 VHD Focused Update
2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Clinical 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
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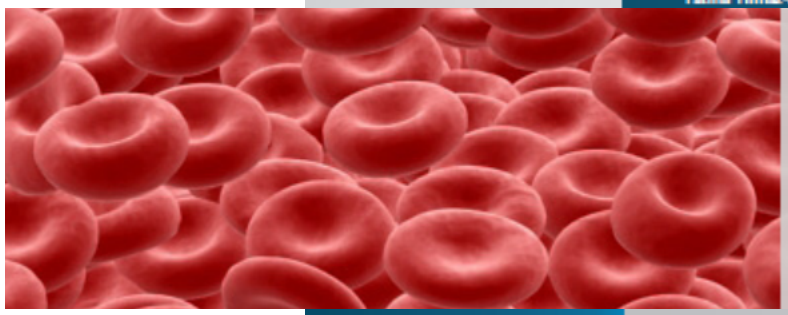
İnfektif Endokarditin Tanısı, Tedavisi ve Önlenmesi: Ulusal Uzlaşı Raporu

Diagnosis, Treatment and Prevention of Infective Endocarditis: Turkish Consensus Report

Serap Şimşek-Yavuz[1], Ahmet Rüçhan Akar[2], Sinan Aydoğdu[3], Denef Berzeg-Deniz[1], Hakan Demir[4], Tuncay Hazırolan[5], Mehmet Ali Özatik[2], Necla Özer[3], Murat Sargın[2], Emine Nursen Topcuoğlu[6], Nesrin Turhan[7], Mehmet Birhan Yılmaz[3], Özlem Azap[1], Seniha Başaran[1], Yasemin Çağ[1], Atahan Çağatay[1], Güle Çınar[1], Sibel Doğan-Kaya[1], Lokman Hızmalı[1], Mehmet Emirhan Işık[1], Nirgül Kılıçaslan[1], Şirin Menekşe[1], Meliha Meriç-Koç[1], Serpil Öztürk[1], Ayfer Şensoy[1], Yasemin Tezer-Tekçe[1], Elif Tükenmez-Tigen[1], Yeşim Uygun-Kızmaz[1], Mutlu Şeyda Velioğlu-Öcalmaz[1], Ayşegül Yeşilkaya[1], Emel Yılmaz[1], Neziha Yılmaz[1], Fatma Yılmaz-Karadağ[1]



Türk Klinik Mikrobiyoloji ve İnfeksiyon Hastalıkları Derneği'nin Yayın Organı

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THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Challenges in Infective Endocarditis

Thomas J. Cahill, MBBS,[a] Larry M. Baddour, MD,[b] Gilbert Habib, MD,[c,d] Bruno Hoen, MD, PhD,[e] Erwan Salaun, MD,[d] Gosta B. Pettersson, MD, PhD,[f] Hans Joachim Schäfers, MD,[g] Bernard D. Prendergast, DM[h]

- Gelişmiş ülkelerde sepsis, pnömoni ve intra-abdominal infeksiyonlardan sonra yaşamı tehdit eden 4. en sık infeksiyon
- Sağ kalım oranları

	Gelişmiş ülkeler	Türkiye
Hastane içi	%80	%72
1 yıllık	%70	
5 yıllık	%60	

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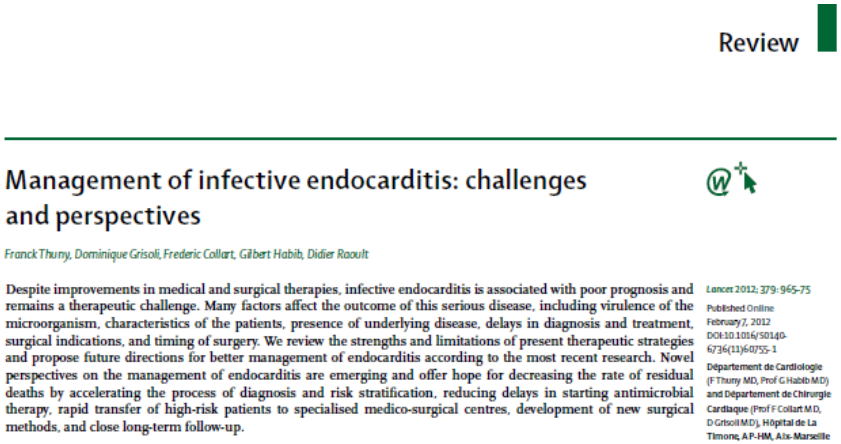
Infective endocarditis in Turkey: aetiology, clinical features, and analysis of risk factors for mortality in 325 cases

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]

- İnsidans
  - 3-10 / 100 000
  - ABD’de yılda 20 000 yeni vaka

- Zamanla daha virulan organizmalar hakim

- Mortalitede değişiklik yok
  - Hastane mortalitesi %15-20
  - 1yıllık mortalite 30%



Review

Management of infective endocarditis: challenges and perspectives

Franck Thuny, Dominique Grisoli, Frederic Collart, Gilbert Habib, Didier Raoult

Despite improvements in medical and surgical therapies, infective endocarditis is associated with poor prognosis and remains a therapeutic challenge. Many factors affect the outcome of this serious disease, including virulence of the microorganism, characteristics of the patients, presence of underlying disease, delays in diagnosis and treatment, surgical indications, and timing of surgery. We review the strengths and limitations of present therapeutic strategies and propose future directions for better management of endocarditis according to the most recent research. Novel perspectives on the management of endocarditis are emerging and offer hope for decreasing the rate of residual deaths by accelerating the process of diagnosis and risk stratification, reducing delays in starting antimicrobial therapy, rapid transfer of high-risk patients to specialised medico-surgical centres, development of new surgical methods, and close long-term follow-up.

Lancet 2012; 379: 965–75
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Département de Cardiologie (F Thuny MD, Prof G Habib MD) and Département de Chirurgie Cardiaque (Prof F Collart M D, D Grisoli M D), Hôpital de La Timone, A P-HM, Aix-Marseille

Lancet 379;965, 2012

Preeminence of *Staphylococcus aureus* in Infective Endocarditis: A 1-Year Population-Based Survey

Christine Selton-Suty,[1] Marie Célard,[2] Vincent Le Moing,[3,4] Thanh Doco-Lecompte,[5] Catherine Chirouze,[6] Bernard Iung,[7,8] Christophe Strady,[9] Matthieu Revest,[10] François Vandenesch,[2] Anne Bouvet,[11] François Delahaye,[12,13] Francois Alla,[14] Xavier Duval,[8,15,16] Bruno Hoen,[6,17] and on behalf of the AEPEI Study Group[a]

Table 3. Distribution of Causative Microorganisms in Patients With Infective Endocarditis

Microorganisms	No. (%) of Patients (n = 497)	
Streptococcaceae	240	(48.3)
Streptococci	180	(36.2)
Oral streptococci[a]	93	(18.7)
Group D streptococci[b]	62	(12.5)
Pyogenic streptococci	25	(5.0)
Enterococci	52	(10.5)
Other Streptococcaceae[c]	8	(1.6)
Staphylococcaceae	180	(36.2)
Staphylococcus aureus	132	(26.6)
Coagulase-negative staphylococci	48	(9.7)
Other microorganisms[d]	42	(8.5)
HACEK group	6	...
Enterobacteriaceae	4	...
Propionibacterium acnes	4	...
Pseudomonas aeruginosa	3	...
Lactobacillus species	2	...
Corynebacterium species	2	...
Coxiella burnetii	2	...
Bartonella quintana	1	...
Tropheryma whipplei	1	...
Candida species	6	...
Miscellaneous[e]	11	...
≥2 Microorganisms[f]	9	(1.8)
No microorganism identified	26	(5.2)

Variable	Whole Population	Mode of Acquisition[a]			Underlying HD			
		Community-Acquired Cases	Healthcare-Associated Cases	*P*	Prosthetic Valve	Previously Known HD	No Previously Known HD	*P*
Pacemaker	26 (5.2)	7 (2.1)	19 (15.6)	…	4 (3.8)	5 (3.8)	17 (6.5)	…
Other location	2 (0.4)	2 (0.6)	0 (0)	…	0 (0)	2 (1.5)	0 (0)	…
Unknown	29 (5.8)	21 (6.3)	6 (4.9)	…	6 (5.8)	9 (6.9)	14 (5.3)	…
Cardiac lesions of IE								
Positive echocardiography	460 (92.6)	307 (91.6)	116 (95.1)	.22	95 (91.3)	119 (90.8)	246 (93.9)	.48
Vegetation	435 (87.5)	289 (86.3)	110 (90.2)	.27	79 (76.0)	114 (87.0)	242 (92.4)	.0001
Dehiscence	19/104 (18.3)	12/69 (17.4)	6/30 (20.0)	.76	19 (18.3)	0 (0)	0 (0)	…
Severe regurgitation	194/492 (39.4)	149/331 (45.0)	30 (24.6)	<.0001	19/102 (18.6)	68/129 (52.7)	107/261 (41.0)	<.0001
Cardiac abscess (echo and surgery)	101 (20.3)	71 (21.2)	18 (14.8)	.12	37 (35.6)	27 (20.6)	37 (14)	<.0001
Microorganisms				<.0001				.01
Streptococci	180 (36.2)	163 (48.7)	9 (7.4)	<.0001	23 (22.1)	50 (38.2)	107 (40.8)	.003
Oral streptococci	93 (18.7)	83 (24.8)	5 (4.1)	<.0001	12 (11.5)	30 (22.9)	51 (19.5)	.08
Group D streptococci	62 (12.5)	57 (17.0)	4 (3.3)	.0001	9 (8.7)	15 (11.5)	38 (14.5)	.29
Pyogenic streptococci	25 (5.0)	23 (6.9)	0 (0)	.003	2 (1.9)	5 (3.8)	18 (6.9)	.11
Enterococci	52 (10.5)	36 (10.7)	13 (10.7)	.98	17 (16.3)	14 (10.7)	21 (8.0)	.06
Other Streptococcaceae	8 (1.6)	7 (2.1)	1 (0.8)	.69	1 (1.0)	6 (4.6)	1 (0.4)	.006
Staphylococcus aureus	132 (26.6)	69 (20.6)	40 (32.8)	.007	22 (21.2)	31 (23.7)	79 (30.2)	.15
Coagulase-negative staphylococci	48 (9.7)	14 (4.2)	32 (26.2)	<.0001	13 (12.5)	9 (6.9)	26 (9.9)	.34
Other microorganisms	42 (8.5)	26 (7.8)	16 (13.1)	.08	17 (16.3)	12 (9.2)	13 (5.0)	.002
≥2 Microorganisms	9 (1.8)	2 (0.6)	4 (3.3)	.04	1 (1.0)	2 (1.5)	6 (2.3)	.76
No microorganism identified	26 (5.2)	18 (5.4)	7 (5.7)	.88	10 (9.6)	7 (5.3)	9 (3.4)	.06
Outcome								
Cardiac surgery	223 (44.9)	165 (49.3)	37 (30.3)	.0003	41 (39.4)	61 (46.6)	121 (46.2)	.45
In-hospital death	113 (22.7)	68 (20.3)	38 (31.1)	.02	27 (26.0)	26 (19.8)	60 (22.9)	.54
Length of hospitalization, days, median (IQR)								
Whole population	43.0 (27.5–67.0)	41.0 (25.0–62.0)	49.0 (30.0–81.0)	.03	43.0 (25.0–59.5)	44.0 (26.0–71.0)	42.0 (29.0–68.0)	.80
Operated patients	47.0 (31.0–71.0)	45.0 (31.0–67.0)	52.0 (32.0–81.0)	.35	51.0 (35.0–79.0)	51.0 (35.0–81.0)	43.0 (31.0–62.0)	.17
Nonoperated patients	38.0 (24.0–62.0)	35.0 (22.0–55.0)	46.0 (30.0–80.5)	.009	36.0 (24.0–50.0)	38.0 (23.0–53.0)	40.0 (27.0–72.0)	.36
Dead patients	26.0 (11.0–44.0)	18.5 (10.5–42.5)	33.0 (22.0–52.0)	.04	19.0 (11.0–42.0)	25.5 (13.0–47.0)	27.0 (11.5–46.0)	.77
Survivors	47.0 (32.0–72.0)	44.0 (31.0–68.0)	54.0 (36.0–94.0)	.008	47.0 (34.0–68.0)	46.5 (32.0–79.0)	45.5 (32.0–72.0)	.99

Values are expressed as no. or proportion (%) of patients, unless otherwise indicated.

Abbreviations: HD, heart disease; ICD, implantable cardiovertor defibrillator; IDU, injection drug use; IE, infective endocarditis; IQR, interquartile range; NYHA, New York Heart Association; PM, pacemaker; SD, standard deviation.

[a] After exclusion of IDU-associated IE and IE of unknown origin.

- 2003-2013
- 105 çalışma
- 36 ülke
- 33 214 olgu

Table 2 Most common microbes per continent

Continent [cases]	Most common microbes
Europe [N = 12,752]	*S. aureus* / VGS/ CoNS / *Enterococcus* spp / *S. bovis*
Asia [N = 12,105]	VGS / *Streptococcus* spp / S. aureus / Staphylococcus spp
North America [N = 1,918]	*S. aureus* / VGS/ CoNS / *Streptococcus* spp / *Enterococcus* spp
Oceania [N = 1,681]	*S. aureus* / *Streptococcus* spp / *Enterococcus* spp / CoNS
Africa [N = 602]	*S .aureus* / Oral streptococci / CoNS / *Streptococcus* spp
South America [N = 452]	*S. aureus* / *Enterococcus* spp / CoNS / HACEK
Multi-continent [N = 3,704]	*S. aureus* / VGS/ CoNS / *Enterococcus* spp / *S. bovis*

Eur J Clin Microbiol Infect Dis (2016) 35:1227–1245
DOI 10.1007/s10096-016-2660-6

REVIEW

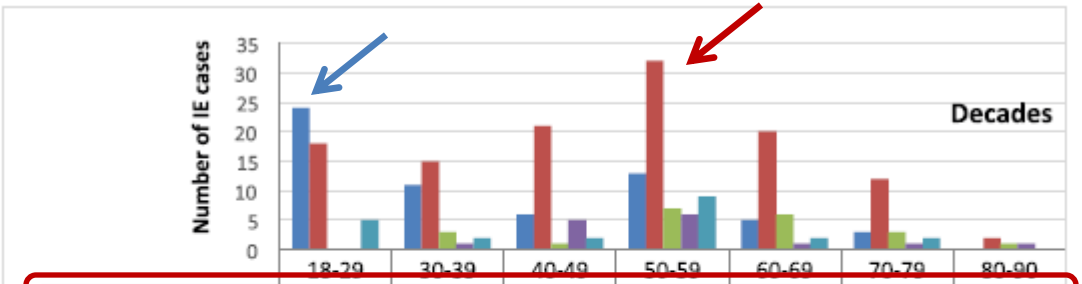
The causative agents in infective endocarditis: a systematic review comprising 33,214 cases

Christiana T. Vogkou[1,2] · Nikolaos I. Vlachogiannis[1,2] · Leonidas Palaiodimos[1,3] · Antonis A. Kousoulis[1,4]

Table 1 Most common microbes in special populations

Special populations [cases]	Most common microbes
HIV [N = 91]	*S. aureus* / *E. faecalis* / CoNS / VGS / *Pseudomonas* spp
Cardiac resynchronization therapy device [N = 505]	*S. aureus* CoNS (equal rates) / *S. pneumoniae* / *E. faecalis*
Dialysis [N = 233]	*S. aureus* / CoNS / *E. faecalis* / VGS / *P. aeruginosa*
Paediatric [N = 1026]	*S. aureus* / VGS / CoNS / *Enterococcus* spp / *S. pneumoniae*
ICU [N = 228]	*S. aureus* / Oral streptococci / Other Group D streptococci / *Enterococcus* spp / Gram (−) bacteria
Transplantation [N = 27]	*Staphylococcus* spp / Polymicrobial / Fungi
Congenital heart defect [N = 672]	VGS / *S. aureus* / CoNS / S. *bovis* / *Enterococcus* spp
Prosthetic valve [N = 994]	CoNS / *S. aureus* / VGS / *Enterococcus* spp / S. *bovis*
Injectable drug user(s) (IDUs) [N = 580]	*S. aureus* / VGS / CoNS / *Enterococcus* spp / *C. albicans*
Cross infection (healthcare associated) [N = 495]	*S. aureus* / *E. faecalis* / VGS / *S. epidermidis* / *S. bovis*
Diabetic [N = 309]	*S. aureus* /Other Group D streptococci / Oral streptococci / CoNS / *Enterococcus* spp
Critically ill [N = 198]	*S. aureus* / *Streptococcus* spp / *Enterococcus* spp / CoNS / *Enterobacter* spp
Epidural abscess [N = 6]	*S. aureus* / CoNS / *E. faecalis*
Immunocompromised (non HIV) [N = 56]	*E. faecalis* / *S. aureus* / *Streptococcus* spp / *E. coli* / *K. ozaenae*

CoNS coagulase-negative staphylococci



	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.

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

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Table 3
Causative microorganisms of 325 cases of infective endocarditis

Causative microorganisms	Native valve	Intracardiac device			Total, n (%)
		Pacemaker/ ICD*, n	Early prosthetic valve, n	Late prosthetic valve, n	
Defined causative agent	122	15	47	69	253 (77.8)
Staphylococcus spp	49	14	23	31	117 (36.1)
Staphylococcus aureus	31	10	10	14	65 (20.1)
MRSA	1	0	5	0	6 (1.9)
MSSA	30	10	5	14	59 (17.3)
CoNS	18	4	13	17	52 (16.0)
Methicillin-resistant CoNS	10	1	11	9	31 (9.6)
Methicillin-sensitive CoNS	8	3	2	8	21 (6.5)
Streptococcus spp	32	0	2	9	63 (19.4)
Viridans Streptococcus	44	0	2	9	55 (17.0)
Streptococcus bovis	4	0	0	0	4 (1.2)
Nutritionally variant streptococci	4	0	0	0	4 (1.2)
Abiotrophia defectiva	3	0	0	0	3 (0.9)
Granulicatella elegans	1	0	0	0	1 (0.3)
Enterococcus spp	11	0	0	11	22 (6.8)
Enterococcus faecalis	10	0	0	9	19 (5.9)
Enterococcus faecium	1	0	0	2	3 (0.9)
Brucella melitensis	5	1	0	9	15 (4.6)
Non-fermentative Gram-negative rods	2	0	12	2	16 (4.6)
Pseudomonas aeruginosa	1	0	6	1	7 (2.2)
Stenotrophomonas maltophilia	0	0	5	1	6 (1.8)
Acinetobacter baumannii	0	0	1	0	2 (0.6)
Acinetobacter lwoffii	1	0	0	0	1 (0.3)
Candida spp	1	0	6	1	8 (2.4)
Candida albicans	0	0	5	0	5 (1.5)
Candida parapsilosis	1	0	1	0	2 (0.6)
Other non-albicans *Candida spp*	0	0	0	1	1 (0.3)
Enterobacteriaceae	0	0	4	2	6 (1.8)
Escherichia coli	0	0	1	1	2 (0.6)
Enterobacter cloacae	0	0	1	0	1 (0.3)
Klebsiella pneumoniae	0	0	1	1	2 (0.6)
Serratia marcescens	0	0	1	0	1 (0.3)
HACEK	1	0	0	2	3 (0.9)
Eikenella corrodens	1	0	0	0	1 (0.3)
Actinobacillus actinomycetemcomitans	0	0	0	2	2 (0.6)
Kytococcus schroeteri	0	0	0	1	1 (0.3)
Bartonella henselae	0	0	0	1	1 (0.3)
Bacillus licheniformis	1	0	0	0	1 (0.3)
Undefined causative agents	44	3	5	20	72 (22.2)
Total	166	18	52	89	325 (100)

* ICD, implantable cardioverter defibrillator; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; CoNS, coagulase-negative staphylococci;

Tablo 1. Türkiye'de 1974-2017 Yılları Arasında İzlenmiş İnfektif Endokardit Olgularını İçeren Çalışmaların Özellikleri

Araştırmacılar	Dönem	Şehir	Olgu Sayısı	Yaş*	Erkek (%)	ARA (%)	Yapay Kapak (%)	IVDU (%)	CIED (%)	Diyaliz (%)	Stafilokok (%)	*Staphylococcus aureus* (%)	MRSA (%)	Streptokok (%)	Enterokok (%)	*Brucella* spp. (%)	Kan Kültürü Negatif (%)	Ameliyat (%)	Nozokomiyal (%)	Kesin İE† (%)	Mortalite (%)
Işık *et al.* (126)	1997-2001	İstanbul	14	41	70	61	23				24			24			54	100		70	
Küçükateş *et al.* (46)	2005-2010	İstanbul	22	47	55	55	41	0			36			27	9	9	50	100			18
Kaya *et al.* (47)	2005-2012	Şanlıurfa	24	41	50		13		4	8.3	21			17	4	33	21	37			8
İnanç *et al.* (49)	2006-2007	Kayseri	27	47	63	67	41				33	11		4	11	4	45	19			15
Çaylan *et al.* (48)	1997-2001	Trabzon	32	47	73		22				37	22		19	9		78	25			41
Zencir *et al.* (33)	2000-2015	Aydın	59	59	43		32					39						27		100	27
Tuğcu *et al.* (34)	2000-2007	İstanbul	68	51	59	40	56		3	12	41	28	4	25	1.5	0	21	59	28	84	25
Sucu *et al.* (35)	1997-2007	Gaziantep	72	45	57	36	29			3	27	10		23	4	4	36	28		100	15
Heper ve Yorukoglu (36)	1995-1999	Ankara	74	25	66	66	14				44	21		29	15	7	11				18
Cancan-Gursul *et al.* (32)	2006-2013	İzmir	80	51	70		12	0	22.5	7.5	49	27	2.5	20	17	12	51	56			15
Agca *et al.* (37)	2009-2014	Bursa	85	52	56	22	40		13		27	8	2	11	5	6	32	27		100	36
Taşbakan *et al.* (38)	2007-2017	İzmir	100	52	65		13	3	42.5			18		32	11		26				14
Erbay *et al.* (39)	2002-2008	Ankara	107	45	71		44										34				27
Akıl *et al.* (40)	2005-2012	Çok Merkezli	112	45	50	18	17	8		5.4	50	35		29	16		16	13		90	29
Şimşek-Yavuz *et al.* (50)	2015-2016	Çok Merkezli	112	55	70	12	33	4	8	13	31	15	3.5	22	8	1	29.5	56	35	77	28
Adademir *et al.* (41)	1997-2004	İstanbul	119	39	69	39	20		2		24	22	11	9	3	3	57	76		100	
Çay *et al.* (42)	2008-2011	Ankara	121	55	53	14	42		10	18	33	16		21	7	6	29	38		100	24
Turak *et al.* (43)	1997-2012	Ankara	157	59	55	15	42		9		30	13		22	7	6	29	39		100	26
Leblebicioğlu *et al.* (30)	2002-2012	Çok Merkezli	158	47	51	39	0				28		6	11	11	6	34	51			31
Özveren *et al.* (44)	1985-2011	İstanbul	174	39	79		15				15		2	29		6	47	100			16
Kocabaş *et al.* (45)	2009-2012	İzmir	194	48	66	22	12		3.1	6	30			16	6		43	52		100	20
Cetinkaya *et al.* (29)	1974-1999	Ankara	228	36	55	64	20	0	0.4		27	24		14	6	5.7	50	37	12	53	23
Elbey *et al.* (31)	2005-2012	Çok Merkezli	248	47	55	28	30		6		29	21	6	11	11	5	37.5	54		100	33
Şimşek-Yavuz *et al.* (4)	2004-2015	İstanbul	325	47	58	34	44	1	5.6	3	36	20	2	19	7	5	22	52	23	86	27
Toplam	1974-2017	Türkiye	2712	47	61	37	27	2	7	9	31	21	5	19	9	7	37	50	25	90	24

*Ortalama. †Modifiye Duke ölçütleriyle. ARA: akut romatizmal ateş, IVDU: damar içi ilaç kullanıcısı, CIED: kardiyak implante edilebilen elektronik cihaz, MRSA: metisiline dirençli *Staphylococcus aureus*, İE: infektif endokardit.

- Etkeni üretmek, tür düzeyinde tanımlamak
- Bakterisidal
- Parenteral
- MİK değeri (antibiyotik seçimi, doz vb)
- Tolerans (yavaş üreyen ya da durağan fazdaki bakteriler)

- Minimal bakterisidal konsantrasyon (MBK), minimal inhibitör konsantrasyondan (MİK) çok yüksektir.
- MBK/MİK ≥ 32
- Streptokoklar arasında %11
- Antibiyotik dozu değişir (MİK yüksekmiş gibi)
- Tedavi süresi daha uzun
- Kombinasyon tedavisi

ORIGINAL ARTICLE

Clinical significance of tolerant strains of streptococci in adults with infective endocarditis

T. Hanslik[1], C. Hartig[1], C. Jurand[2], L. Armand-Lefevre[2], V. Jubault[1], E. Rouveix[3], O. Dubourg[3], J. Prinseau[1], A. Baglin[1] and M. H. Nicolas-Chanoine[2]

[1]Fédération de Médecine Interne, [2]Service de Microbiologie and [3]Service de Cardiologie, Hôpital Ambroise Paré, Université de Versailles Saint-Quentin-en-Yvelines, Assistance Publique-Hôpitaux de Paris, Paris, France

Clin Microbiol Infect 2003; 9: 852–857

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			NS
Patients evaluated by transesophageal echocar			NS
Duke's classification			
Definite infective end			NS
Possible infective end			NS
Severity criteria at prese			
Major arterial emboli			NS
Vegetation size ≥10 r			NS
Severe heart failure			NS
Intracardiac extension			NS
Heart block			NS
Antibiotic treatment bef diagnosis of endocarditi			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.

Penisilin toleransı %42

ORIGINAL ARTICLE

Clinical significance of tolerant strains of streptococci in adults with infective endocarditis

T. Hanslik[1], C. Hartig[1], C. Jurand[2], L. Armand-Lefevre[2], V. Jubault[1], E. Rouveix[1], O. Dubourg[3], J. Prinseau[1], A. Baglin[1] and M. H. Nicolas-Chanoine[2]

[1]Fédération de Médecine Interne, [2]Service de Microbiologie and [3]Service de Cardiologie, Hôpital Ambroise Paré, Université de Versailles Saint-Quentin-en-Yvelines, Assistance Publique-Hôpitaux de Paris, Paris, France

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 1
MIC ranges of antimicrobial agents tested

Organisms (No. of isolates) and antimicrobial agent	MIC (mg/l) range	No of strains		
		Susceptible	Intermediate	Resistant
Group C strepts (68)				
Penicillin	≤0.016–0.06	68		
Erythromycin	≤0.016– > 16.0	65	2	1
Cefotaxime	≤0.016–0.125	68		
Meropenem	≤0.016–0.06	68		

Abstract

A total of 105 clinical strains of Group C and Group G streptococci were examined for their susceptibility to penicillin, cefotaxime, erythromycin, meropenem and vancomycin using a broth microdilution method. Minimum bactericidal concentrations of the antimicrobial agents and phenotypes of strains resistant to erythromycin were also evaluated. No resistance to penicillin, cefotaxime, meropenem and vancomycin was found in years 1995–2002, but there was 6.7% resistance to erythromycin. No tolerance was seen for penicillin and vancomycin, but there were strains tolerant to cefotaxime, erythromycin and meropenem. The resistance phenotypes of erythromycin-resistant isolates were determined by the double disc test with erythromycin and clindamycin which showed inducible MLS (57.1%) and M phenotype (42.8%) resistance. This in vitro finding shows that classical antimicrobial agents used for the treatment of GCS and GGS have good activity against clinically significant isolates, but the presence of macrolide resistance and tolerant isolates suggests that careful surveillance of the streptococcal isolates should be carried out.

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Keywords: Group C Streptococci; Group G Streptococci; Antibiotic susceptibility; MLS resistance

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In vitro susceptibility, tolerance and MLS resistance phenotypes of Group C and Group G streptococci isolated in Turkey between 1995 and 2002

Alper Ergin [a,*], Serpil Ercis [b], Gülsen Hasçelik [b]

[a] *School of Health Services, Hacettepe University, 06100 Sihhiye, Ankara, Turkey*
[b] *Department of Microbiology and Clinical Microbiology, School of Medicine, Hacettepe University, 06100 Sihhiye, Ankara, Turkey*

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Tablo 19. Streptokoksik İnfektif Endokarditin Antimikrobik Tedavisi (3,65,207)

Mikroorganizma	Antimikrobik	Günlük Doz, Doz Aralığı, Uygulama Yolu	Süre (Hafta) Doğal Kapak	Süre (Hafta) Yapay Kapak	Yorum
Penisilin G MIC ≤0.125 µg/ml olan viridans streptokoklar ve SGG	Penisilin G veya Seftriakson* + Gentamisin†	12-18 MÜ/gün, 6 dozda, IV 2 gr/gün, tek doz, IV/IM 3 mg/kg, tek doz, IV	2 2 2		Kısa süreli tedavi sadece komplike olmayan ve yakınmaların 3 aydan daha kısa süredir devam ettiği doğal kapak IE'sinde kullanılmalıdır.
	Penisilin G veya Seftriakson*	18 MÜ/gün, 6 dozda, IV 2 gr/gün, tek dozda, IV/IM	4 4	6 6	>65 yaş, VIII. kraniyal sinir hasarı veya böbrek işlev bozukluğu olanlarda yeğlenir.
Penisilin G MIC >0.125 ve <0.5 µg/ml arasında olan viridans streptokoklar ve SGG	Penisilin G veya Seftriakson* + Gentamisin†	24 MÜ/gün, 6 dozda, IV 2 gr/gün, tek dozda, IV/IM 3 mg/kg/gün, tek dozda, IV/IM	4 4 2	6 6 6	Nefrotoksik veya ototoksik etki gelişmesi halinde gentamisin kesilmelidir.
Penisilin G MIC ≥0.5 ve ≤2 µg/ml arasında olan viridans streptokoklar, SGG, *Abiotrophia* spp., *Granulicatella* spp. ve *Gemella* spp.	Penisilin G veya Ampisilin veya Seftriakson* + Gentamisin†	24 MU/gün, 6 dozda, IV 200 mg/kg/gün, 4-6 dozda, IV 2 gr/gün, tek dozda, IV/IM 3 mg/kg/gün, tek dozda, IV/IM	4 4 4 4	6 6 6 6	Nefrotoksik veya ototoksik etki gelişmesi halinde gentamisin kesilmelidir.
Penisilin G MIC >2 µg/ml olan dirençli streptokoklar veya β-laktam alerjisi	Vankomisin‡ veya Teikoplanin§	30 mg/kg/gün, 2 dozda, IV 10 mg/kg/gün, tek dozda, IV	4 4	6 6	Nefrotoksisite riski yüksek hastalarda teikoplanin yeğlenmelidir.

MIC: minimum inhibitör konsantrasyon, SGG: *Streptococcus gallolyticus* subsp. *gallolyticus* (eski *Streptococcus bovis* biyotip I).
* Seftriakson MIC değeri ≤0.5 µg/ml olması halinde kullanılmalıdır.
† Böbrek işlevleri ve serum gentamisin düzeyi haftada bir kontrol edilmelidir. Streptokoksik İE'de gentamisin günde tek doz olarak da kullanılabilir. Tek doz kullanılan hastalarda gentamisin serum vadi (doz öncesi) düzeyi <1 µg/ml, pik düzeyi (injeksiyondan 1 saat sonra) ~10-12 µg/ml olmalıdır.
‡ Vankomisin serum vadi düzeyinin (doz öncesi) 10-15 µg/ml, pik düzeyinin (doz yapıldıktan hemen sonra) ise 30-45 µg/ml olması sağlanmalıdır.
§ Teikoplanin, 10 mg/kg/gün dozunda ve serum vadi düzeyi (doz öncesi) ≥20 µg/ml olacak şekilde kullanılmalıdır.

CLSI M100-ED29:2019 Performance Standards for Antimicrobial Susceptibility Testing, 29th Edition

ß Hemolitik Streptekoklar		
Antibiyotikler	**MIC Değerleri µg/ml**	
	S	**R**
Penisilin	≤0.12	-
Ampisilin	≤0.25	-
Vankomisin	≤1	-
Daptomisin	≤1	-

CLSI M100-ED29:2019 Performance Standards for Antimicrobial Susceptibility Testing, 29th Edition

Viridan Streptokoklar		
Antibiyotikler	**MIC Değerleri µg/ml**	
	S	**R**
Penisilin	≤0.12	≥4
Ampisilin	≤0.25	≥8
Vankomisin	≤1	-
Daptomisin	≤1	-

S. mitis, S. mutans,
S. oralis, S. sanguinis, S. sobrinus
S. milleri grubu (S. anginosus, S. constellatus ve S. intermedius)

Table 2. Recommended therapy for viridans group streptococcal native valve infective endocarditis, based on MIC.

Description, recommended therapies
Highly susceptible to penicillin G (MIC, ≤0.12 μg/mL)
Penicillin G, 12–18 million U per day for 4 weeks, or
Ceftriaxone, 2 g per day for 4 weeks, or
Penicillin G
for 2 w
Ceftriaxo
weeks
Vancomy
Relatively r
Penicillin
kg per
Ceftriaxo
day[a] fo
Vancomy
Resistant t
Penicillin
3[a] mg/
Ceftriaxo
day[a] fo
Vancomy

NOTE. Data are modified from Baddour et al. [1]. Doses are based on normal renal function. GM, gentamicin.

[a] For strains of viridans group streptococci that are highly susceptible or relatively resistant to penicillin G, GM dosing should be once daily; for resistant strains, dosing should be thrice daily.

[b] Vancomycin is indicated only for patients intolerant of penicillin G and ceftriaxone.

[c] Vancomycin dosage should be adjusted to achieve peak values of 30–45 μg/mL trough concentrations of 10–15 μg/mL.

MİK>2 µg/ml ise enterokoka bağlı İE gibi tedavi

Penicillin G–Resistant Viridans Group Streptococcal Endocarditis and
herican Heart
for the
ndocarditis

nd W. Lance George[3,4]
liated Infectious Diseases
and [3]Department of Medicine,
System, and [4]UCLA School of

R	>0.5 µg/ml

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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, Micr
[g] Siyami Ersek Thoracic and Cardiovascular Surgery H

325 İE olgusu
253 etken
63 streptokok→penisilin duyarlı

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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 hastalardan alınan
kan kültürlerinden izole edilen
50 tane viridans grubu streptokok suşunun %50'si penisilin dirençli

- %57.3 penisiline azalmış duyarlılık
- MİK> 4 µg/ml olan suş yok

Tablo 1. Hematolojik Kanserli Hastaların Boğaz Kültürlerinden İzole Edilen VGS'lerin Penisilin Duyarlılığına Etki Edebilecek Faktörlerin Değerlendirilmesi

Risk Faktörleri	Penisiline Duyarlı n (%)	Azalmış Penisilin Duyarlılığı n (%)	*p*
Yaş, yıl, ortalama (SS)	54.41 (18.97)	51.49 (15.84)	0.471
Erkek cinsiyet (n=53)	21 (65.6)	32 (74.4)	0.408
Hematolojik kanser tipi			
Akut myeloblastik lösemi (n=12)	3 (9.4)	9 (20.9)	0.216
Akut lenfoblastik lösemi (n=9)	5 (15.6)	4 (9.3)	0.484
Kronik lenfositer lösemi (n=16)	8 (25.0)	8 (18.6)	0.504
Multipl myelom (n=13)	7 (21.9)	6 (14.0)	0.370
Hodgkin lenfoması (n=9)	4 (12.5)	5 (11.6)	1.000
Non-Hodgkin lenfoma (n=10)	3 (9.4)	7 (16.3)	0.502
Diğer* (n=6)	2 (6.3)	4 (9.3)	1.000
Hastalık süresi (ay), ortalama (SS)	22.91 (31.90)	20.47 (22.02)	0.696
Hastanede yatma öyküsü (n=36)	15 (46.9)	21 (48.8)	0.866
Bir önceki hastanede yatma zamanı (ay), ortalama (SS)	3.867 (2.326)	2.476 (1.965)	0.610
Bir önceki hastanede kalış süresi (gün), ortalama (SS)	17.933 (24.534)	19.810 (26.254)	0.820
Hastanede yatma sayısı	2.000 (1.069)	2.191 (1.692)	0.703
Antibiyotik kullanım öyküsü (n=24)	8 (47.1)	16 (72.7)	0.102
β-laktam kullanımı† (n=21)	8 (25.0)	13 (30.2)	0.618
Kinolon kullanımı† (n=11)	2 (6.3)	9 (20.9)	0.103
Altta yatan hastalıklar			
Diabetes mellitus	2 (6.3)	1 (2.3)	0.572
Renal yetmezlik	4 (12.5)	1 (2.3)	0.157
Kronik karaciğer hastalığı	1 (3.1)	3 (7.0)	0.632
İleri yaş (>65 yıl)	9 (28.1)	10 (23.3)	0.632
Kemoterapi	27 (84.4)	38 (88.4)	0.615
Sitozin arabinozid kullanımı	6 (18.8)	10 (23.3)	0.615
Fludarabin kullanımı	5 (15.6)	5 (11.6)	0.963
Steroid tedavisi	7 (21.9)	9 (20.9)	0.921
Sigara kullanımı	9 (28.1)	14 (32.6)	0.680

*Kronik myeloid lösemi, hoffing in hastalığı, aplastik anemi

Hematolojik Kanserli Hastaların Orofarinksinden İzole Edilen Viridans Grubu Streptokoklarda Penisilin Duyarlılığı

Penicillin Susceptibility of Viridans Group Streptococci Isolated from the Oropharynx of Patients with Hematological Malignancy

Selda Sayın-Kutlu[1], Demet Ökke[2], Melek Demir[3], Ebru Tepeli[4], İsmail Sarı[5]

Klimik Dergisi 2012; 25(1): 6-9

- Şubat-Haziran 2015
- İE riski olan 49 hasta; protez kapak, kapak hastalığı, romatizmal kapak hastalığı
- Ağız mukozasından sürüntü örnekleri
- E test

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.

Vankomisin direnci yok

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

Table 2. Antibiotic resistance rates and resistance genes reported in the literature regarding species belonging to the *Streptococcus bovis/Streptococcus equinus* complex (SBSEC).

Isolates (*n*)	Origin (Human or Animal)	Body Site	Study Period	SBSEC Species/ Subspecies (*n*) [a]	Ery-R (%)	Ery-R Gene (%)	Cli-R (%)	Tetracyclines-R (%) [b]	Tet-R Gene [c]	Other Antibiotics (%) [d]	Country	Ref.
22	Human	Various	2010–2012	SGSP (22)	31.8	*erm*(B) (100)	31.8	68.2	*tet*(O) *tet*(M)	Pen (0) Ctx (0) Van (0)	Italy	[46]
25	Human	Blood	1990–2003	SGSG (20) SGSP (4) SI (1)	48	n.a.[h]	n.a.	64	n.a.	Gen (8) Lev (4) Pen (0) Van (0) in (0)	Italy	[60]
45	Human	Blood	2003–2010	SGSG (14) SGSP (24) SISI (2) SL (5)	33.3	n.d.	30.2	n.a.	n.a.	Sxt (20.2) Lev (15.6) Pen (0) Str (0) Rif (0) Li (0) Q-D (0)	Spain	[19]
100	Human	Blood	n.a.	*S. bovis*	46	n.a.	26	65	n.a.	Pen (3) Van (0) Lin (0) Dap (0) Q-D (6)	International collection	[63]
45	Human	Carriage	n.a.	*S. bovis*	8.9	n.a.	n.d.	n.a.	n.a.	Pen (13.3) Cro (0) Van (0)	Israel	[61]
48	Human	Blood	1996–2001	SGSG (2) SGSP (42) SI (4)	65	*erm*(B) (54.2) *erm*(T) (41.7) *erm*(B)+*erm*(T) (4.2)	41	n.a.	n.a.	Pen (0) Van (0)	China	[24]
23	Human	Peritoneal dialysis	2000–2010	*S. bovis*	47.8	n.a.	43.5	n.a.	n.a.	Pen (30.4)	China	[64]
172	Human	Blood	2000–2012	SGSG (126) SGSP (31) SI (15)	54.7	n.a.	54.1	n.a.	n.a.	Gen (19.8) Lev (16.9) Pen (0.6) Cro (0) Van (0) Lin (0) Dap (0) Tig (0)	Taiwan	[43]

International Journal of *Molecular Sciences*

MDPI

Review

An Overview on *Streptococcus bovis/Streptococcus equinus* Complex Isolates: Identification to the Species/Subspecies Level and Antibiotic Resistance

Arianna Pompilio [1,2], Giovanni Di Bonaventura [1,2] and Giovanni Gherardi [3,*]

Table 2. *Cont.*

Isolates (*n*)	Origin (Human or Animal)	Body Site	Study Period	SBSEC Species/ Subspecies (*n*) [a]	Ery-R (%)	Ery-R Gene (%)	Cli-R (%)	Tetracyclines-R (%) [b]	Tet-R Gene [c]	Other Antibiotics (%) [d]	Country	Ref.
60	Human	Blood	1996–2000	SGSG (4) SGSP (53) SI (3)	63.3	*erm*(B) (63.2) *erm*(T) (36.8)	63.3	75	*tet*(M) [e]	Pen (0) Ctx (0) Van (0) Chl (0)	Taiwan	[65]
66	Human (20) Animal (44) Reference (2)	Various	1981–2011	SG	16.7	*erm*(B) (63.7)*mef*(A) (9.1) *erm*(B)+*mef*(A) (9.1) no genes (18.2)	10.6	57.6	*tet*(M) *tet*(O) *tet*(L) *tet*(T)	Ctx:15.2 Chl:4.5 Pen:0 an:0	Japan	[62]
128	Human (125) Animal (3)	Bl		SGSG (121)					*tet*(M)	Pen (0)	France Belgium Netherlands	[66]
118	Human										Spain	[20]
41	Human (18) Animal (23)	Various	1990–2010	SGSG	46.3	*erm*(B) (94.7) o genes (5.1)	48.8	36.6 [g]	*tet*(M)	Fos (51.2) Q-D (14.6) Gen (12.2) Lev (12.2) Sxt (7.3) Van (2.4)	Spain	[67]
107	Human	Blood	1988–2005	SGSG (69) SGSP (38)	60.2	n.a.	54.5	n.a.	n.a.	Sxt (85.3) Pen (0)	Spain	[68]
64	Human	Blood	1987–2003	SGSG (42) SGSP (22)	60	n.a.	50	n.a.	n.a.	Sxt (60) Pen (0) Ctx (0) Van (0)	Spain	[69]
18	Human	Blood	1998–2003	*S. bovis*	78	*erm*(B) (92.9) *mef*(A) (7.1)	72	n.a.	n.a.	Tel (39) Pen (11)	Spain	[25]

Hayvanlarda penisilin direnci yok

- Streptekoklarda henüz korkulacak düzeyde penisilin direnci söz konusu değil

- İE riski nedeni ile penisilin profilaksisi alanlar!

- Malignitesi olanlar!

CLSI M100-ED29:2019 Performance Standards for Antimicrobial Susceptibility Testing, 29th Edition

Stafilokoklar			
Antibiyotikler	**Mikroorganizma alt türü**	**MIC Değerleri µg/ml**	
		S	**R**
Penisilin	Tüm staf.	≤0.12	≥0.25
Oksasilin	*S. aureus* *S. epidermidis* Diğer	≤2 - ≤0.25	≥4 ≥0.5 ≥0.5
Vankomisin	*S. aureus* Diğer	≤2 ≤4	≥16 ≥32
Daptomisin	Tüm staf.	≤1	-

Tablo 23. Stafilokoksik İnfektif Endokarditlerin Antimikrobik Tedavisi (3,65,207)

Mikroorganizma	Antimikrobik	Günlük Doz, Doz Aralığı, Uygulama Yolu	Süre (Hafta) Doğal Kapak	Süre (Hafta) Yapay Kapak	Yorum
Metisiline duyarlı stafilokoklar*	Nafsilin veya	12 gr, 6 dozda, IV	4-6	≥6	Ülkemizde nafsilin ve flukloksasilin bulunamamaktadır.
	Flukloksasilin veya	12 gr, 6 dozda, IV	4-6	≥6	
	Sefazolin†	6 gr, 3 dozda, IV	4-6	≥6	
	+				
	Gentamisin	3 mg/kg, tek doz, IV	Verilmez	2	
	+				
	Rifampisin‡	900 mg, tek doz, oral/IV	Verilmez	≥6	
	Daptomisin§ veya	8-12 mg/kg, tek doz, IV	4-6	≥6	Sadece β-laktamları tolere edemeyen veya β-laktam alerjisi olan hastalarda kullanılmalıdır.
	Vankomisin	30 mg/kg/gün, 2 dozda, IV	4-6	≥6	
Metisiline dirençli vankomisine duyarlı (MIC ≤2 µg/ml) stafilokoklar	Vankomisin‖	30 mg/kg/gün, 2 dozda IV	4-6	≥6	Kardiyak veya ekstrakardiyak tüm apse odakları uygun cerrahi girişimlerle kontrol altına alınmalıdır.
	+				
	Gentamisin¶ (duyarlıysa)	3 mg/kg, tek doz, IV	Verilmez	2	
	+				
	Rifampisin (duyarlıysa)	900 mg, 3 doz, oral-IV	Verilmez	≥6	
	Daptomisin§	8-12 mg/kg, tek doz, IV	4-6		
Metisiline duyarlı stafilokoklar (IVDU'da sağ kalp endokarditi)**	Nafsilin veya	12 gr, 6 dozda, IV	2		Ülkemizde nafsilin ve flukloksasilin bulunamamaktadır.
	Flukloksasilin	12 gr, 6 dozda, IV			
	Siprofloksasin	1500 mg, 2 dozda, oral	2		Hastanede yatırılamayan komplike olmamış olgularda suşun her iki ajana da duyarlı olduğu gösterilmeli ve hasta uyumu yakından izlenmelidir.
	+				
	Rifampisin	600 mg, 2 dozda, oral			

MIC: Minimum inhibitör konsantrasyon, IVDU: damar içi ilaç kullanıcısı.

* Metisiline duyarlı olan stafilokoklar, genellikle penisiline dirençlidir; var olan duyarlılık testleri stafilokoklarda penisilin duyarlılığını saptamak için güvenilir olmadığı için penisiline duyarlı olarak belirlenmiş stafilokokların tedavisinde de bu tedavi seçenekleri kullanılmalıdır

† MSS apsesi olan hastalarda sefazolin kullanılmamalıdır. Bu hastalarda tek başına sefotaksim veya sefazolin + vankomisin kullanılabilir.

‡ Rifampisin, varfarinin hepatik metabolizmasını artırır; bu nedenle yapay kapak nedeniyle varfarin kullanan hastalarda varfarin dozunun dikkatle ayarlanması gerekir.

§ Daptomisinin, seftarolin, sefazolin, seftriakson, trimetoprim-sülfametoksazol (345) veya fosfomisinle kombine edilmesi düşünülebilir (65).

‖ Vankomisin serum vadi düzeyinin (doz öncesi) 15-20 µg/ml olması sağlanmalıdır.

¶ Gentamisine dirençliyse, duyarlı olduğu başka bir aminoglikozid verilebilir. Tüm aminoglikozidlere dirençliyse, duyarlı olması halinde florokinolonlar eklenebilir.

**Sadece antistafilokoksik penisilin kullanılabilen; tedavi yanıtı iyi; metastatik infeksiyonu, ampiyemi, kardiyak veya ekstrakardiyak komplikasyonu, yapay kapak veya eşlik eden sol kalp tutulumu olmayan; vejetasyonu <20 mm ve HIV ile infekte ise $CD4^+$ sayısı >200/µl olan hastalarda kısa süreli tedavi verilebilir. Bu durumlar dışında veya ülkemizde olduğu gibi antistafilokoksik penisilinlerin bulunamaması halinde, stafilokoksik sol kalp endokarditlerinde önerilen tedavi rejimleri kullanılmalıdır.

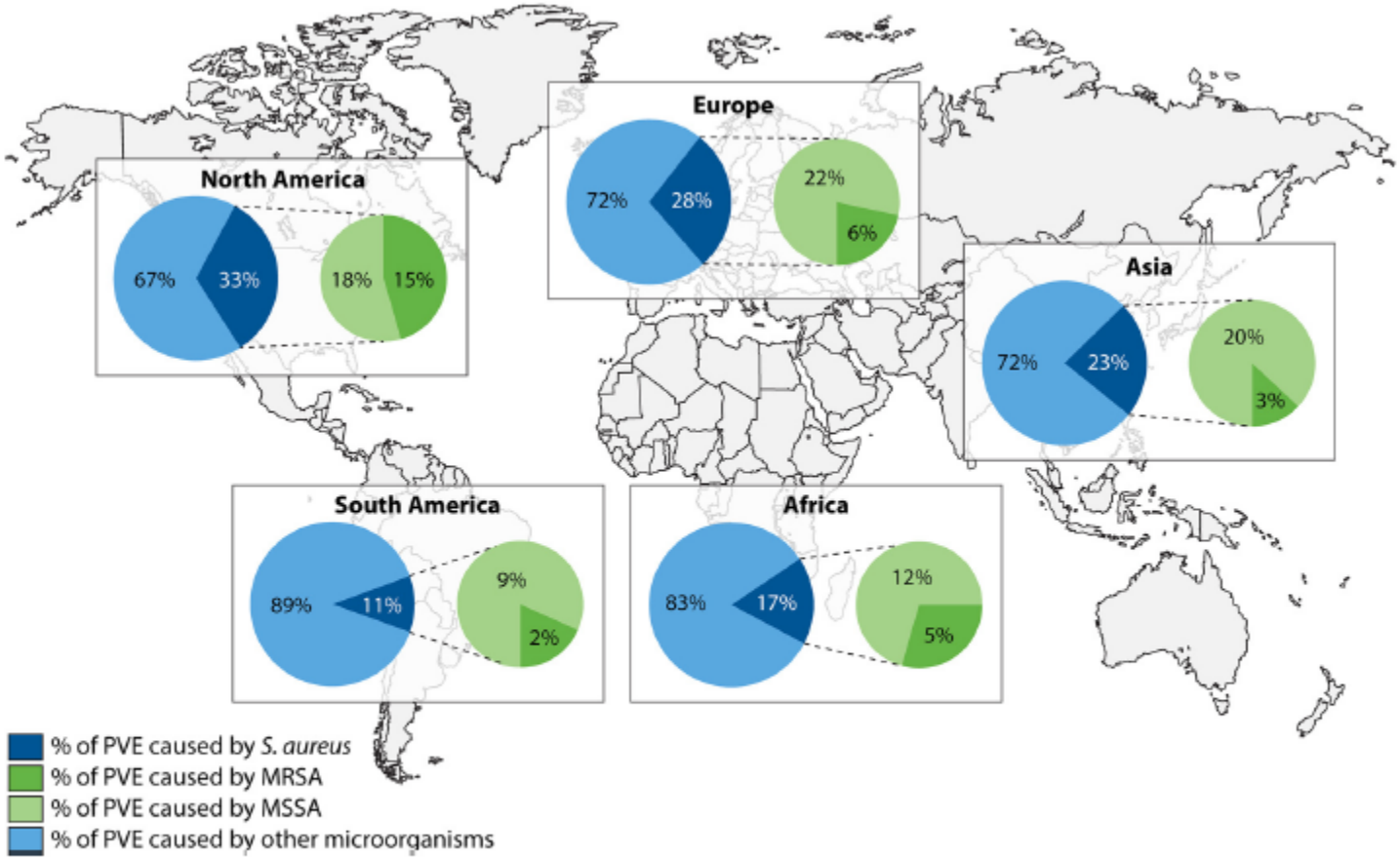

FIG 5 Global epidemiology of MRSA involved in prosthetic valve endocarditis (PVE). The causative agents of PVE differ geographically (4, 6). Data from Wang et al. (6) were collected between June 2000 and August 2005 from 556 patients with infective prosthetic valve endocarditis in 53 sites worldwide ($P = 0.003$ for *Staphylococcus aureus*; $P = 0.001$ for MRSA [methicillin-resistant *Staphylococcus aureus*]). MSSA, methicillin-sensitive *Staphylococcus aureus*.

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REVIEW

Methicillin-Resistant *Staphylococcus aureus* Prosthetic Valve Endocarditis: Pathophysiology, Epidemiology, Clinical Presentation, Diagnosis, and Management

April 2019 Volume 32 Issue 2 e00041-18

Alicia Galar,[a,b] Ana A. Weil,[c,d] David M. Dudzinski,[d,e] Patricia Muñoz,[a,b,f,g] Mark J. Siedner[c,d]

Table 1. WHO priority pathogens list for research and development (R&D) of new antibiotics [5].

Priority 1: Urgency "Critical" #
Acinetobacter baumannii, carbapenem-resistant
Pseudomonas aeruginosa, carbapenem-resistant §
Enterobacteriaceae *, carbapenem-resistant, 3rd generation cephalosporin-resistant
Priority 2: Urgency "High"
Enterococcus faecium, vancomycin-resistant
Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant
Helicobacter pylori, clarithromycin-resistant
Campylobacter **spp.**, fluoroquinolone-resistant
Salmonella **spp.**, fluoroquinolone-resistant
Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant
Priority 3: Urgency "Medium"
Streptococcus pneumoniae, penicillin-non-susceptible
Haemophilus influenzae, ampicillin-resistant
Shigella **spp.**, fluoroquinolone-resistant

molecules

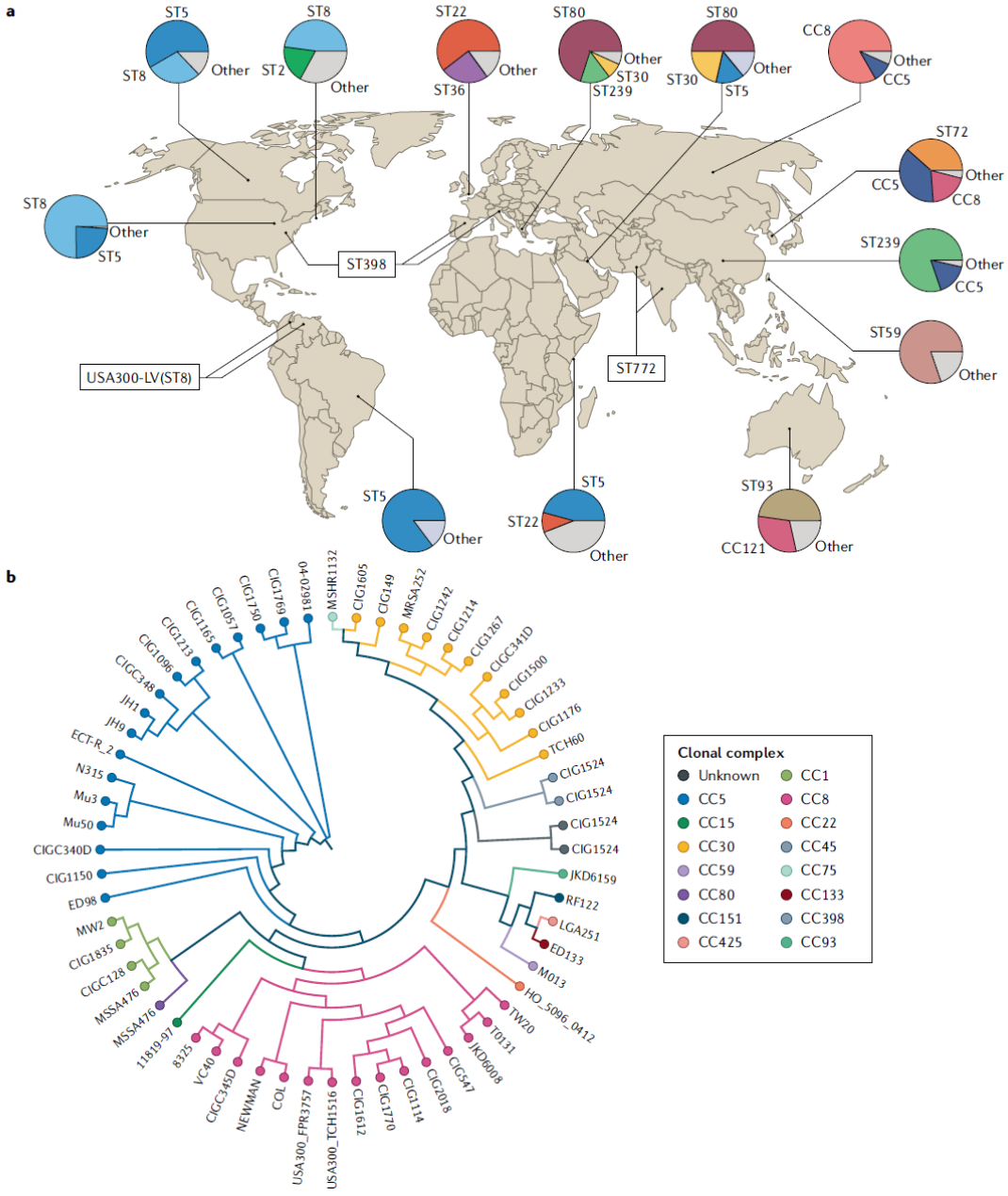
MDPI

Review

Fight Against Antimicrobial Resistance: We Always Need New Antibacterials but for Right Bacteria

Raphaël E. Duval [1,2,*], Marion Grare [3] and Béatrice Demoré [4,5]

Molecules **2019**, *24*, 3152; doi:10.3390/molecules24173152



ANTIMICROBIAL RESISTANCE

Methicillin-resistant *Staphylococcus aureus*: an overview of basic and clinical research

*Nicholas A. Turner[1], Batu K. Sharma-Kuinkel[1], Stacey A. Maskarinec[1], Emily M. Eichenberger[1], Pratik P. Shah[1], Manuela Carugati[1,2], Thomas L. Holland[1] and Vance G. Fowler Jr[1,3]**

Vankomisin Duyarlılığı

- Disk difüzyon ya da otomatize sistemler azalmış duyarlılığı belirlemede yetersiz
- VRSA (MİK≥16 µg/ml) saptanabilir, VISA (4-8 µg/ml) ya da hVISA saptanamaz
- MİK belirlenmeli (BMD)
- E test (tedavi başarısızlığını göstermede daha iyi)

YALE JOURNAL OF BIOLOGY AND MEDICINE 90 (2017), pp.269-281.

REVIEW YJBM

Vancomycin Resistance in *Staphylococcus aureus*

Will A. McGuinness, Natalia Malachowa, and Frank R. DeLeo*

Laboratory of Bacteriology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT

- VRSA; oldukça az
- 2002'de ilk VRSA
- VISA; ABD ve Avrupa'da <%0.3 (azalmış daptomisin duyarlılığı)
- hVISA; MİK değeri duyarlı bulunan ancak orta duyarlı alt popülasyon içeren suşlar (azalmış daptomisin duyarlılığı)

YALE JOURNAL OF BIOLOGY AND MEDICINE 90 (2017), pp.269-281.

REVIEW

YJBM

Vancomycin Resistance in *Staphylococcus aureus*

Will A. McGuinness, Natalia Malachowa, and Frank R. DeLeo*

Laboratory of Bacteriology, Rocky Mountain Laboratories, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, MT

- 62 klinik olgu
- 10 tane endokardit
- Stafilokoklarda daptomisin direnci %0.04
- Tedavi altında azalmış duyarlıklık %5
- hVISA %15, VISA %38-85

Please cite this article in press as: Stefani S, et al. Insights and clinical perspectives of daptomycin resistance in *Staphylococcus aureus*: A review of the available evidence. Int J Antimicrob Agents (2015), http://dx.doi.org/10.1016/j.ijantimicag.2015.06.008

Table 1
Clinical reports of daptomycin (DAP) resistance.

Reference/location	Case description (*n*)	Age (years) and co-morbidities	Previous treatment with glycopeptides	Dosage of DAP	Time until development of non-susceptibility after usage (days)	DAP MIC shift	Strain characteristics	Salvage treatment	Resistance mechanism
Rezai et al., USA [62]	Bacteraemia and osteomyelitis (2)		NA	6 mg/kg		NA	NA	NA	ND
Mangili et al., USA [63]	Septic thrombophlebitis (1)	54/cirrhosis	VAN	4 mg/kg initial and after 4 days 6 mg/kg	28	Susceptible by KB to 2 mg/L	MRSA	LNZ and then VAN + GEN Death	ND
Hayden et al., USA [64]	Osteomyelitis (2)	86/total knee replacement; 61/IHD	VAN	6 mg/kg	35; 42	0.25–4 mg/L; 0.5–4 mg/L	MRSA (27 strains in the two cases, unrelated by PFGE, hDAP by PAP; one strain hVISA)	NS; DAP	ND
Vikram et al., USA [65]	Bacteraemia, vertebral osteomyelitis (1)	52/DM, micronodular cirrhosis of the liver, pulmonary fibrosis	VAN	6 mg/kg	28	0.5–4 mg/L	MRSA (5 isolates). VAN MIC 2–4 mg/L	LNZ, Q/D, RIF. Death	ND
Hirschwerk et al., USA [66]	Bacteraemia (1)	92/permanent pacemaker	VAN	7 mg/kg	42	0.75–2 mg/L	MRSA (5 serial isolates). VAN MIC of 2 mg/L; all related isolates	NA. Death	ND
Marty et al., USA [67]	Bacteraemia and probable vertebral osteomyelitis, immunocompromised (1)	61/bone marrow transplant	LNZ first, after VAN and GEN	6 mg/kg	20	0.25–4 mg/L	MRSA (4), all equal by PFGE	LNZ and then VAN + RIF	ND; lower bactericidal activity by time-to-kill experiments
Skiest, USA [68]	Septic arthritis and bacteraemia (1)	64/DM, obesity, breast cancer in remission	VAN	Initial dose 8 mg/kg followed by 6 mg/kg	28 weeks over the course of 2 years	7 to 4 mg/L	Initial MRSA infection; after amputation the patient developed an MRSA infection. Another MRSA	LNZ	ND
Tsukimori et al., Japan [69]	Aortic prosthesis infection (1)	45/aortic aneurysm	VAN	6 mg/kg/day	10	7 to >1 mg/L	MRSA isolates	LNZ and CLI	ND
Mariani et al., USA [70]	Bacteraemia and prosthetic joint infection (1)	64/total hip replacement	VAN	1 g i.v. q12h	46	0.5–8 mg/L	MRSA. VAN MIC 4 mg/L	NA	ND

International Journal of Antimicrobial Agents xxx (2015) xxx–xxx

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International Journal of Antimicrobial Agents

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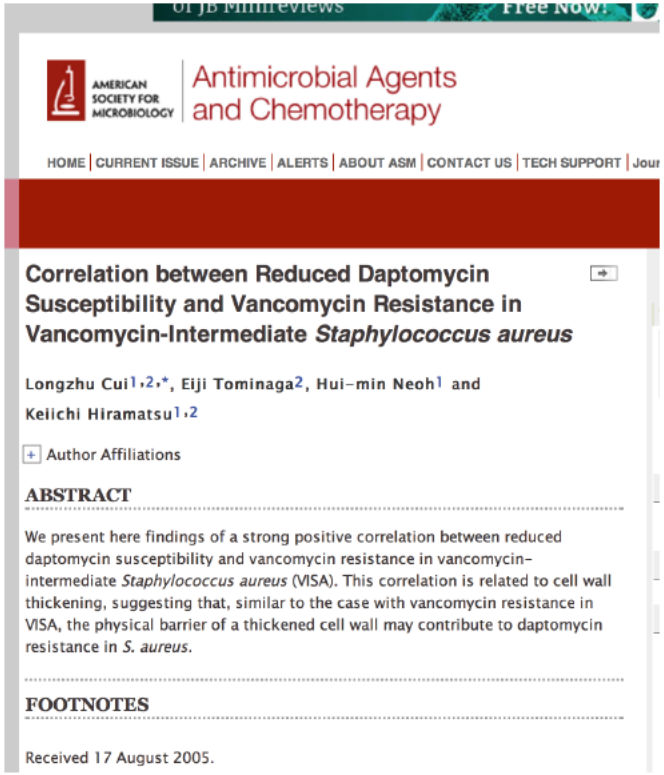
Review

Insights and clinical perspectives of daptomycin resistance in *Staphylococcus aureus*: A review of the available evidence

Stefania Stefani[a,*], Floriana Campanile[a], Maria Santagati[a], Maria Lina Mezzatesta[a], Viviana Cafiso[a], Giovanni Pacini[b]

VISA-Daptomisin Direnci



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Correlation between Reduced Daptomycin Susceptibility and Vancomycin Resistance in Vancomycin-Intermediate *Staphylococcus aureus*

Longzhu Cui[1,2,*], Eiji Tominaga[2], Hui-min Neoh[1] and Keiichi Hiramatsu[1,2]

Author Affiliations

ABSTRACT

We present here findings of a strong positive correlation between reduced daptomycin susceptibility and vancomycin resistance in vancomycin-intermediate *Staphylococcus aureus* (VISA). This correlation is related to cell wall thickening, suggesting that, similar to the case with vancomycin resistance in VISA, the physical barrier of a thickened cell wall may contribute to daptomycin resistance in *S. aureus*.

FOOTNOTES

Received 17 August 2005.

VISA'da azalmış daptomisin duyarlılığı ile vankomisin direnci arasında güçlü bir pozitif korelasyon

Hücre duvarının kalınlaşması ile daptomisine duyarlılığın azalması

- Duvardaki teikoik asit içeriğinde artış ile duvar kalınlaşması
- Membran fosfolipid kompozisyonun değiştirilmesi ile membran akışkanlığının değişmesi
- Hücre yüzey elektrik yükünün değişmesi (pozitif yüklenme) sonucu elektrostatik geri püskürtme

International Journal of Antimicrobial Agents xxx (2015) xxx–xxx

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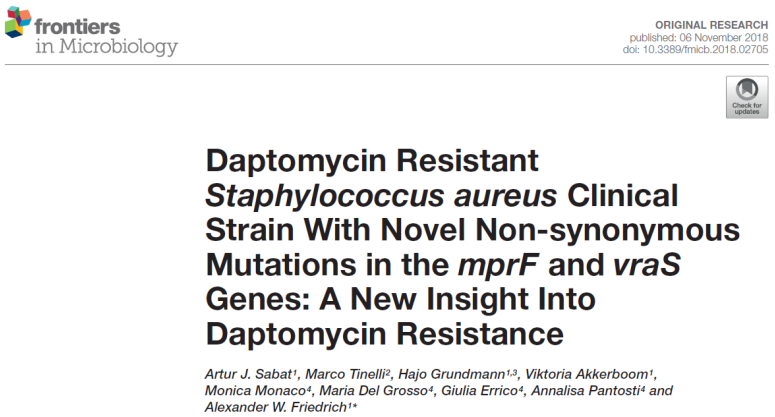
Review

Insights and clinical perspectives of daptomycin resistance in *Staphylococcus aureus*: A review of the available evidence

Stefania Stefani[a,*], Floriana Campanile[a], Maria Santagati[a], Maria Lina Mezzatesta[a], Viviana Cafiso[a], Giovanni Pacini[b]

- MprF ve vraS genleri
- Yeni mutasyonlar
- Daptomisin direncindeki anahtar genlerin ekspresyonunun antibiyotik tarafından azaltıldığı



- Mutlaka vankomisin MİK değerleri belirlenmeli

- hVISA sorun oluşturabilir

CLSI M100-ED29:2019 Performance Standards for Antimicrobial Susceptibility Testing, 29th Edition

Enterokoklar			
Antibiyotikler	**Mikroroganizma alt türü**	**MIC Değerleri µg/ml**	
		S	**R**
Penisilin	Tüm ent.	≤8	≥16
Ampisilin	Tüm ent.	≤8	≥16
Vankomisin	Tüm ent.	≤4	≥32
Daptomisin	*E. faecium* Diğer	≤4 ≤2	≥8 ≥8

Tablo 20. Enterokoksik İnfektif Endokarditin Antimikrobik Tedavisi (3,65,207)

Mikroorganizma	Antimikrobik	Günlük Doz, Doz Aralığı, Uygulama Yolu	Süre (Hafta) Doğal Kapak	Süre (Hafta) Yapay Kapak	Yorum
Penisilin ve gentamisine dirençli olmayan enterokoklar	Ampisilin veya	12 gr, 4-6 dozda, IV	4-6	6	Belirtileri <3 ay sürenlerde 4, >3 ay sürenlerde 6 hafta.
	Penisilin G +	24 MU/gün, 6 dozda, IV	4-6	6	
	Gentamisin	3 mg/kg/gün, 3 dozda, IV/IM	2-6	6	Kreatinin klirensi >50 ml/dakika olanlarda kullanılabilir.
					Nefrotoksik veya ototoksik etki gelişmesi halinde gentamisin kesilmelidir.
	Ampisilin +	6 gr, 6 dozda, IV	6	≥6	Kreatinin klirensi <50 ml/dakika olanlarda önerilir.
	Seftriakson[7]	4 gr, 2 dozda, IV	6	≥6	
Penisiline dirençli ve gentamisine yüksek düzeyde dirençli olmayan enterokoklar veya β-laktam alerjisi	Vankomisin veya	30 mg/kg/gün, 2 dozda, IV	6	≥6	Nefrotoksisite riski yüksek hastalarda teikoplanin yeğlenmelidir.
	Teikoplanin +	10 mg/kg/gün, tek dozda, IV	6	≥6	
	Gentamisin	3 mg/kg, 3 dozda, IV/IM	6	≥6	
Penisiline duyarlı ve gentamisine yüksek düzeyde dirençli olan enterokoklar (gentamisin MIC >500 µg/ml, streptomisin MIC <2000 µg/ml)	Ampisilin +	200 mg/kg/gün, 6 dozda, IV	4-6	6	Nefrotoksisite riski yüksek veya VIII. sinir hasarı olanlarda ampisilin ve seftriakson kombinasyon rejimi de kullanılabilir.
	Streptomisin	15 mg/kg/gün, 2 dozda, IV/IM	4-6	6	
Penisiline duyarlı ve gentamisin ve streptomisine yüksek düzeyde dirençli olan enterokoklar (gentamisin MIC >500 µg/ml, streptomisin MIC >2000 µg/ml)	Ampisilin +	6 gr, 6 dozda, IV	6	≥6	Bu kombinasyonun tedavi başarısının, ampisilin ve gentamisinle benzer olduğu bildirilmiştir.
	Seftriakson*	4 gr, 2 dozda, IV	6	≥6	
Penisiline, aminoglikozidlere ve vankomisine dirençli enterokoklar	Linezolid veya	1200 mg/2 dozda, IV	>6	>8	Linezolid kullanımı ciddi kemik iliği baskılanması, nöropati ve ilaç etkileşimlerine neden olabilir. Bu hastalar IE ekibi tarafından izlenmelidir. Kür için kapak replasmanı gerekebilir.
	Daptomisin +	10-12 mg/kg/tek dozda, IV	>6	>8	
	Ampisilin	12 gr, 6 dozda, IV	>6	>8	

MIC: Minimum inhibitör konsantrasyon.

*Bu kombinasyonun, *Enterococcus faecalis* suşlarına karşı etkinliği gösterilmiştir. *E. faecium* suşlarına karşı etkinliği bilinmemektedir.

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

VIRULENCE
2016, VOL. 7, NO. 3, 252–266
http://dx.doi.org/10.1080/21505594.2016.1159366

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REVIEW

Epidemiology of antimicrobial resistance in bloodstream infections

Murat Akova

TABLE 4. ANTIMICROBIAL SUSCEPTIBILITY OF *ENTEROCOCCUS* STRAINS ISOLATED FROM HUMANS ($N=56$) AND TURKEY ($N=51$)

	Antimicrobials[a]																	
	AMP			*AMX*			*VAN*			*CIP*			*TET*			*ERY*		
Strains	*S*	*I*	*R*	*S*	*I*	*R*	*S*	*I*	*R*	*S*	*I*	*R*	*S*	*I*	*R*	*S*	*I*	*R*
Human strains	*n* (%)																	
E. faecalis (*n*=45)	38 (84.44)	0	7 (15.56)	39 (86.67)	1 (2.22)	5 (11.11)	21 (46.67)	16 (35.56)	8 (17.78)	10 (22.22)	21 (46.67)	14 (31.11)	5 (11.11)	2 (4.44)	38 (84.45)	6 (13.33)	21 (46.67)	18 (40)
E. faecium (*n*=5)	5 (100)	0	0	5 (100)	0	0	2 (40)	2 (40)	1 (20)	2 (40)	2 (40)	1 (20)	1 (20)	0	4 (80)	0	3 (60)	2 (40)
E. gallinarum (*n*=6)	5 (83.33)	0	1 (16.67)	6 (100)	0	0	0	1 (16.67)	5 (83.33)	0	4 (66.67)	2 (33.33)	0	0	6 (100)	0	5 (83.33)	1 (16.67)
Total (*n*=56)	48 (85.71)	0	8 (14.29)	50 (89.28)	1 (1.79)	5 (8.93)	23 (41.07)	19 (33.93)	14 (25)	12 (21.43)	27 (48.21)	17 (30.36)	5 (8.93)	3 (5.36)	48 (85.71)	6 (10.71)	29 (51.79)	21 (37.50)
Turkey strains																		
E. faecalis (*n*=41)	32 (78.05)	1 (2.44)	8 (19.51)	32 (78.05)	2 (4.88)	7 (17.07)	22 (53.66)	13 (31.71)	6 (14.63)	19 (46.34)	17 (41.46)	5 (12.20)	3 (7.32)	0	38 (92.68)	5 (12.20)	7 (17.07)	29 (70.73)
E. faecium (*n*=9)	2 (22.22)	0	7 (77.78)	2 (22.22)	1 (11.11)	6 (66.67)	3 (33.33)	4 (44.45)	2 (22.22)	0	2 (22.22)	7 (77.78)	0	0	9 (100)	0	0	9 (100)
E. gallinarum (*n*=1)	0	0	1 (100)	0	0	1 (100)	0	1 (100)	0	1 (100)	0	0	0	0	1 (100)	0	0	1 (100)
Total (*n*=51)	34 (66.67)	1 (1.96)	16 (31.37)	34 (66.67)	3 (5.88)	14 (27.45)	25 (49.02)	18 (35.29)	8 (15.69)	20 (39.22)	19 (37.25)	12 (23.53)	3 (5.88)	0	48 (94.12)	5 (9.8)	7 (13.73)	39 (76.47)

[a]All examined human and turkey strains were susceptible to gentamicin (120 μg); results not presented in the table.
S, susceptible; I, intermediate; R, resistant; the specific values used for disk diffusion test for *Enterococcus* spp. are described in the Clinical and Laboratory Standards Institute Supplement.[31]
AMP, ampicillin (10 μg); AMX, amoxicillin/clavulanic acid (20/10 μg); VAN, vancomycin (30 μg); CIP, ciprofloxacin (5 μg); TET, tetracycline (30 μg); ERY, erythromycin (15 μg).

ÇİD
İnsan → %32
Hindi→ %43

MICROBIAL DRUG RESISTANCE
Volume 25, Number 2, 2019
Mary Ann Liebert, Inc.
DOI: 10.1089/mdr.2018.0221

Antimicrobial Resistance and Biofilm Formation in *Enterococcus* spp. Isolated from Humans and Turkeys in Poland

Anna Woźniak-Biel,[1] Gabriela Bugla-Płoskońska,[2] Jakub Burdzy,[2] Kamila Korzekwa,[2] Sebastian Ploch,[3] and Alina Wieliczko[1]

TABLE 6. PRESENCE OF RESISTANT GENES IN *ENTEROCOCCUS* SPP. ISOLATED FROM HUMANS ($N=56$) AND TURKEYS ($N=51$)

	Resistant genes, n (%)										
Isolates	blaZ	vanA	vanB	vanC-1	tetK	tetO	tetM	ermA	ermB	ermC	aac(6')Ie-aph(2")Ia
Human isolates											
E. faecalis ($n=45$)	0	0	0	1 (2.22)	0	21 (46.67)	38 (84.44)	2 (4.44)	19 (42.22)	0	13 (28.89)
E. faecium ($n=5$)	0	0	0	0	0	5 (100.00)	4 (80.00)	0	2 (40.00)	0	0
E. gallinarum ($n=6$)	0	1 (16.67)	0	6 (100.00)	0	4 (66.67)	6 (100.00)	0	3 (50.00)	0	0
Total ($n=56$)	0	1 (1.79)	0	7 (12.50)	0	30 (53.57)	48 (85.71)	2 (3.57)	24 (42.86)	0	13 (23.21)
Turkey isolates											
E. faecalis ($n=41$)	2 (4.88)	5 (12.19)	0	0	0	3 (7.32)	32 (78.05)	5 (12.19)	27 (65.85)	0	4 (9.76)
E. faecium ($n=9$)	0	1 (11.11)	0	0	0	1 (11.11)	7 (77.78)	3 (33.33)	7 (77.78)	0	4 (44.44)
E. gallinarum ($n=1$)	0	0	0	1 (100.00)	0	0	1 (100.00)	1 (100.00)	1 (100.00)	0	0
Total ($n=51$)	2 (3.92)	6 (11.76)	0	1 (1.96)	0	4 (7.84)	40 (78.43)	9 (17.65)	35 (68.63)	0	8 (15.69)

MICROBIAL DRUG RESISTANCE
Volume 25, Number 2, 2019
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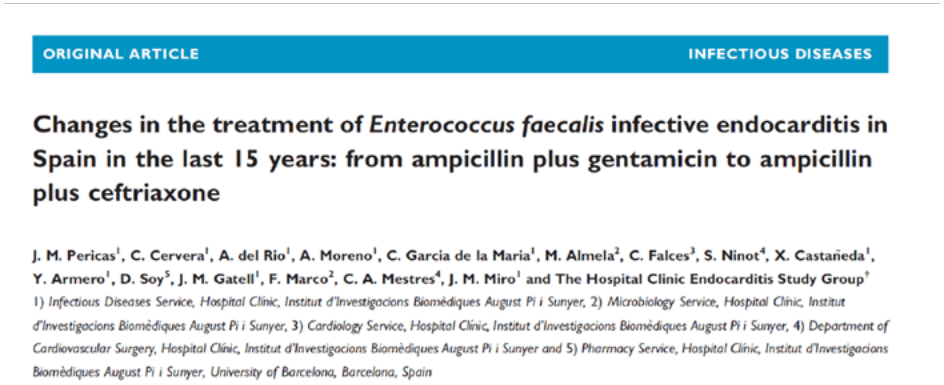
Antimicrobial Resistance and Biofilm Formation in *Enterococcus* spp. Isolated from Humans and Turkeys in Poland

Anna Woźniak-Biel,[1] Gabriela Bugla-Płoskońska,[2] Jakub Burdzy,[2] Kamila Korzekwa,[2] Sebastian Ploch,[3] and Alina Wieliczko[1]

- İE etkeni olan enterokok suşlarında yüksek düzey aminoglikozid direncinde (HLAR) artış
- ABD %22
- Diğer ülkeler %38
- Hem gentamisin hem streptomisin duyarlılığı çalışılmalı



ORIGINAL ARTICLE INFECTIOUS DISEASES

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

Clin Microbial Infect 2014; 20(12)

ORIGINAL ARTICLE INFECTIOUS DISEASES

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1997-2011

30 olgu (7 HLAR)→ Amp (8g / gün) + Genta (3 mg/kg/gün)

39 olgu (18 HLAR)→ Ampisilin + Seftriakson

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 Kirdar 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 etken
22 enterokok penisilin, vankomisin duyarlı ve HLAR yok

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

Table 1 Characteristics of glycopeptide resistance phenotypes in *Enterococcus*

Resistance	Acquired								Intrinsic
	High		Variable	Moderate	Low				Low
Phenotype	VanA	VanM	VanB	VanD	VanE	VanG	VanL	VanN	VanC
Vancomycin MIC (mg/L)	64–1,000	>256	4–1,000	64–128	8–32	≤16	8	16	2–32
Teicoplanin MIC (mg/L)	16–512	96	0.5–1	4–64	0.5	Sensitive	≤0.5	≤0.5	0.5–1
Modification	D-Ala-D-Lac	D-Ala-D-Lac	D-Ala-D-Lac	D-Ala-D-Lac	D-Ala-D-Ser	D-Ala-D-Ser	D-Ala-D-Ser	D-Ala-D-Ser	D-Ala-D-Ser
Location	Plasmid or chromosome	Plasmid or chromosome	Plasmid or chromosome	Plasmid or chromosome	Chromosome	Chromosome	Chromosome	Plasmid	Chromosome
Transferrable	Yes	Yes	Yes	No	No	Yes	No	Yes	No
Expression	Inducible	Inducible	Inducible	Constitutive or inducible	Inducible	Inducible	Inducible	Constitutive	Constitutive or inducible
Main Species	*E. faecalis*, *E. faecium*	*E. faecium*	*E. faecalis*, *E. faecium*	*E. faecalis*, *E. faecium*	*E. faecalis*	*E. faecalis*	*E. faecalis*	*E. faecium*	*E. gallinarum*, *E. casseliflavus*

Table 2 Surveillance of vancomycin-resistant enterococci around the world

Species	Percent of *Enterococcus* isolates resistant to vancomycin by region (no of isolates)					
	Europe[8] 2013	US[11] 2009–2010	Worldwide[15] 2007–2012	Canada[50] 2007–2011	Asia-Pacific[118] 2007–2008	Latin America[118] 2007–2008
E. faecium	8.8 (729)	79.4 (2,572)	–	22.4 (60)	14.1 (270)	48.1 (54)
E. faecalis	1.0 (126)	8.5 (444)	10.3 (27)	0.1 (1)	0.01 (440)	3.1 (195)
All enterococci	4.0 (855)	35.5 (3,016)	–	6.0 (61)	11.9 (710)	12.9 (249)

Note: Adapted by permission of Oxford University Press from Cattoir V, Leclercq R. Twenty-five years of shared life with vancomycin-resistant enterococci: is it time to divorce? *J Antimicrob Chemother*. 2013;68(4):731–742.[14]

Abbreviations: VRE, vancomycin-resistant *Enterococcus*; US, United States.

Infection and Drug Resistance

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REVIEW

Vancomycin-resistant enterococcal infections: epidemiology, clinical manifestations, and optimal management

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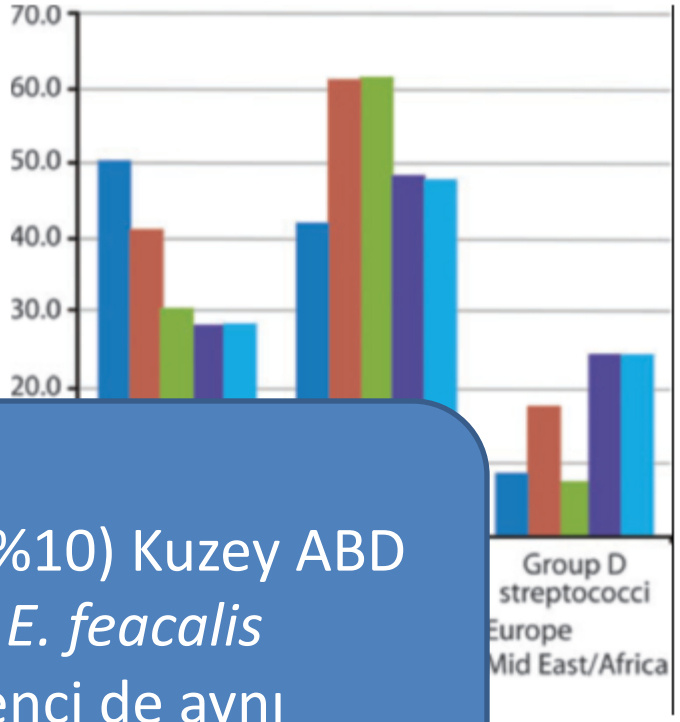
Infection and Drug Resistance
24 July 2015
Number of times this article has been viewed

Tristan O'Driscoll[1]
Christopher W Crank[2]

[1]Department of Pharmacy Practice, Chicago College of Pharmacy, Downers Grove, IL, USA; [2]Pharmacy Services, Rush-Copley Medical Center, Aurora, IL, USA

Abstract: Since its discovery in England and France in 1986, vancomycin-resistant *Enterococcus* has increasingly become a major nosocomial pathogen worldwide. Enterococci are prolific colonizers, with tremendous genome plasticity and a propensity for persistence in hospital environments, allowing for increased transmission and the dissemination of resistance elements. Infections typically present in immunosuppressed patients who have received multiple courses of antibiotics in the past. Virulence is variable, and typical clinical manifestations include

- 2000-2006
- 28 ülke
- 64 merkez
- 4794 İE hastası



12 suş VRE→ 8'i (%10) Kuzey ABD
E. faecium > *E. feacalis*
Ampisilin direnci de aynı

TABLE 1. List of pathogens included in the th
pathogens used for comparative analysis

Enterococci	N	Oral streptococci	N	Gro stre	
E faecalis	453	*S. mitis*	79	*S. bo*	
E faecium	19	*S. mutans*	64	*S. go*	
E durans	6	*S. oralis*	42	*S. eq*	
E casseliflavus	2	*S. sanguis*	31	*S. po*	
E gallinarum	1	*S. salivarius*	23	Grou	
Enterococci NIS[b]	19	*S. gordonii*	12		
		S. anginosus	17		
		S. constellatus	5		
		S. intermedius	5		
		S. milleri group NIS[b]	4		
		S. acidominimus	7		
		S. parasanguis	1		
		S. viridans NIS[b]	533		
TOTAL	500		823		293

[a]'*S. bovis*' refers to the results of species identification according to the former, outdated classification of group D streptococci.
[b]Not identified to species level.

cocci and group D
nong the five ICE

ORIGINAL ARTICLE INFECTIOUS DISEASES

Enterococcal endocarditis in the beginning of the 21st century: analysis from the International Collaboration on Endocarditis-Prospective Cohort Study

C. Chirouze[1,2], E. Athan[3], F. Alla[4], V. H. Chu[5], G. Ralph Corey[5], C. Selton-Suty[6], M.-L. Erpelding[4], J. M. Miro[7], L. Olaison[8], B. Hoen[1,2] and on behalf of the International Collaboration on Endocarditis Study Group*

1) CHRU Besançon, Service de Maladies Infectieuses et Tropicales, 2) Université de Franche-Comté, UMR CNRS 6249, Besançon, France, 3) Department of Infectious Diseases, Barwon Health, Geelong, Australia, 4) INSERM, Epidémiologie, CHU Nancy, Nancy, France, 5) Duke University Medical Center, Durham, North Carolina, USA, 6) Service de Cardiologie, Centre Hospitalier Universitaire, Nancy, France, 7) Hospital Clinic – IDIBAPS, University of Barcelona, Barcelona, Spain and 8) Department of Infectious Diseases, Institute of Biomedicine, University of Gothenburg, Gothenburg, Sweden

- Mortalite %16-29
- VRE İE mortalite ↑
- Mortalite-Bakteriyemi süresi; *E. faecium* > *E. Feacalis*
- VRE İE yüksek risk faktörleri; Organ nakli
  HD
  SVK

HHS Public Access
Author manuscript
Curr Infect Dis Rep. Author manuscript; available in PMC 2015 May 15.

Published in final edited form as:
Curr Infect Dis Rep. 2012 August ; 14(4): 339–349. doi:10.1007/s11908-012-0270-8.

Enterococcal Endocarditis: Can We Win the War?

Jose M. Munita,
Laboratory for Antimicrobial Research, University of Texas Medical School at Houston, Houston, TX, USA. Clínica Alemana – Universidad del Desarrollo School of Medicine, Santiago, Chile

ELSEVIER

Journal of Infection
Volume 63, Issue 6, December 2011, Pages 420-428

Single center experience of a vancomycin resistant enterococcal endocarditis cohort ☆

Graeme N. Forrest [a], Ryan S. Arnold [b], James S. Gammie [c], Bruce L. Gilliam [d]

- Hücre yüzey yükünü değiştirerek antibiyotiğin geri püskürtülmesi
- Kardiyolipin moleküllerinin dağılımını değiştirerek antibiyotiğin hedefinden saptırılması (*E. feacalis)*
- Daptomisin direnci % 0.6

J Antimicrob Chemother 2018; **73**: 1–11
doi:10.1093/jac/dkx349 Advance Access publication 20 October 2017

Journal of Antimicrobial Chemotherapy

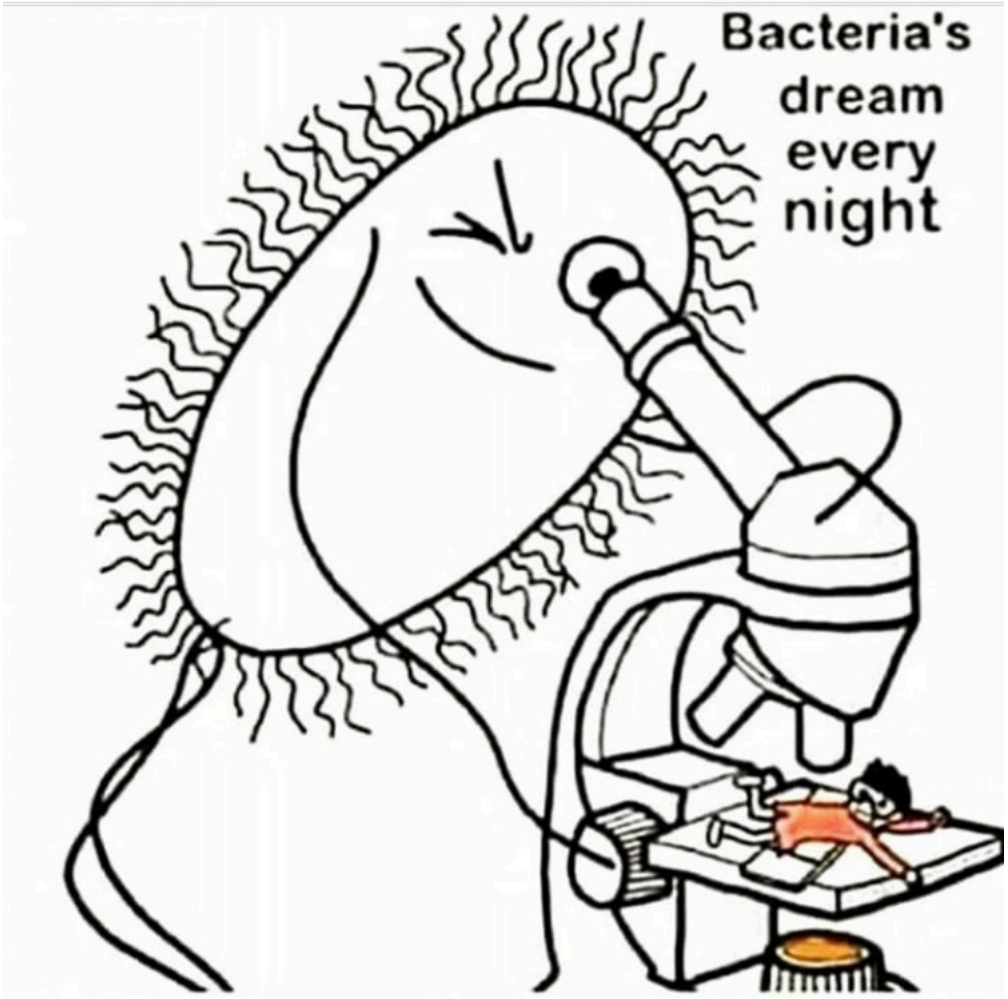
Daptomycin

Mohsen Heidary[1], Azar Dohkt Khosravi[2,3], Saeed Khoshnood[3]*, Mohammad Javad Nasiri[4], Saleh Soleimani[5] and Mehdi Goudarzi[4]

Table 1. Prevalence of daptomycin resistance worldwide

Location/ reference	Period	Bacteria	Patients	No. of resistant bacteria	MIC (mg/L)	Resistance mechanism	Study
USA[74]	2004	*S. aureus*	adult	–	–	ND	case report
USA[75]	2005	MRSA	adult	–	0.5–4	ND	case report
North America[76]	2005	*S. aureus*	both	2	–	ND	short communication
		CoNS		2			
		E. faecalis		0			
		E. faecium		0			
		β-haemolytic streptococci		0			
USA[77]	2005	MRSA	adult	–	0.25–4	ND	case report
USA[78]	2005	MRSA	adult	–	–	ND	case report
Europe[76]	2005	*S. aureus*	both	0		ND	short communication
		CoNS		1			
		E. faecalis		0			
		E. faecium		0			
		β-haemolytic streptococci		0			
USA[79]	2006	MRSA	adult	–	0.5–8	ND	case report
USA[3]	2006	MRSA	adult	4	0.25–4	lower bactericidal activity	case report
USA[80]	2006	MRSA	adult	–	1–4	ND	case report
USA[81]	2006	MRSA	adult	5	0.75–2	ND	case report
USA[82]	2007	VISA	adult	29	1–8	MprF I420N mutation	case report
USA[83]	2008	daptomycin-non-susceptible *S. aureus*	adult	10	0.125–4	ND	original article
		VISA					
		MRSA					
Taiwan[84]	2008	MRSA	adult	11	1–4	ND	case report
USA[85]	2008	MSSA	NS	4	0.125–2	ND	original article
USA[86]	2008	MRSA	adult	5	0.5–4	ND	case report
USA[87]	2008	MRSA	adult	4	1–4	MprF T345A mutation	case report
Taiwan[88]	2008	MRSA	adult	12	0.5–2	ND	case report
UK[89]	2009	MRSA	adult	6	0.25–4	ND	case report
USA[90]	2009	MRSA	adult	4	–	ND	case report
USA[91]	2009	MRSA	adult	2	0.5–2	ND	case report
Taiwan[92]	2009	MRSA	adult	10	0.5–2	ND	case report
Italy[93]	2010	MRSA	adult	–	–	ND	case report
Singapore[70]	2010	daptomycin-non-susceptible *S. aureus*	adult	6	0.19–4	ND	case report
Taiwan[94]	2010	MRSA	adult	–	0.5–4	ND	case report
UK[95]	2011	group G *Streptococcus*	adult	–	0.19–4	ND	case report
		MRSA					
Australia[96]	2011	vancomycin-unresponsive *S. aureus*	adult	8	0.25–2	ND	case report
Taiwan[97]	2011	daptomycin-non-susceptible *S. aureus*	adult	7	0.25–1	ND	case report
USA[98]	2012	MRSA	adult	6	0.25–1.5 and 8	ND	case report
Australia[99]	2012	MRSA	adult	3	–	ND	case report
Canada[100]	2012	MRSA	adult	3	1 to >4	ND	case report
USA[101]	2013	MRSA	adult	3	0.38–3	ND	case report
USA[102]	2013	MRSA	both	10	2–4	ND	original article
		MSSA					
France[40]	2013	MRSA	adult	3	0.25–2	ND	case report
Spain[103]	2014	MRSA	adult	7	<0.5–2	ND	letter to editor

ND, not determined; NS, not stated.


Bacteria's
dream
every
night