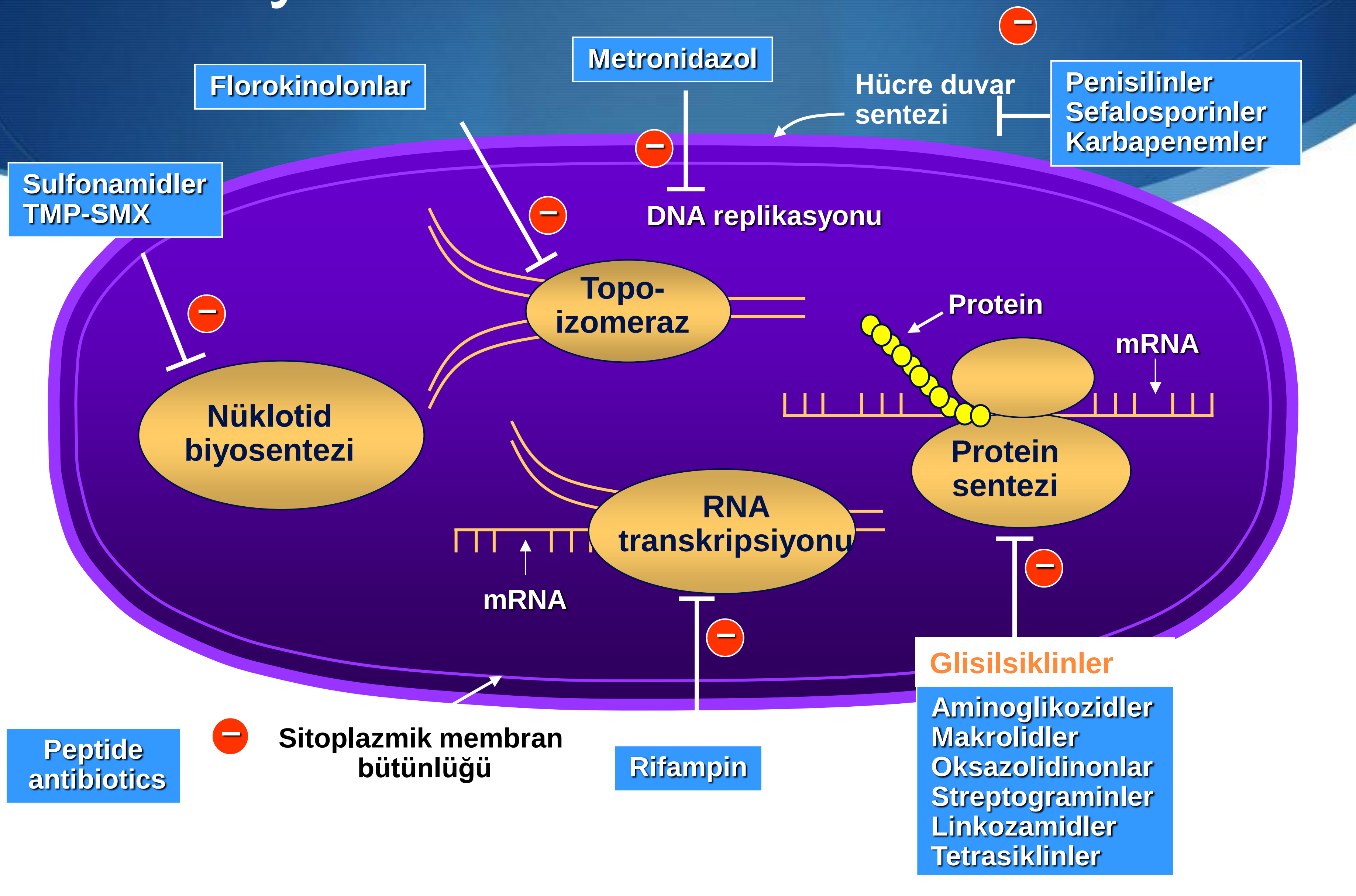
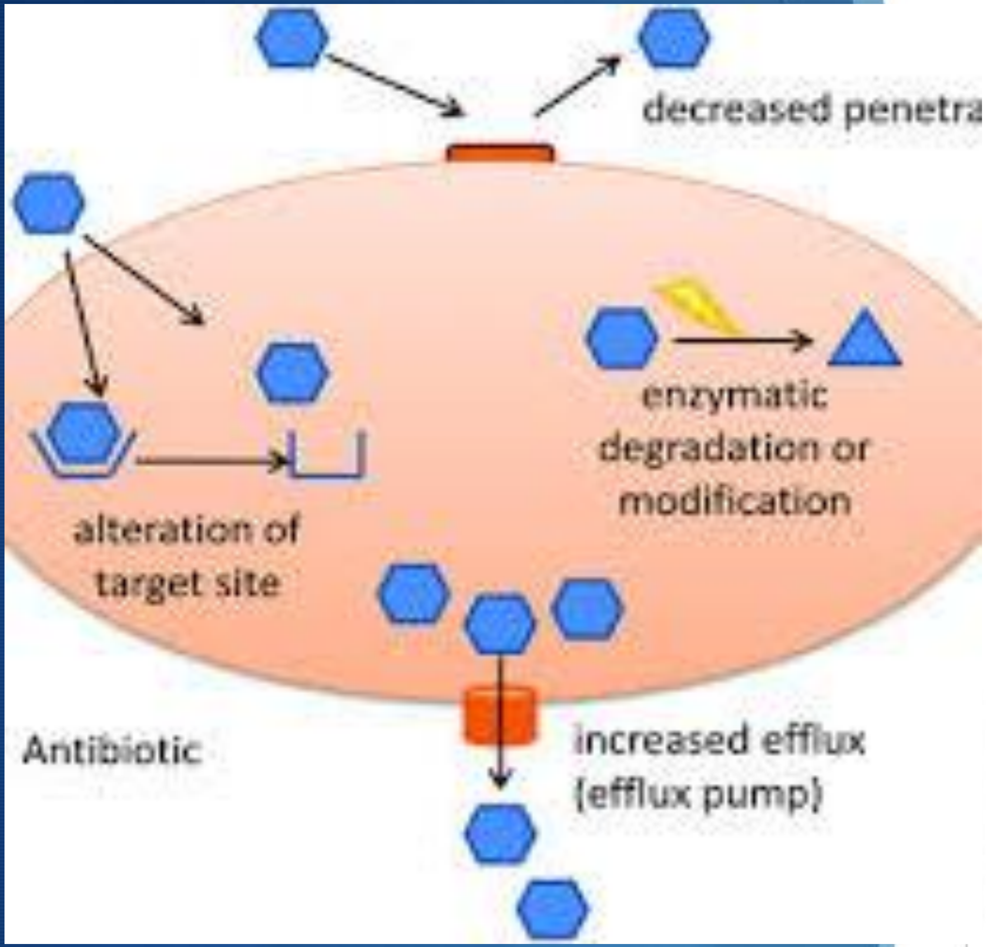
Gram-Negatif Bakterilerde Antibiyotik Direnç Mekanizmaları ve Epidemiyoloji

LÜTFİYE MÜLAZIMOĞLU
MARMARA ÜNİVERSİTESİ TIP FAKÜLTESİ

Antibiyotiklerin Etki Mekanizmaları

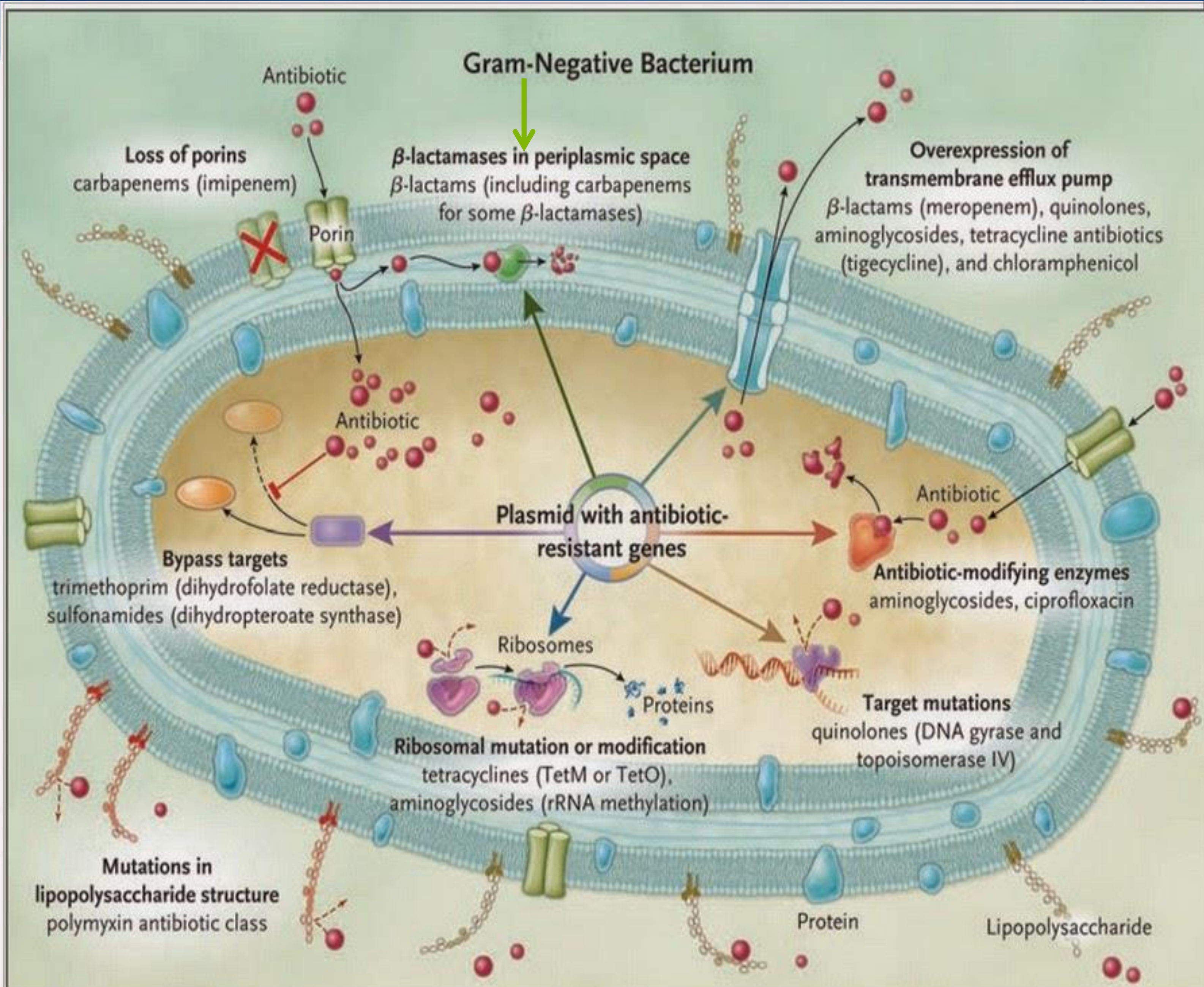


Chopra I. *Curr Opin Pharmacol* 2001;1:464



Direnç Mekanizmaları

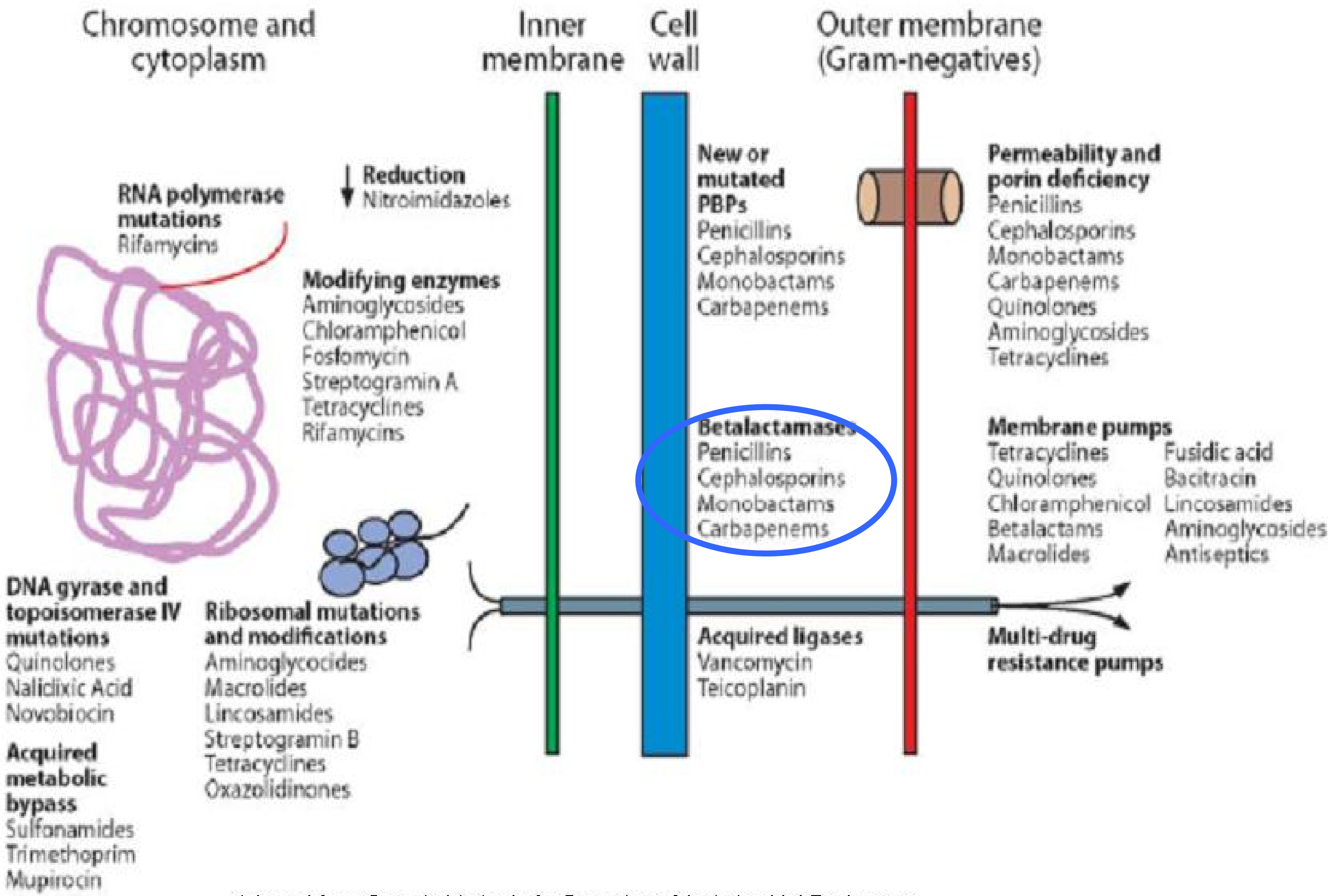
- Azalmış penetrasyon
- Hedef bölgede değişiklik
- Artmış sızma
- Enzimatik yıkım ya da değiştirme



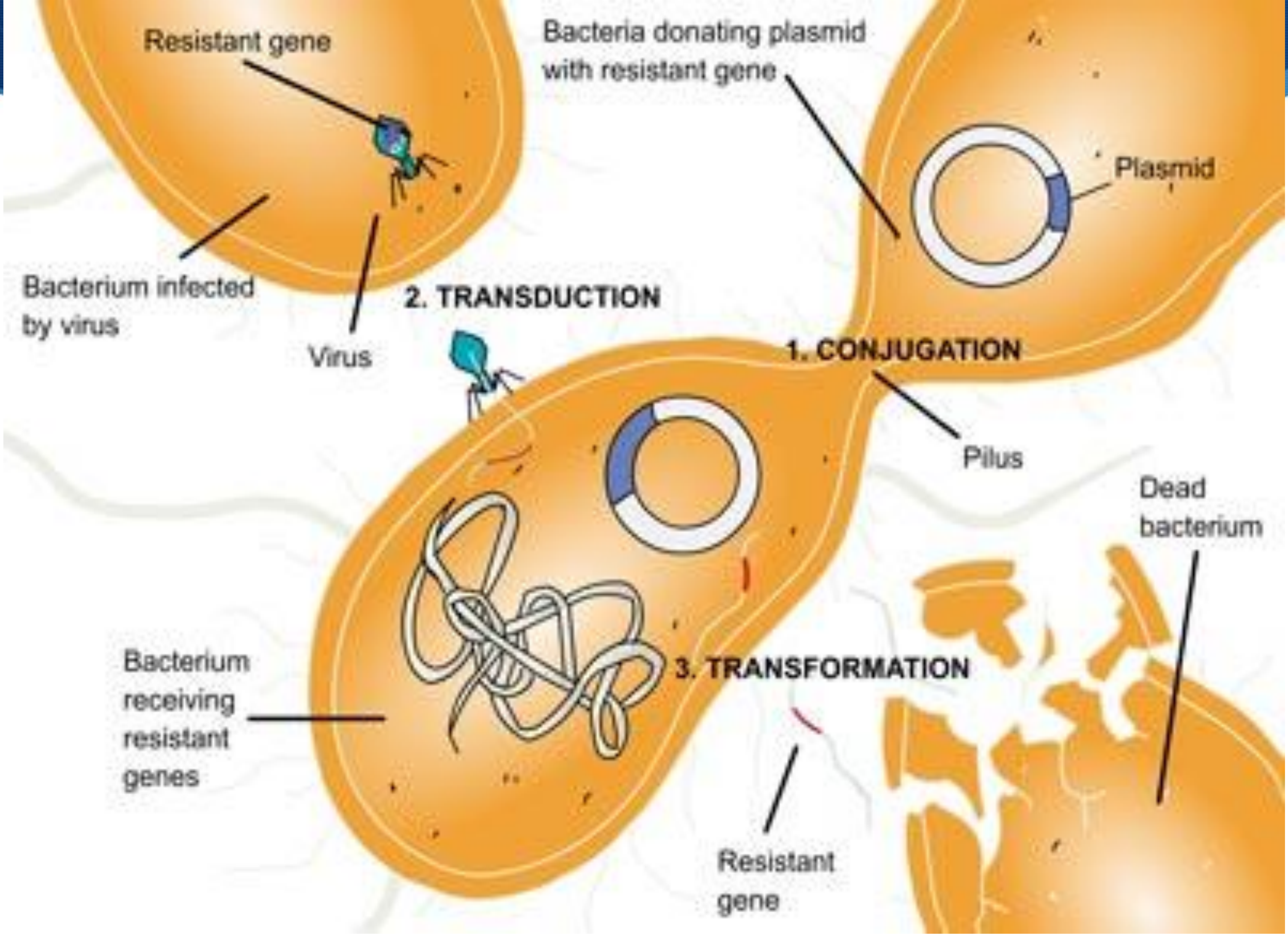
Gram-Negative Bacterium
Antibiotic
Loss of porins
carbapenems (imipenem)
Porin
β-lactamases in periplasmic space
β-lactams (including carbapenems for some β-lactamases)
Overexpression of transmembrane efflux pump
β-lactams (meropenem), quinolones, aminoglycosides, tetracycline antibiotics (tigecycline), and chloramphenicol
Antibiotic
Plasmid with antibiotic-resistant genes
Antibiotic
Bypass targets
trimethoprim (dihydrofolate reductase), sulfonamides (dihydropteroate synthase)
Antibiotic-modifying enzymes
aminoglycosides, ciprofloxacin
Ribosomes
Proteins
Target mutations
quinolones (DNA gyrase and topoisomerase IV)
Ribosomal mutation or modification
tetracyclines (TetM or TetO), aminoglycosides (rRNA methylation)
Mutations in lipopolysaccharide structure
polymyxin antibiotic class
Protein
Lipopolysaccharide

(NEJM, 2010

MECHANISMS OF RESISTANCE and ANTIBIOTICS

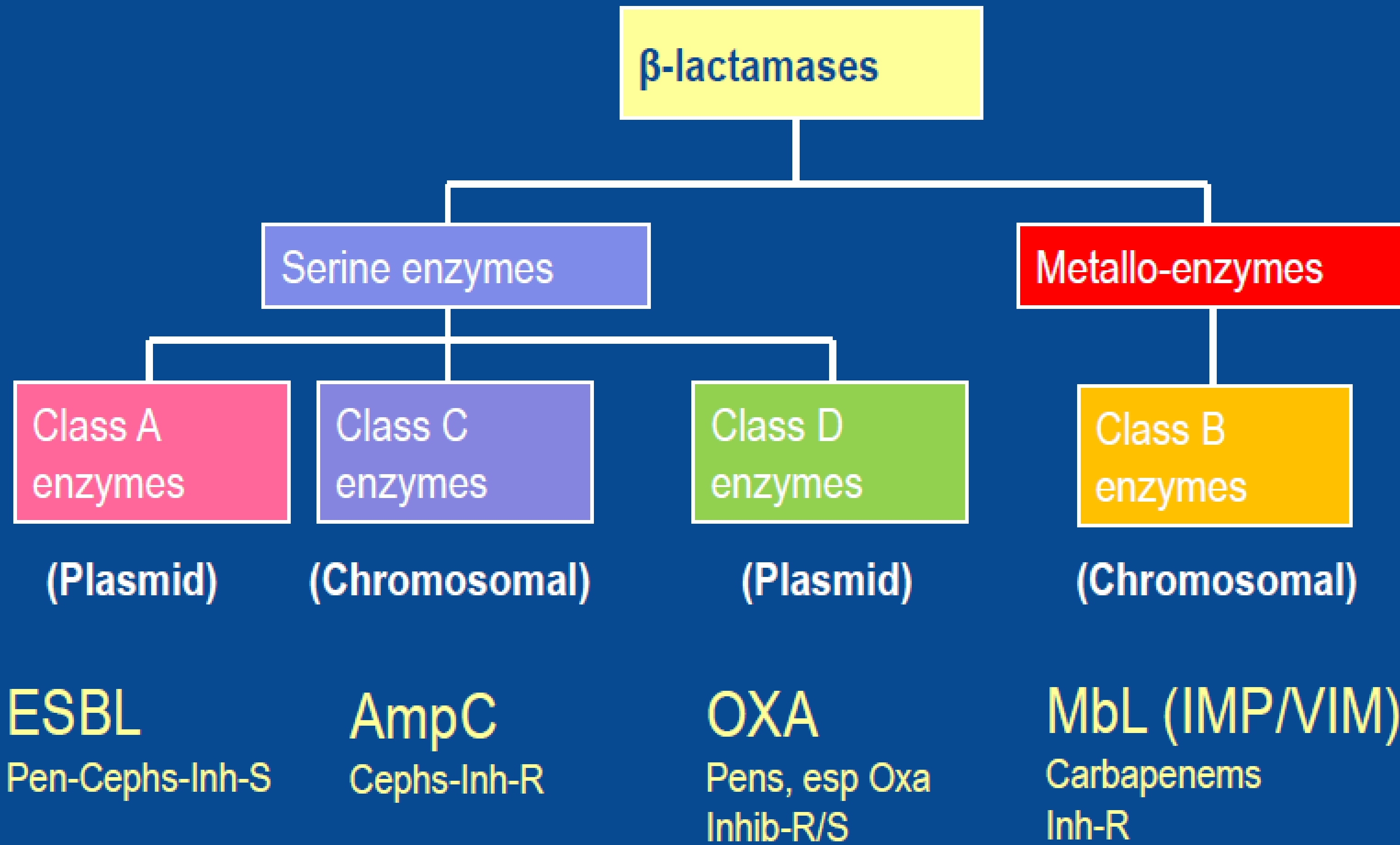


Adapted from Genetic Methods for Detection of Antimicrobial Resistance
ARNFINN SUNDSFJORD,1, 2, 3 GUNNAR S. SIMONSEN,2, 3 BJØRG C. HALDORSEN,2
HÅKON HAAHEIM,2 STIG-OVE HJELMEVOLL,2 PIA LITTAUER2 and KRISTIN H. DAHL1,2
1Department of Microbiology and Virology, University of Tromsø, 2Reference Centre for Detection of Antimicrobial Resistance, Department of Microbiology, University Hospital of Northern-Norway and 3Division of Infectious Disease Control, Norwegian Institute of Public Health, Oslo, Norway



Wiley Science

Classification of β-lactamases



Bush. Rev Inf Dis 1987;10:681; Bush et al. Antimicrob Agents Chemother 1995;39:1211–1233
Bush. Curr Opin Investig Drugs 2002;3:1284–1290

GSBL üretimi için risk faktörleri

- **huzurevinde kalıyor olma**
- **daha önce seftazidim veya aztreonam kullanımı**
- **yüksek APACHE skoru**
- **üriner kateter varlığı**
- **mekanik ventilatöre bağlı olma**
- **Türkiyede bir hastanede yatıyor olmak**
    - ***Jacoby G. CID 1998;27:81-83***
    - **Paterson DL,Mülazımoglu L. Ann Intern Med. 2004 Jan 6;140(1):26-32**

2008 EARS

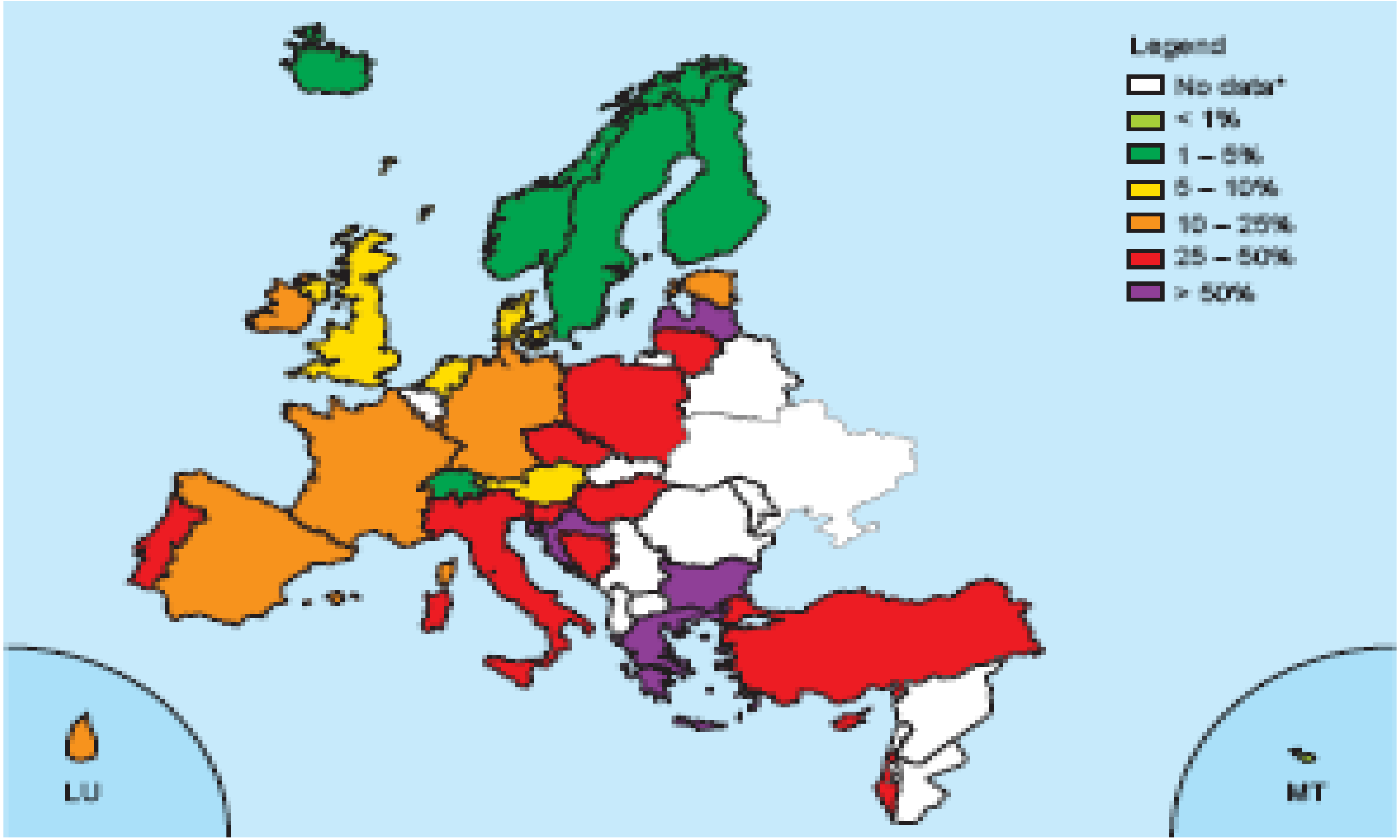
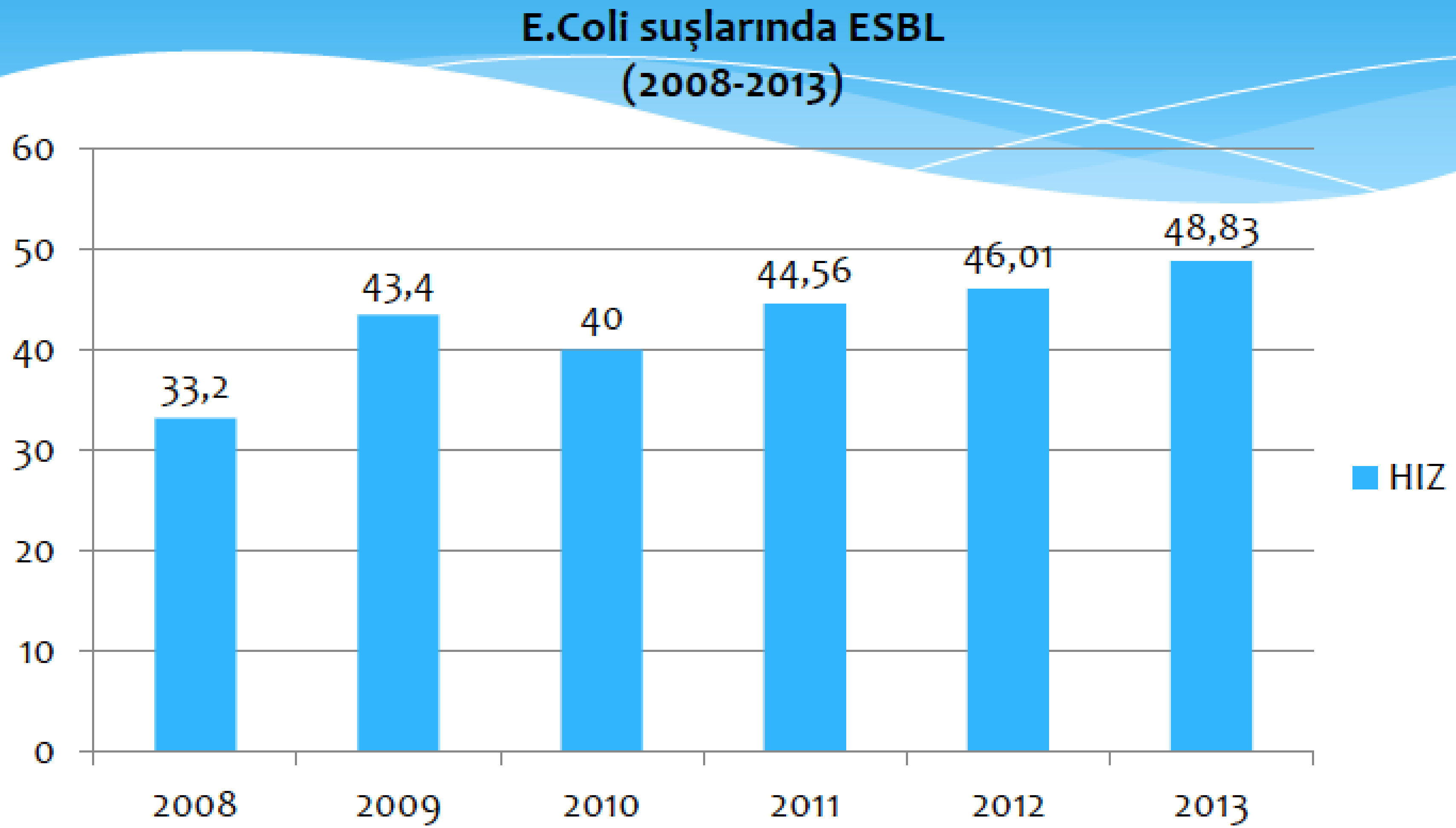


Figure 5.22. *Klebsiella pneumoniae*: proportion of invasive isolates resistant to 3rd generation cephalosporins in 2008.
* These countries did not report any data or reported less than 10 isolates.

GSBL' lerin Laboratuvarda Tespiti

Hastane Enfeksiyonlarında

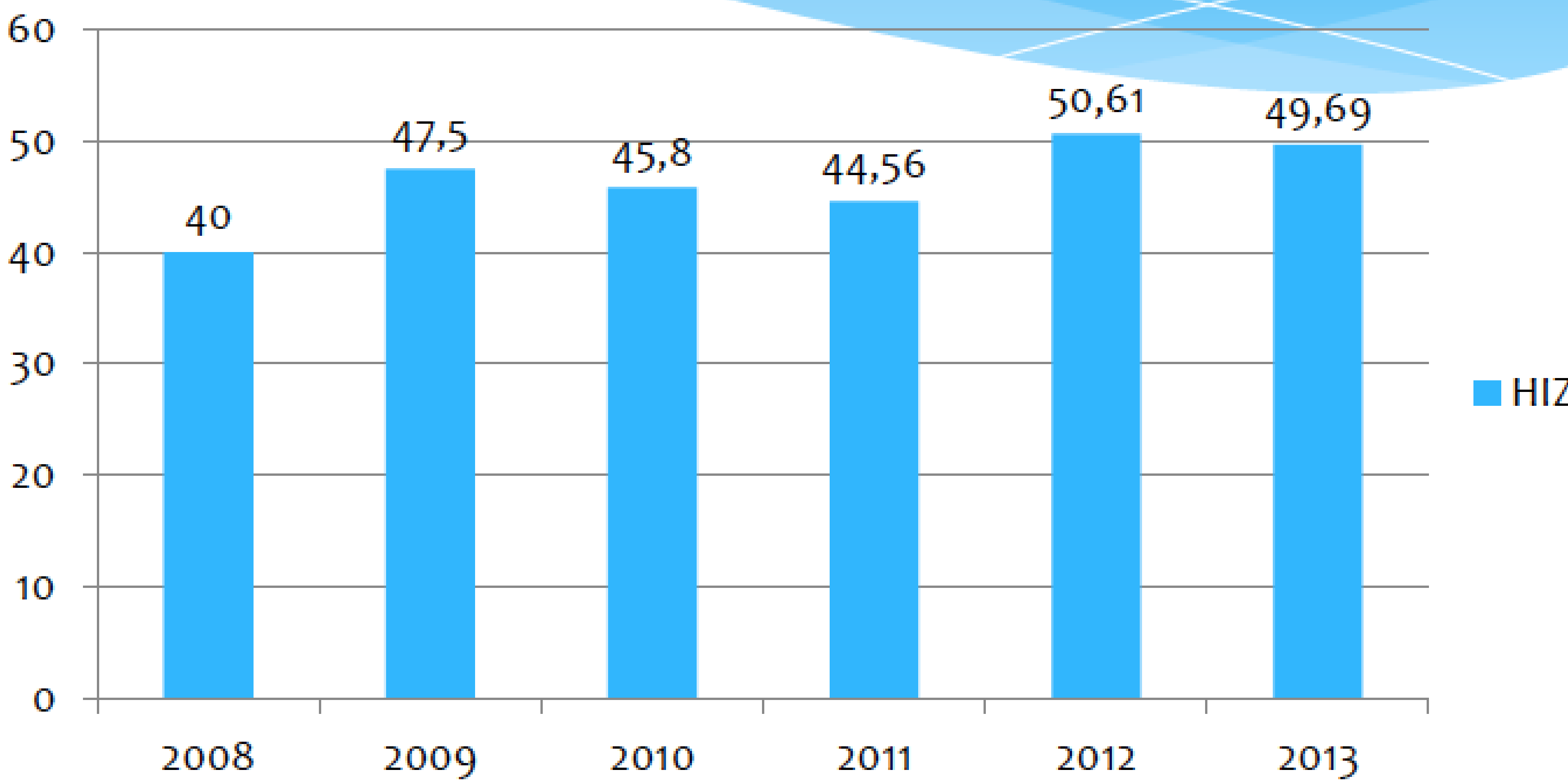


Dirençli izolatlar / Test edilen izolat sayısı X 100

Erhan Kabasakal

Hastane Enfeksiyonlarında

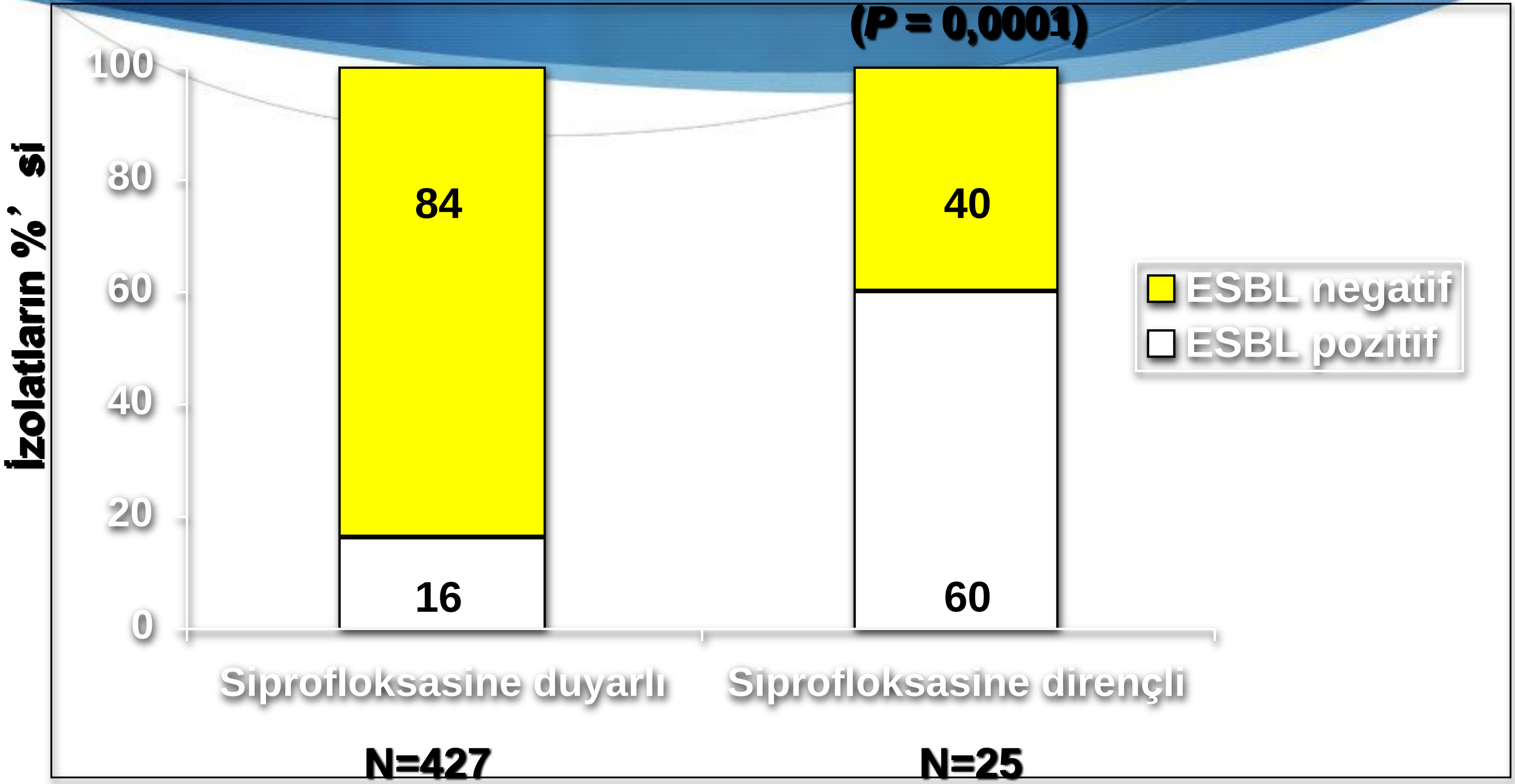
Klebsiella Pneumoniae suşlarında ESBL
(2008-2013)



Dirençli izolatlar / Test edilen izolat sayısı X 100

Erhan Kabasakal

Siprofloksasin Direnci ve ESBL Üretimi



Paterson DL,Mulazimoglu L.et al.*Clin Infect Dis*. 2000;30:473-478.

Dışkı taraması-400 örnek

- **79 suşta ESBL(+)** **%20**
- ***E.coli* 75 adet**
- **Klebsiella 4 adet**
- **TEM --> 46**
- **SHV -->12**
- **CTX-M grup 1-->77**
- **CTX-M 15-->78**
- **CTX-M 9-14-->4**

- **Tigen E-Korten V.2010**

Genişlemiş spektrumlu beta-laktamaz (GSBL) yapan *Escherichia coli* ve *Klebsiella pneumoniae* kökenleri ile gelişen toplum kökenli üriner sistem enfeksiyonlarında risk faktörleri

	Çalışma grubu (n=62) GSBL (+)	Kontrol grubu (n=60) GSBL(-)	p
Yaş	54,7± 18 yaş (17-88)	57,7±20,2 yaş (19-87 yaş	>0,05
Cinsiyet			
Erkek	33 (%53,2)	15 (%25)	
Kadın	29 (%46,8)	45 (%75	
ÜSE öncesi antibiyotik kullanım süresi (gün)	10,6±5,44 (1-21)	7±4,05 (1-14)	p=0,016
Son 15 günde antibiyotik kullanımı	32 (%54,2)	23 (%39)	>0,05
Son 3 ayda antibiyotik kullanımı	28 (%47,5)	9 (%15,3)	<0,001
Önceden operasyon öyküsü	27 (%45)	3 (%5,1)	<0,001
Son 15 günde hastanede yatış	15 (%24,6)	5 (%8,6)	p=0,02
Son 3 ayda hastanede yatış	22 (%36,7)	4 (%6,9)	<0,001
Altta yatan hastalık (malignite, taş, BPH, DM)	57 (%58,8)	40 (%41,2)	p=0,032

ÜSE: Üriner Sistem Enfeksiyonu; BPH: Benign prostat hipertrofisi; DM: Diabetes Mellitus

Yılmaz E, Akalın H
KLİMİK 2007
/J Chemother. 2008 Oct;20(5):581-5.
Yilmaz E1, Akalin H, Ozbey S, Kordan Y, Sinirtaş M, Gürcüoglu E, Ozakin C, Heper Y, Mistik R, Helvaci S.

Clin Microbiol Infect. 2010

Risk factors for extended-spectrum beta-lactamase positivity in uropathogenic Escherichia coli isolated from community-acquired urinary tract infections.

Azap OK1, Arslan H, Serefhanoğlu K, Colakoğlu S, Erdoğan H, Timurkaynak F, Senger SS.

- 510 hasta
- GSBL (6.3%) / (17.4%)
- multivariat analiz:
- Üç epizod/ yıl
- Son üç ayda betalaktam kullanımı
- Prostat hastalığı
- GSBL pozitif grupda SXT-Genta-Cip simultane direnç %39.2

Int J Clin Pract. 2015 Feb 16.

Comparison of community-onset healthcare-associated and hospital-acquired urinary infections caused by extended-spectrum beta-lactamase-producing Escherichia coli and antimicrobial activities.

Saltoglu N1, Karali R, Yemisen M, Ozaras R, Balkan II, Mete B, Tabak F, Mert A, Hondur N, Ozturk R.

- **2009-2011 173 GSBL pozitif E.coli kaynaklı üriner sistem infeksiyonu- %74 kadın**
- **%43.4 toplum başlangıçlı sağlık hizmeti ile ilişkili (CO-HCA)**
- **%56.6 hastene kökenli**
    - **duyarlılık**
- nitrofurantoin, %97.6
- amikasin %89
- trim -sulfa %29.4
- kinolon %17.9

J Antimicrob Chemother. 2005 Nov;56(5):914-8. Epub 2005 Sep 20.

Risk factors for ciprofloxacin resistance among Escherichia coli strains isolated from community-acquired urinary tract infections in Turkey.

Arslan H1, Azap OK, Ergönül O, Timurkaynak F; Urinary Tract Infection Study Group.

- 611 hasta
- *E.coli* siprofloksasin direnci
  - %17 non-komplike
  - %38 komplike
- 50 yaş üstü [odds ratio (OR): 1.6;
- Son bir yılda birden fazla kez siprofloksasin kullanımı(OR: 2.8);
- Komplike ÜSİ (OR: 2.4);

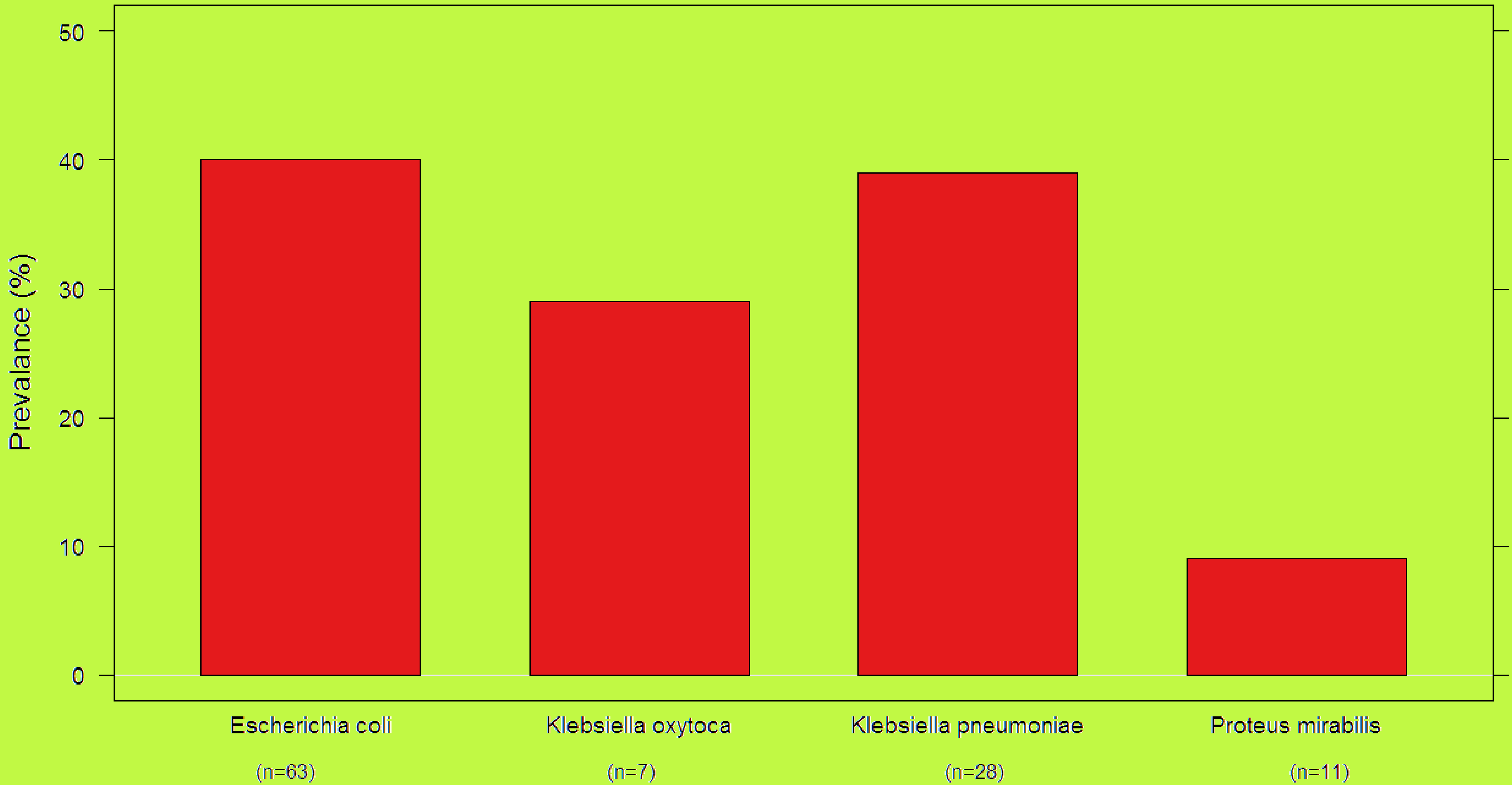
Toplum başlangıçlı kinolon (siprofloksasin) direnci risk faktörleri

- **Son altı ayda antibiyotik kullanımı OR: 4.3**
- **Sağlık bakımı**
- **Altta yatan hastalık**

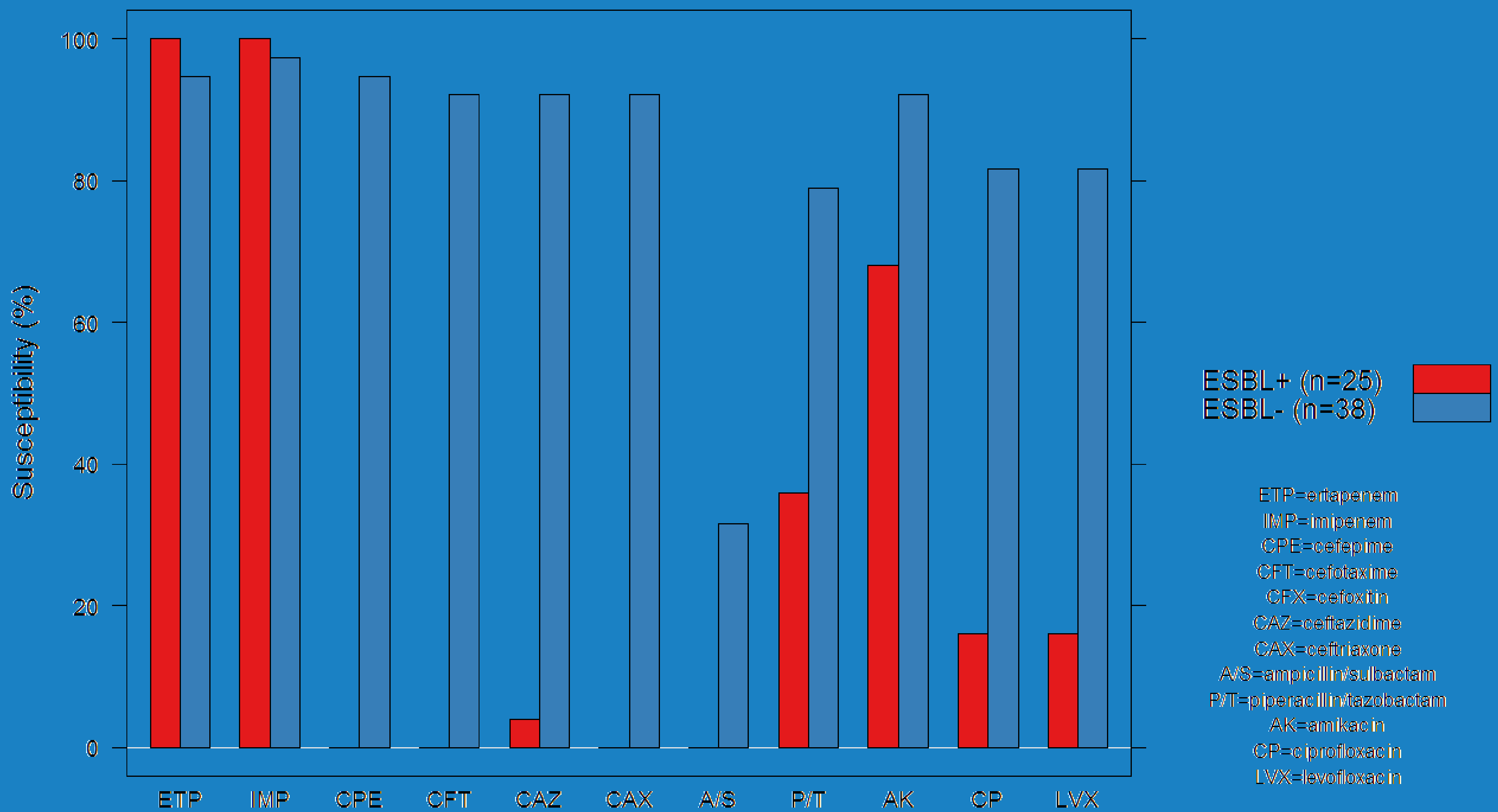
- **Q R li suşların %75.4 ü GSBL pozitif**

  - **Tüzün T, Sayın Kutlu S, Kutlu M, Kaleli İ. KLİMİK 2015**

SMART Study: Prevalence of ESBL+ Isolates
All Sites, Turkey, 2011 (IAIs only)

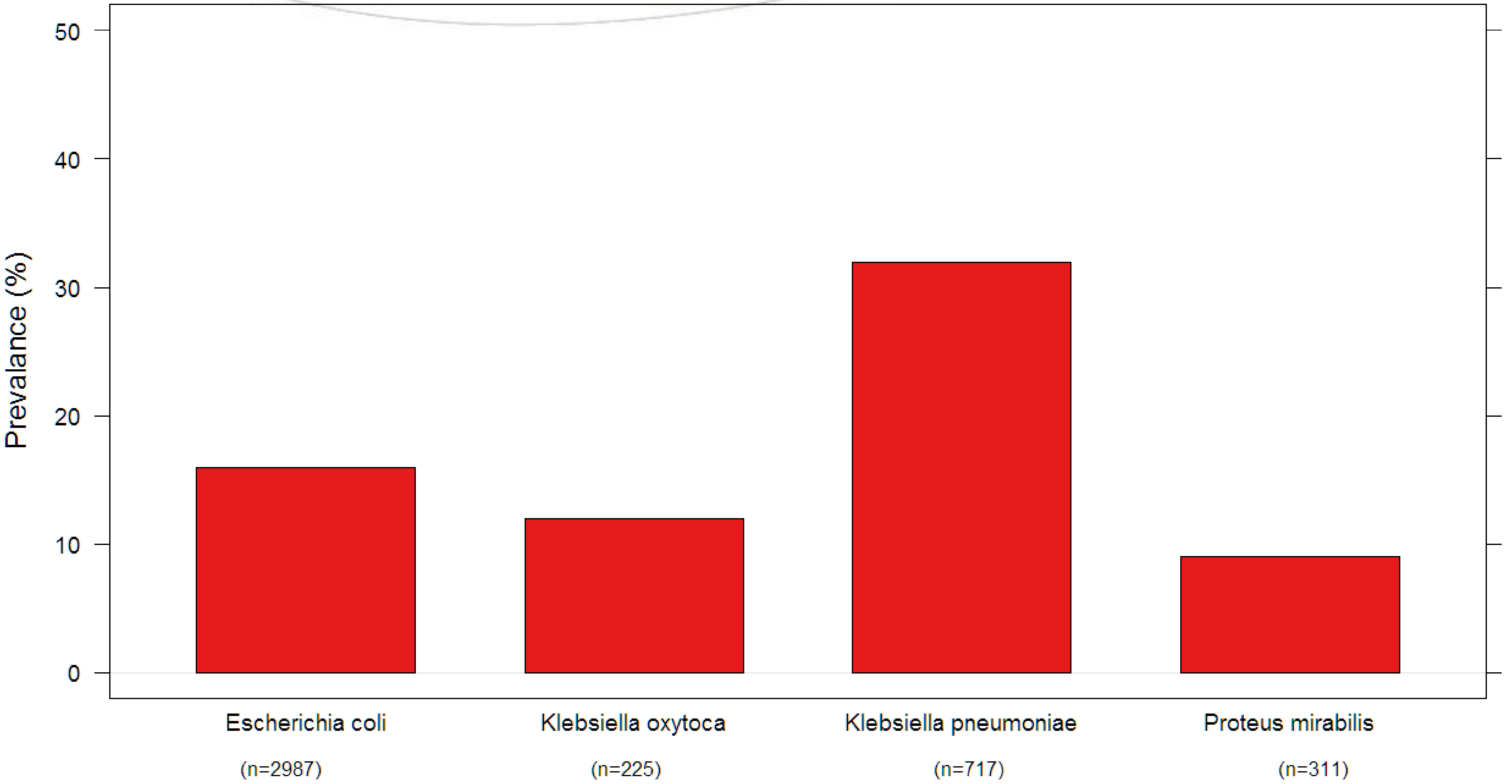


SMART Study: Susceptibility of Escherichia coli by ESBL
All Sites, Turkey, 2011 (IAIs only)



Based on EUCAST 2012 breakpoints.

SMART Study: Prevalence of ESBL+ Isolates All Sites, Europe, 2011



Includes: IAIs and UTIs.

Marmara PEAH

- **2013 IAI TK 34 etken**
- **GSBL %2.94**

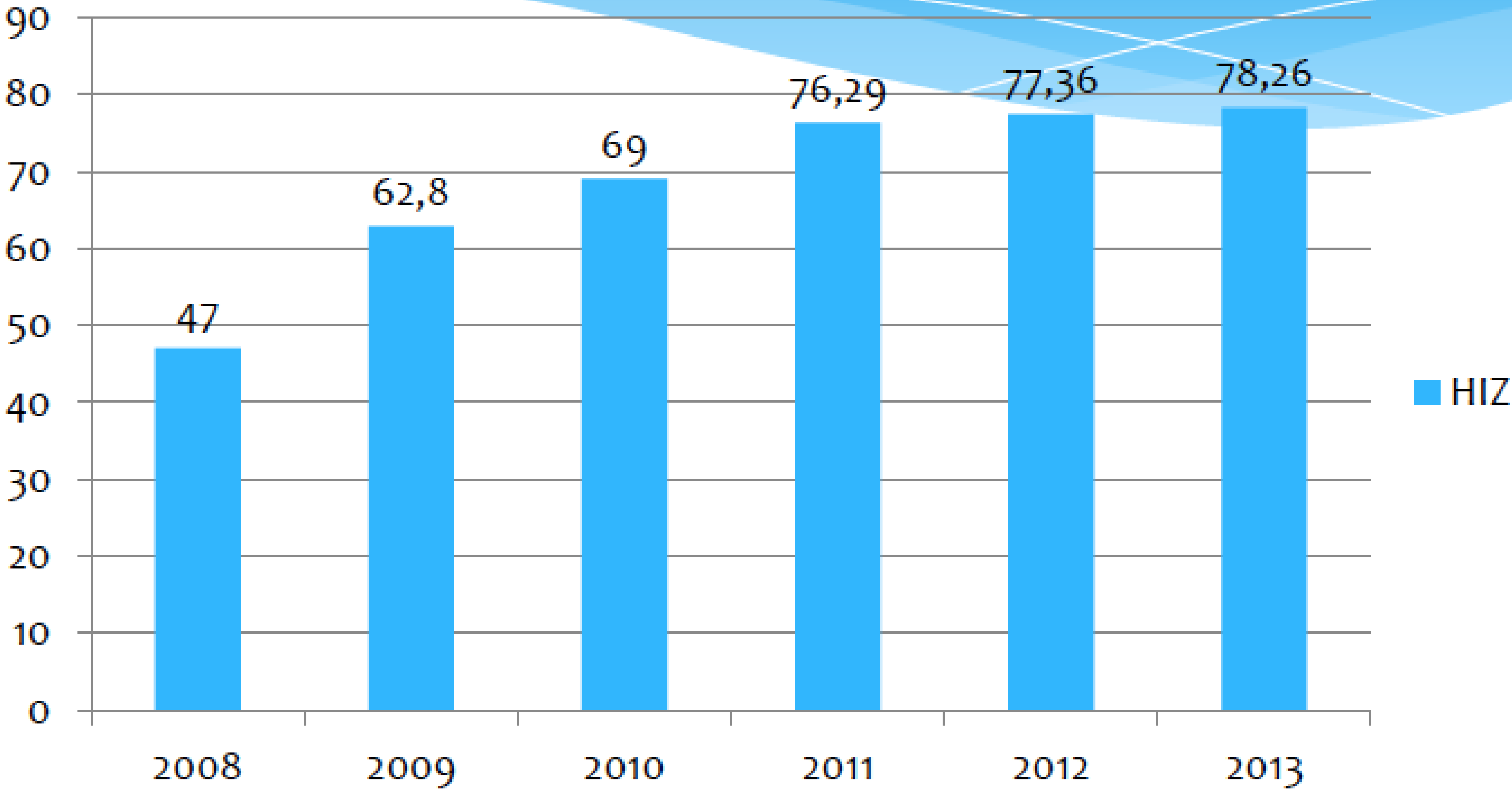
- **2014**
- **GSBL %20**

Marmara PEAH 2014

	GSBL
E. coli	%70,37
K. pneumoniae	%82,54
	kolistin R
Acinetobacter	1,18

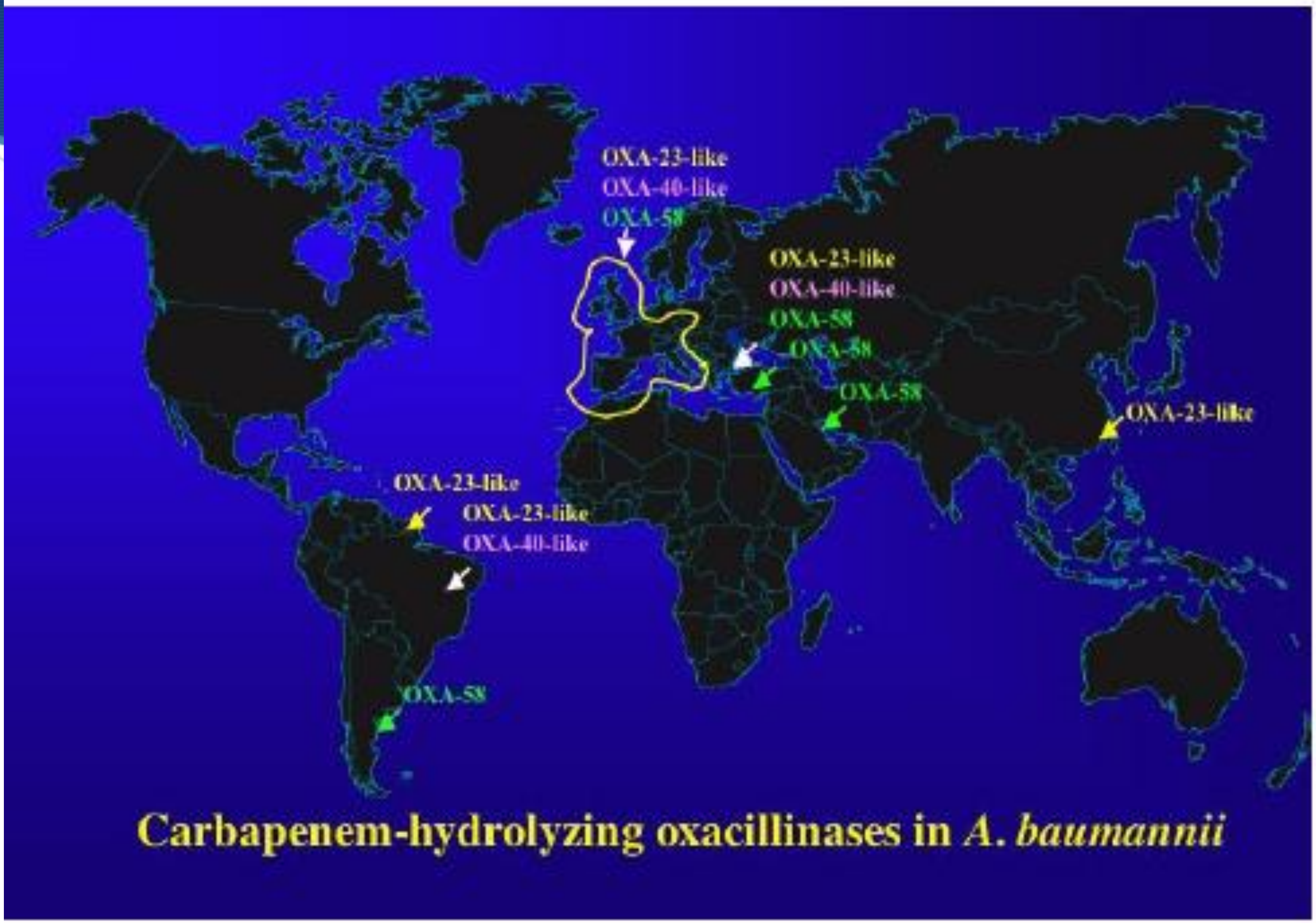
Hastane Enfeksiyonlarında

Karbapenem dirençli *Acinetobacter baumannii*
(2008-2013)



Dirençli izolatlar / Test edilen izolat sayısı X 100

Erhan Kabasakal


OXA-23-like
OXA-40-like
OXA-58
OXA-23-like
OXA-40-like
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OXA-58
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OXA-23-like
OXA-23-like
OXA-23-like
OXA-40-like
OXA-58
Carbapenem-hydrolyzing oxacillinases in *A. baumannii*

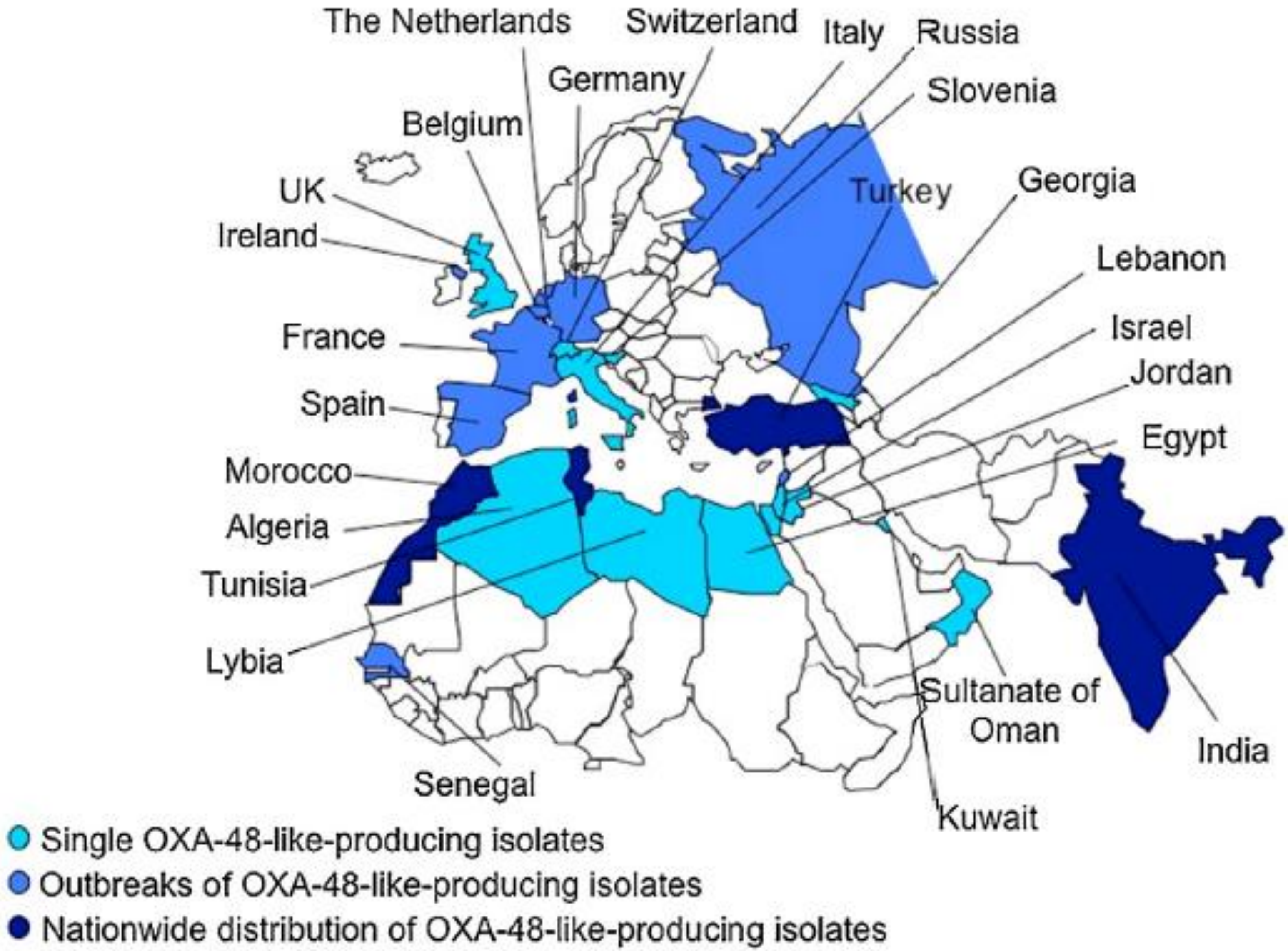


Fig. 2. Worldwide spread of OXA-48 producing strains.
Diffusion des souches OXA-48 dans le monde.

Blood stream infections due to OXA-48-like carbapenemase-producing *Enterobacteriaceae*: treatment and survival

Ilker Inanç Balkan [a,*], Gökhan Aygün [b], Selda Aydın [a], Sibel Islak Mutcalı [a], Zehra Kara [c], Mert Kuşkucu [b], Kenan Midilli [b], Vicdan Şemen [b], Şükrü Aras [d], Mücahit Yemişen [a], Bilgül Mete [a], Reşat Özaras [a], Neşe Saltoğlu [a], Fehmi Tabak [a], Recep Öztürk [a]

Patient characteristics

	Total ($n = 36$)	Survivors[a] ($n = 18$)	Non-survivors[a] ($n = 18$)	p-Value[b]
Demographics				
Age, years, mean ± SD	54.9 ± 15.8	56.2 ± 15.6	53.5 ± 16.4	0.606
Gender, male, n (%)	18 (50)	9 (50)	9 (50)	1
Unit of hospitalization, n (%)				0.6
Internal medicine	15 (41.6)	6 (53)	9 (50)	
Intensive care	14 (38.8)	8 (44)	6 (33)	
Surgical	7 (19.4)	4 (22)	3 (16)	
Hospital length of stay, mean ± SD	71.8 ± 52.1	70.8 ± 47.2	71.85 ± 63.9	0.854

KPC

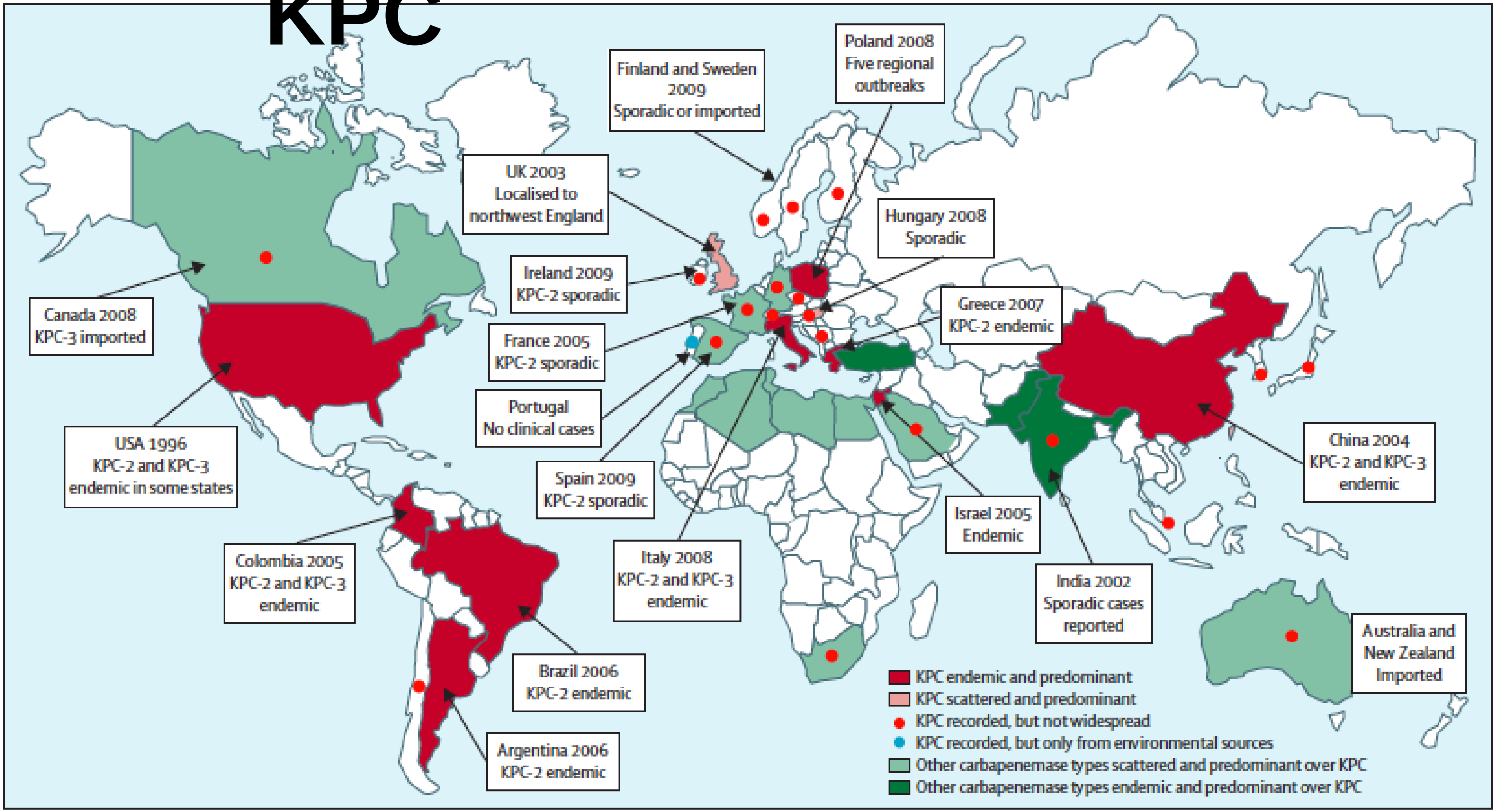
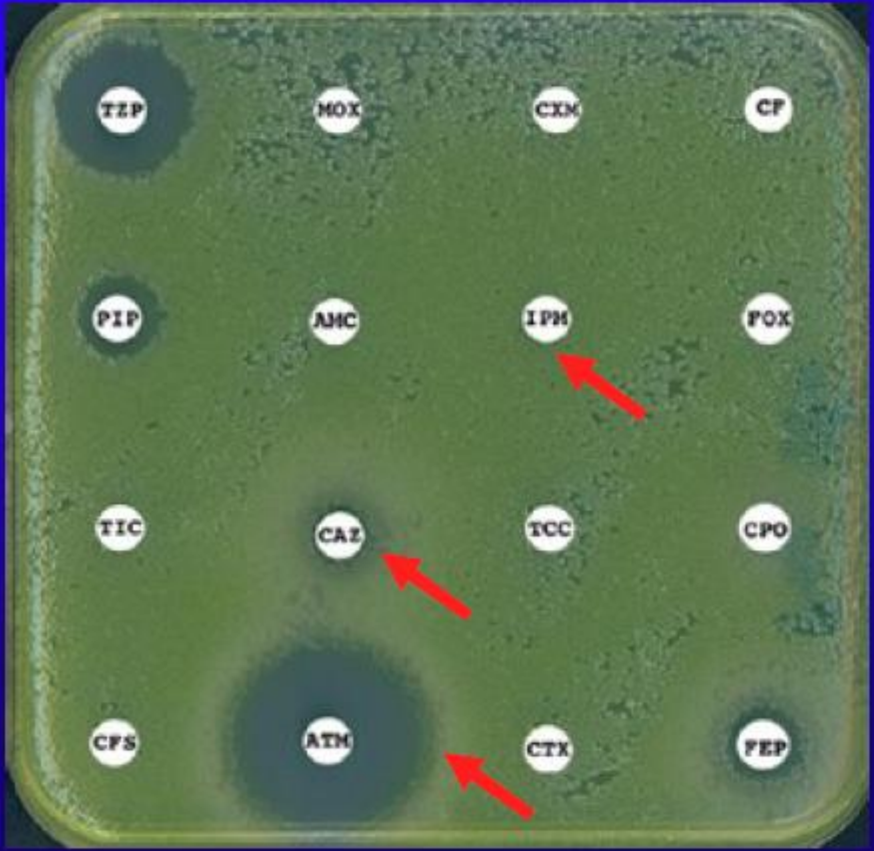


Figure: Epidemiological features of producers of *Klebsiella pneumoniae* carbapenemases by country of origin
Other carbapenemase types include VIM, OXA-48, or NDM. KPC=*Klebsiella pneumoniae* carbapenemase.

Lancet Infect Dis 2013; 13: 785–96

Metallo-enzymes; class B carbapenemases



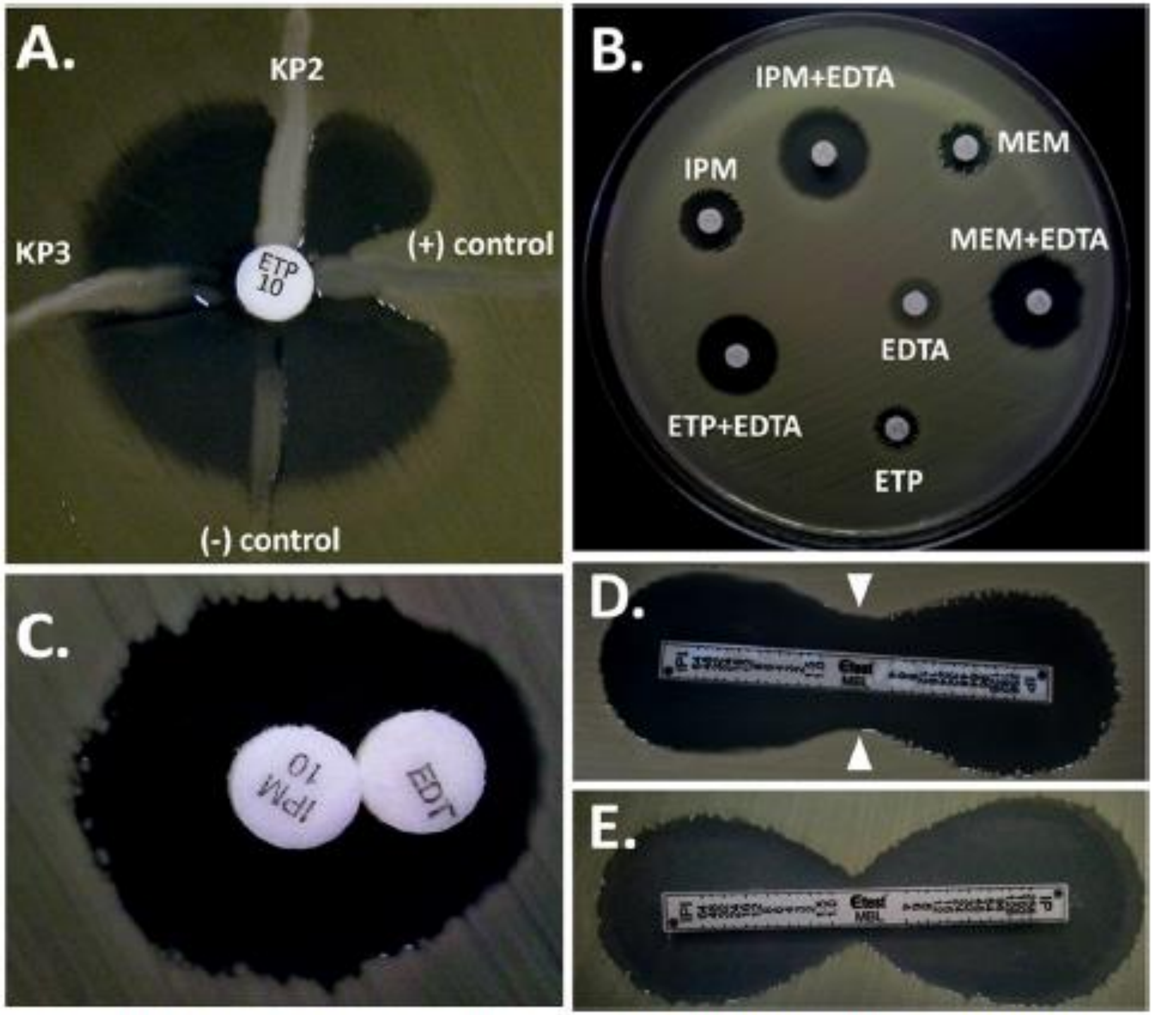


FIG. 1. Phenotypic detection of carbapenemases in a *K. pneumoniae* NDM-1 strain isolated from a nasal wash specimen (KP2). (A) Modified Hodge test, using ETP, for detection of carbapenemase, performed by the CLSI reference method. (B) Carbapenem-EDTA combined disk test for MBL. The *K. pneumoniae* isolate was inoculated to the surface of a Mueller-Hinton agar plate. Disks containing 10 μg/ml ETP, IMP, and MEM alone or ETP, IMP, and MEM plus 10 μl of 0.5 M EDTA (pH 8.0) were placed on the agar. EDTA was also added to a blank disk as a control. (C) EDTA-IMP disk synergy test for MBL. (D) Equivocal MBL Etest result demonstrating a large zone of inhibition. Arrowheads indicate the deformation of the ellipse (i.e., phantom zone). (E) Negative (control) MBL Etest results demonstrating a characteristic sharp-edged ellipse and a large zone of inhibition.

NDM-Niye Hindistan?????

- Hindistanda antibiyotik satışları serbest
- Jenerik ilaç cenneti
- Karbapenem kullanımı gelişmiş ülkelere kıyasla 25 kat yüksek
- Hijyen kötü-musluk suyu dahi kontamine
- %5-15 taşıyıcılık

Figure 1.3 Worldwide distribution of different metallo-beta-lactamases

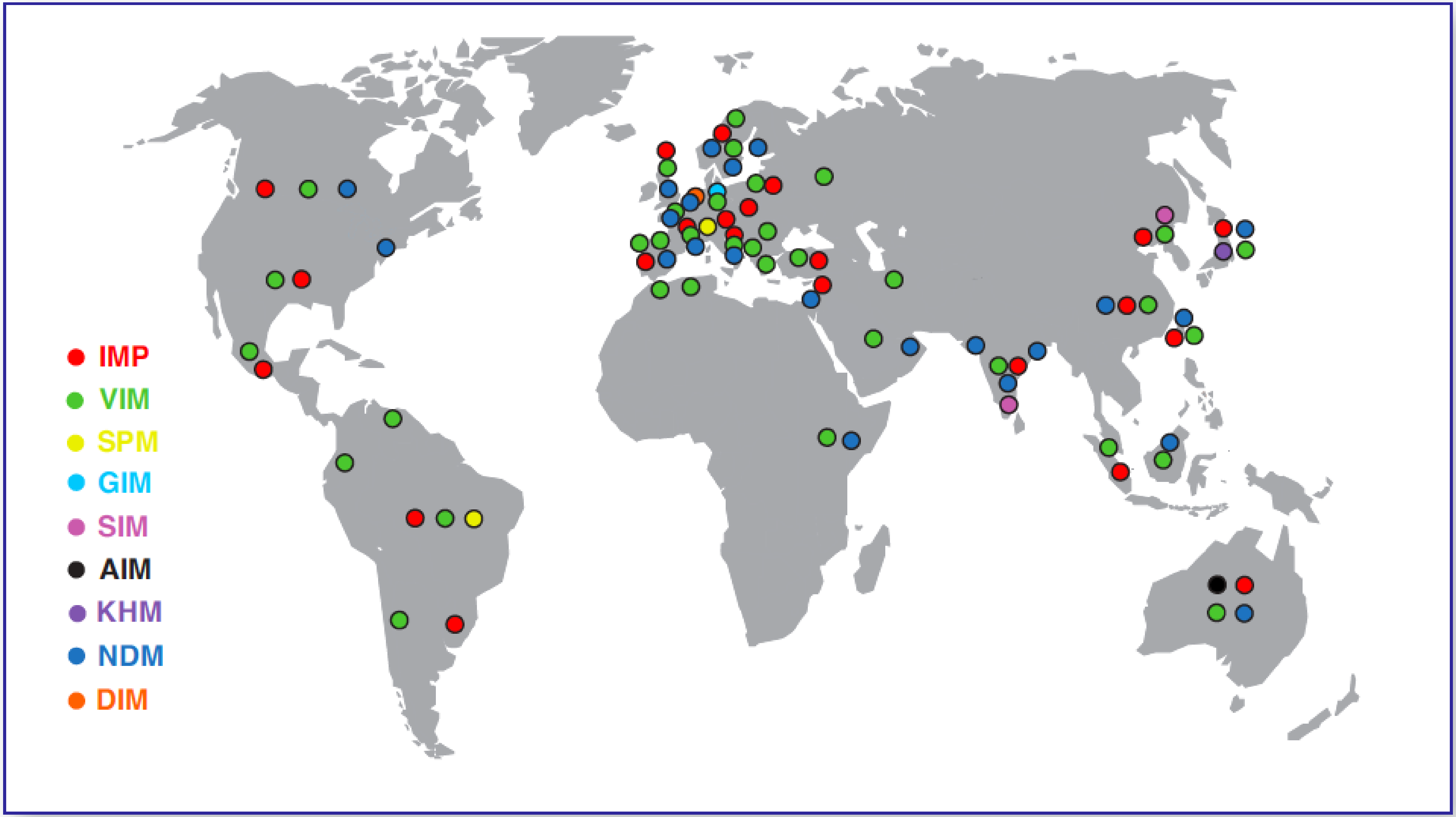


Figure 4.1 Annual antibiotic use for human and veterinary practice in Denmark

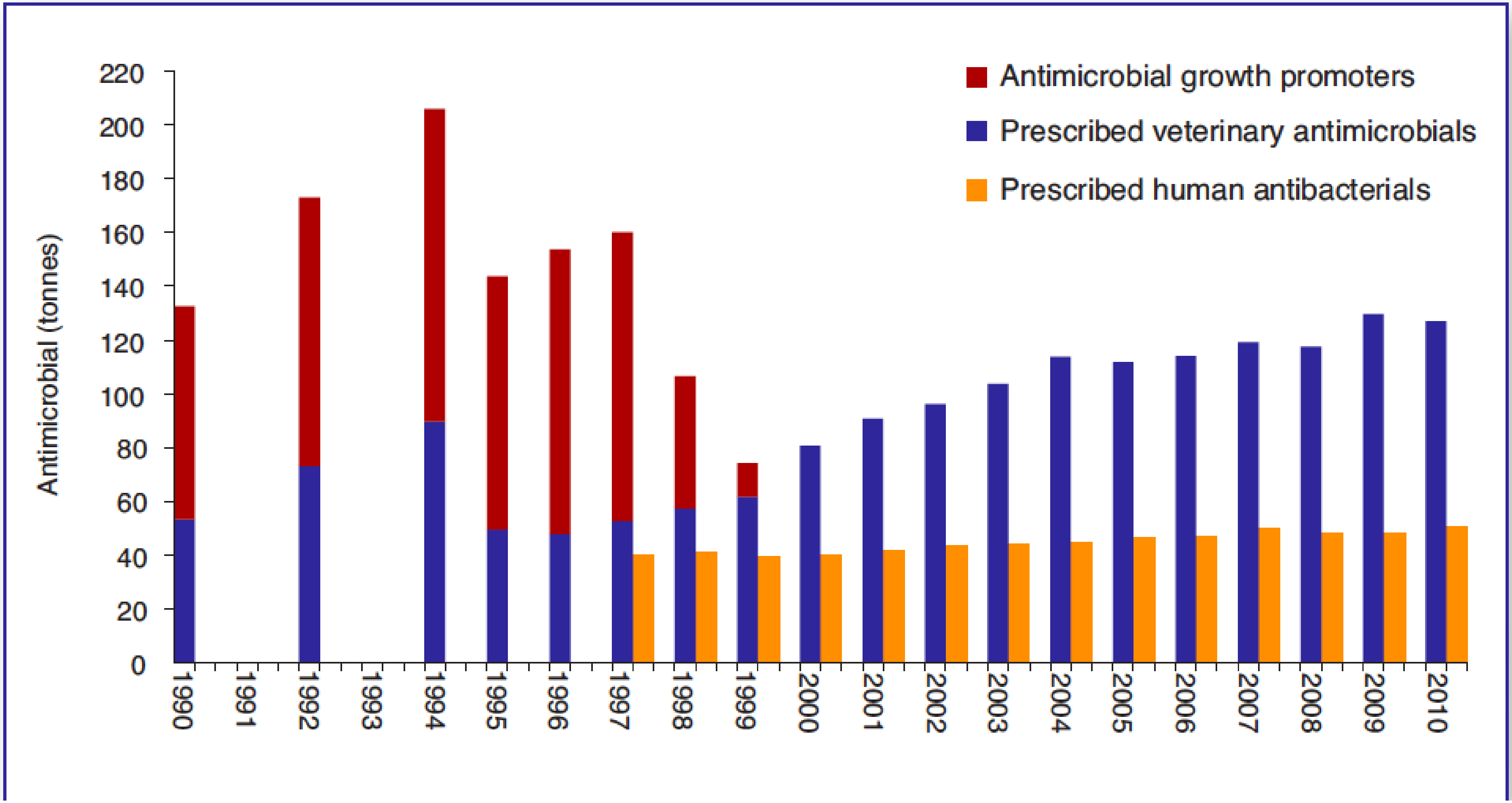
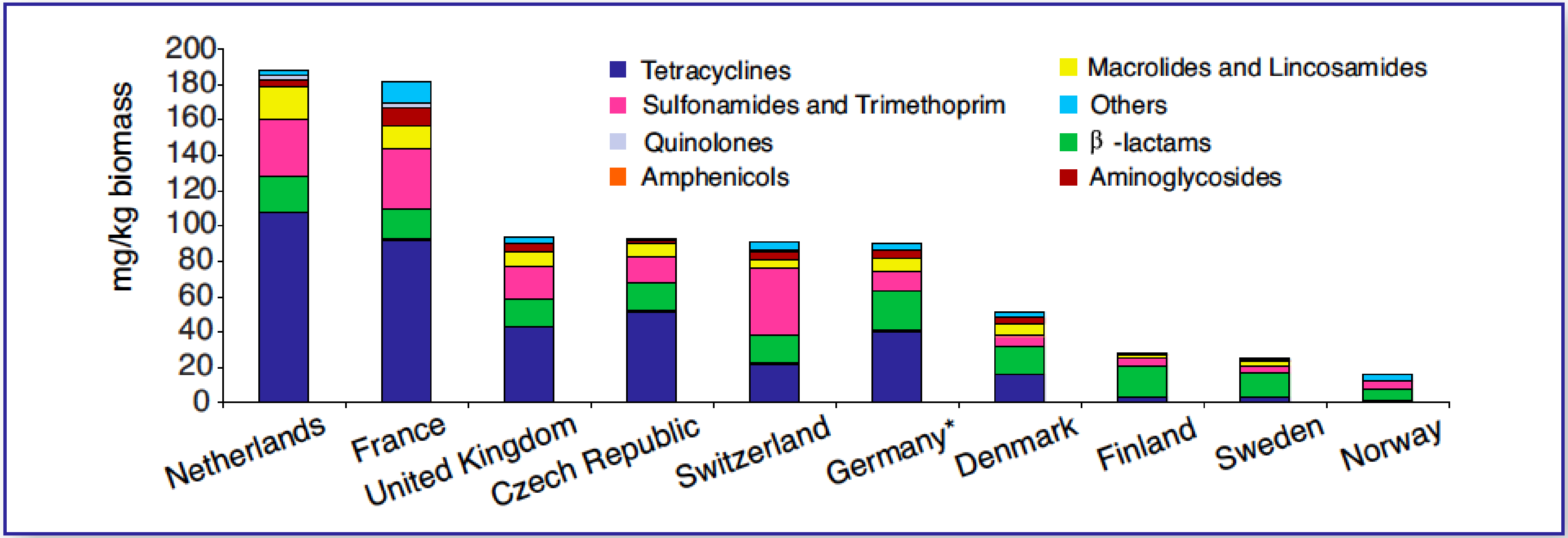


Figure 4.3 Estimated antimicrobial use to produce one kilogram of meat in different countries



Amounts in mg of veterinary antibacterial agents sold in 2007 per kg biomass of pig meat, poultry meat and cattle meat produced plus estimated live weight of dairy cattle. *2005 data

Source: Reproduced from [122] with permission from Oxford University Press.

TABLE 19-2 Ambler Classification of β-Lactamases

Class	*Active Site*	*Enzyme Type*	*Substrates*	*Examples*
A	Serine	**Penicillinases**		
		Broad-spectrum	Benzylpenicillin, aminopenicillins, carboxypenicillins, ureidopenicillins, narrow-spectrum cephalosporins	PC1 in *Staphylococcus aureus* TEM-1, SHV-1 in *Escherichia coli, Klebsiella pneumoniae*, and other gram-negative bacteria
		Extended-spectrum (ESBL)	Substrates of broad-spectrum plus oxymino-β-lactams (cefotaxime, ceftazidime, ceftriaxone) and aztreonam	In Enterobacteriaceae: TEM-derived, SHV-derived, CTX-M–derived; PER-1, VEB-1, VEB-2, GES-1, GES-2, IBC-2 in *Pseudomonas aeruginosa*
		Carbapenemases	Substrates of extended-spectrum plus cephamycins and carbapenems	KPC-1, KPC-2, KPC-3 in *K. pneumoniae*; NMC/IMI, SME family
B	Metallo-β-lactamases (Zn^{2+})	**Carbapenemases**	Substrates of extended-spectrum plus cephamycins and carbapenems	IMP, VIM, GIM, SPM, SIM lineages in *P. aeruginosa*, *Acinetobacter* spp.
C	Serine	**Cephalosporinases**	Substrates of extended-spectrum plus cephamycins	AmpC-type enzymes in Enterobacteriaceae, *Acinetobacter baumannii*
D	Serine	**Oxacillinases**		
		Broad-spectrum	Aminopenicillins, ureidopenicillins, cloxacillin, methicillin, oxacillin, and some narrow-spectrum cephalosporins	OXA-family in *P. aeruginosa*
		Extended-spectrum	Substrates of broad-spectrum plus oxymino-β-lactams and monobactam	OXA-derived in *P. aeruginosa*
		Carbapenemases	Substrates of extended-spectrum plus cephamycins and carbapenems	OXA-derived in *Acinetobacter* spp.

Adapted from Jacoby GA, Munoz-Price LS. The new β-lactamases. *N Engl J Med*. 2005;352:380-391.

DÜZELTME

Table 1. Prominent Mechanisms of Carbapenem Resistance Among Enterobacteriaceae

Carbapenemases	Ambler Molecular Class	Requirement for Enzymatic Activity	Gene Location	Geographic Distribution[a] [6, 11–14]
KPC	A	Serine	Plasmid	US, Colombia, Brazil, Argentina, Greece, Italy, Malta, Israel, China
NDM	B	Zinc	Plasmid	India, Pakistan, Bangladesh, United Kingdom
VIM	B	Zinc	Plasmid	Greece
IMP	B	Zinc	Plasmid	Japan, Taiwan
OXA-48-types	D	Serine	Plasmid	Turkey, Morocco, Algeria, Tunisia, India
Other mechanisms				
ESBL or AmpC-type β-lactamase + OMP mutation	A/C	Serine	Plasmid or chromosomal	Worldwide[b]

Abbreviations: ESBL, extended-spectrum β-lactamase; IMP, "active on imipenem"; KPC, *Klebsiella pneumoniae* carbapenemase; NDM, New Delhi metallo-β-lactamase; OMP, outer membrane porin; VIM, Verona integron–encoded metallo-β-lactamase.

[a] Locations with the highest prevalence for each carbapenem resistance mechanism.

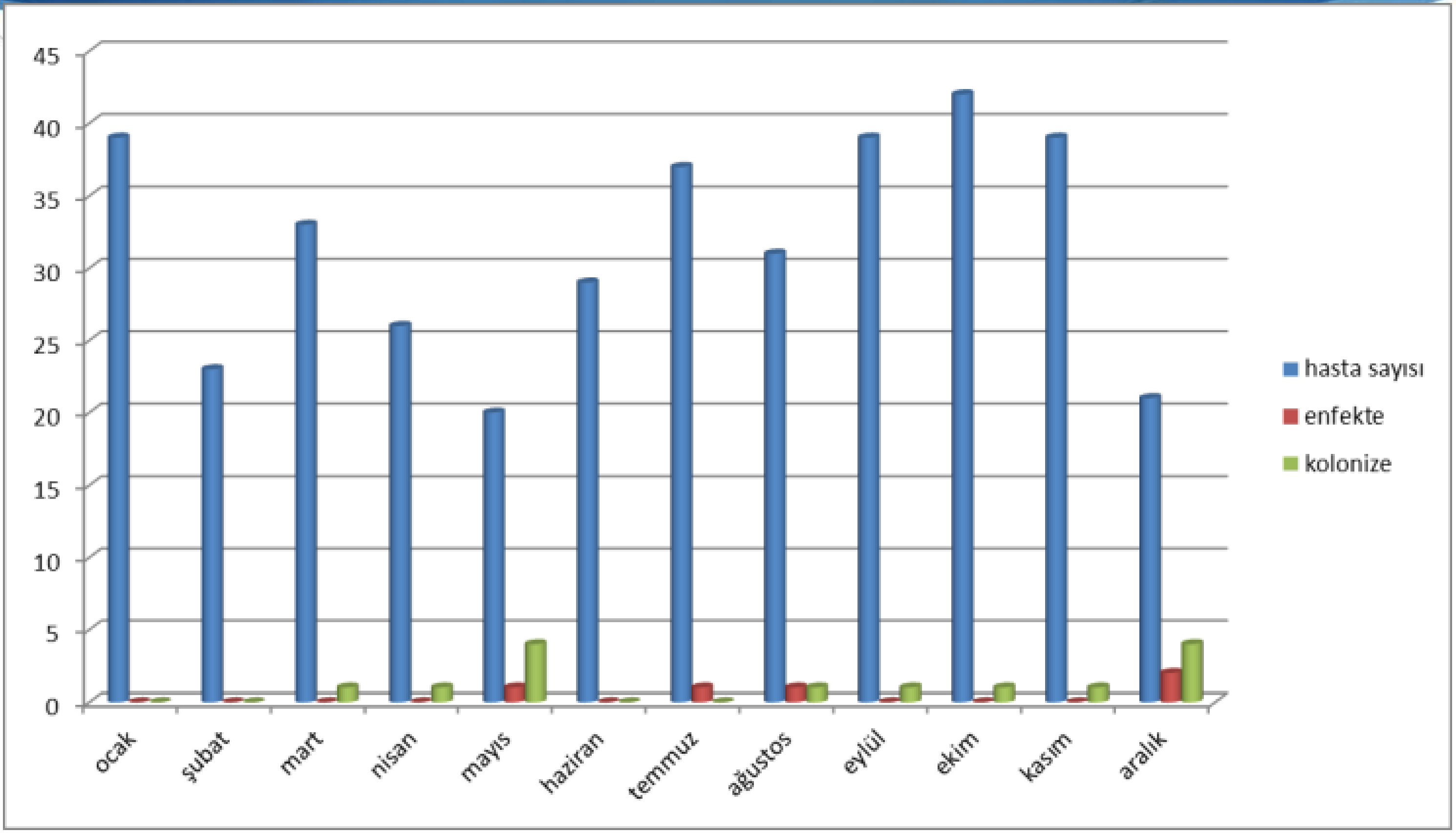
[b] Carbapenem resistance is more commonly due to carbapenemase production than these mechanisms in the geographic locations listed above.

Comparison of the two most common causes of carbapenem resistance in Enterobacteriaceae: Klebsiella pneumoniae carbapenemase (KPC) and New Delhi Metallo-β-Lactamase (NDM) type β-lactamases	KPC	NDM
β-lactamase type	Serine	Metallo-β-lactamase
Ambler cass	A	B
Most commonly affected species	K. pneumoniae	K. pneumoniae
Other species commonly affected	E. coli, E. cloacae	E. coli, E. cloacae
Common MLST types	ST258	Variable
Geographic epicenter	NE USA	India, Pakistan
β-lactam antibiotics affected	Penicillins, cephalosporins, carbapenems	Penicillins, cephalosporins, carbapenems
Phenotypic detection	Modified Hodge Test (MHT) positive	Unknown (positive MHT likely)
Inhibitors	Boronic acid	EDTA

Marmara PEAH karbapenemaz verisi 2014-2015

- 18 hasta
- 17 K.pneumoniae
  - 9 OXA 48;
  - 8 NDM
    (bir suş: NDM ve OXA 48 birlikte)
- 1 E.cloacae IMP

MARMARA PEAH 2014 DAHİLİ YBÜ CRE ETKEN/KOLONİZASYON DAĞILIMI



Carbapenemases in *Enterobacteriaceae*

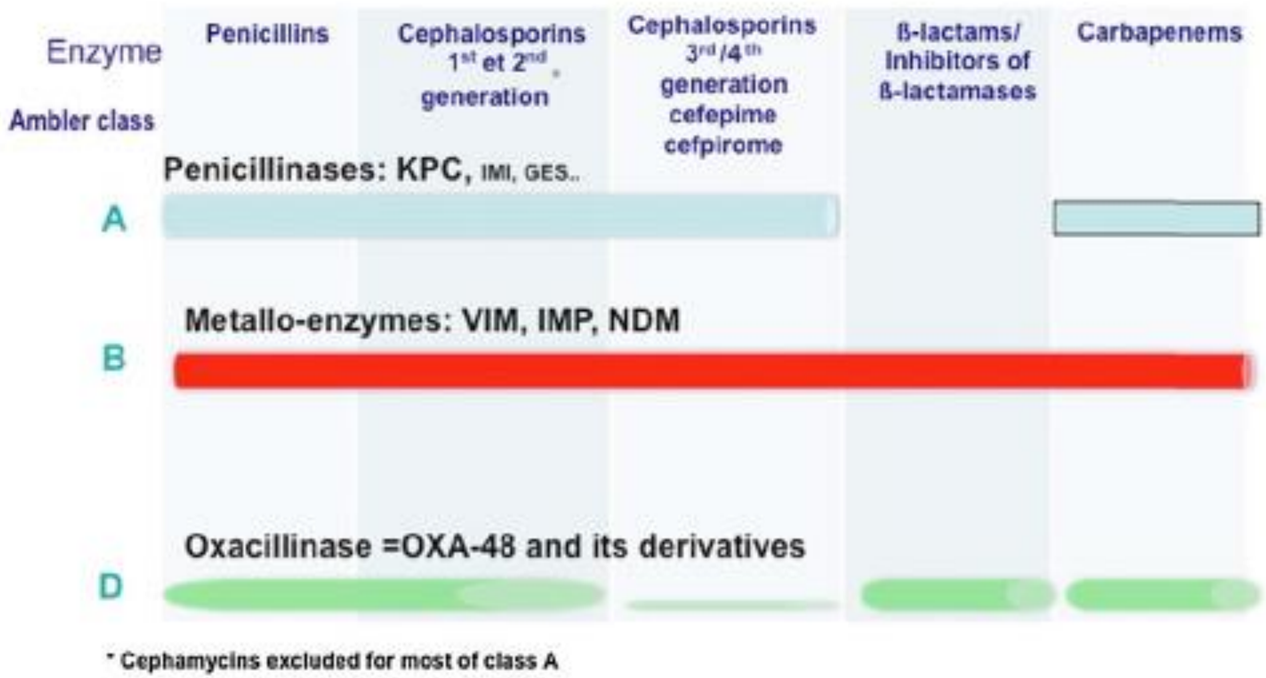


Fig. 1. Activity spectrum of carbapenemases in Enterobacteriaceae.

P. Nordmann / Médecine et maladies infectieuses 44 (2014) 51–56

Deaths Attributable to Carbapenem-Resistant *Enterobacteriaceae* Infections
Matthew E. Falagas et al.

2012 dek yapılmış 12 çalışma

7 çalışmada %26 ila %44 karbepenem direnci ilişkili mortalite

Maliyet

- 4.55 kat maliyet artışı
- 11.9 kat antibiyotik maliyet artışı

- Yenilmez E et al; 2015 KLİMİK

Karbapenemaz risk faktörleri

- **Antibiyotik kullanımı**
- **Diyabet**
- **Travma**
- **Malignensi**
- **MV**
- **Kateter**
- **Uluslararası seyahat**

Organism & carbapenemase	Imipenem MIC (µgm/ml)					Meropenem MIC (µgm/ml)				
	2	4	8	16	64	2	4	8	16	64
VIM (6)										
E. coli (2)	-	-	1	1	-			-	1	1
A. baumannii (1)	-	-	-	1	-			-	-	1
P. aeruginosa (3)	1	2	-	-	-		1	1	1	-
KPC (15)										
E. coli (1)	1	-	-	-	-	-	-	1	-	-
K. pneumoniae (5)	-	-	1	4	-	-	-	-	2	3
A. baumannii (9)	-	-	-	8	1	-	-	-	-	9
NDM-1 (59)										
E. coli (14)	2	4	6	2	-	-	3	4	5	2
K. pneumoniae (30)	-	3	8	19	-	-	-	3	8	19
A. baumannii (15)	-	-	-	14	1	-	-	-	-	15

[Table/Fig-4]: Correlation of MIC with carbapenemase production among GNB

DOI: 10.7860/JCDR/2014/10794.5322

Original Article

Microbiology Section

Comparative Evaluation of Multiplex PCR and Routine Laboratory Phenotypic Methods for Detection of Carbapenemases among Gram Negative Bacilli

RACHANA SOLANKI, LAVANYA VANJARI, SREEVIDYA SUBRAMANIAN, APARNA B, NAGAPRIYANKA E, VEMU LAKSHMI

Journal of Clinical and Diagnostic Research. 2014 Dec, Vol-8(12): DC23-DC26

FENOTİPİK ÖZELLİKLER

	AMX	AMC	TZP	CTX	CAZ	IMP	ETP	MER	ATM
KPC	R	S/I	R	R	R	S/I/R	I/R	S/I/R	R
KPC + ESBL	R	I/R	R	R	R	I/R	I/R	I/R	R
IMP/VIM/NDM	R	R	I/R	R	I/R	S/I/R	I/R	S/I/R	S
IMP/VIM/NDM + ESBL	R	R	I/R	R	R	I/R	R	S/I/R	R
OXA-48/OXA-181	R	R	S/I/R	S/I	S	S/I	S/I	S/I	S
OXA-48/OXA-181 + ESBL	R	R	I/R	R	R	I/R	I/R	I/R	R

AMX, amoxycillin; AMC, amoxycillin–clavulanic acid; TZP, piperacillin–tazobactam; CTX, cefotaxime; CAZ, ceftazidime; IMP, imipenem; ETP, ertapenem; MER, meropenem; ATM, aztreonam.

Identification and screening of carbapenemase-producing *Enterobacteriaceae*

P. Nordmann[1], M. Gniadkowski[2], C. G. Giske[3], L. Poirel[1], N. Woodford[4], V. Miriagou[5] and the European Network on Carbapenemases*

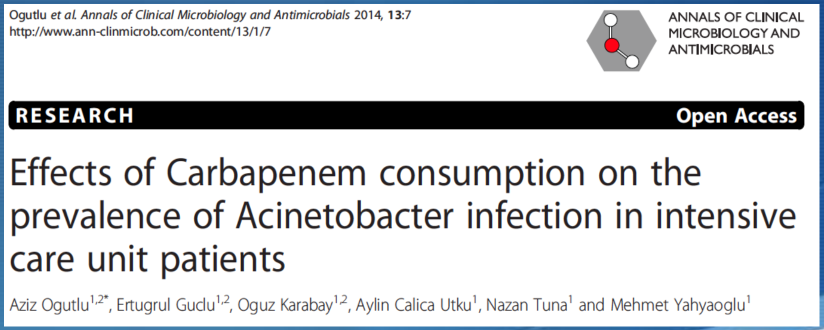
HIZLI TANIMA

			E faecium, Listeria spp			
Nucleic acid microarray BC-GN	Nanosphere, Inc, Northbrook, IL	Blood	*Escherichia coli/Shigella* spp, *Klebsiella pneumonia, Klebsiella oxytoca, P aeruginosa, Serratia marcescens, Acinetobacter* spp, *Proteus* spp, *Citrobacter* spp, *Enterobacter* spp	KPC, NDM, CTX-M, VIM, IMP, OXA	2.5	Yes
Multiplex nucleic acid amplification test	BioFire, Inc, Salt Lake City, UT	Blood	*Enterococcus* spp, *Listeria monocytogenes, Staphylococcus* spp, *S aureus, Streptococcus* spp, *S agalactiae, S pyogenes, S pneumoniae, A baumannii, Haemophilus influenzae, Neisseria meningitides, P aeruginosa, E cloacae complex, E coli, K oxytoca, K pneumoniae, S marcescens, Proteus* spp, *Enterobacteriaceae* spp, *C albicans, C parapsilosis, C tropicalis, C glabrata, C krusei*	*mecA, vanA, vanB*, KPC	1	Yes

licrobiology Laboratory and ASP

CHROMAGAR
CHROMADID

Gibi ayırt edici besiyerleri



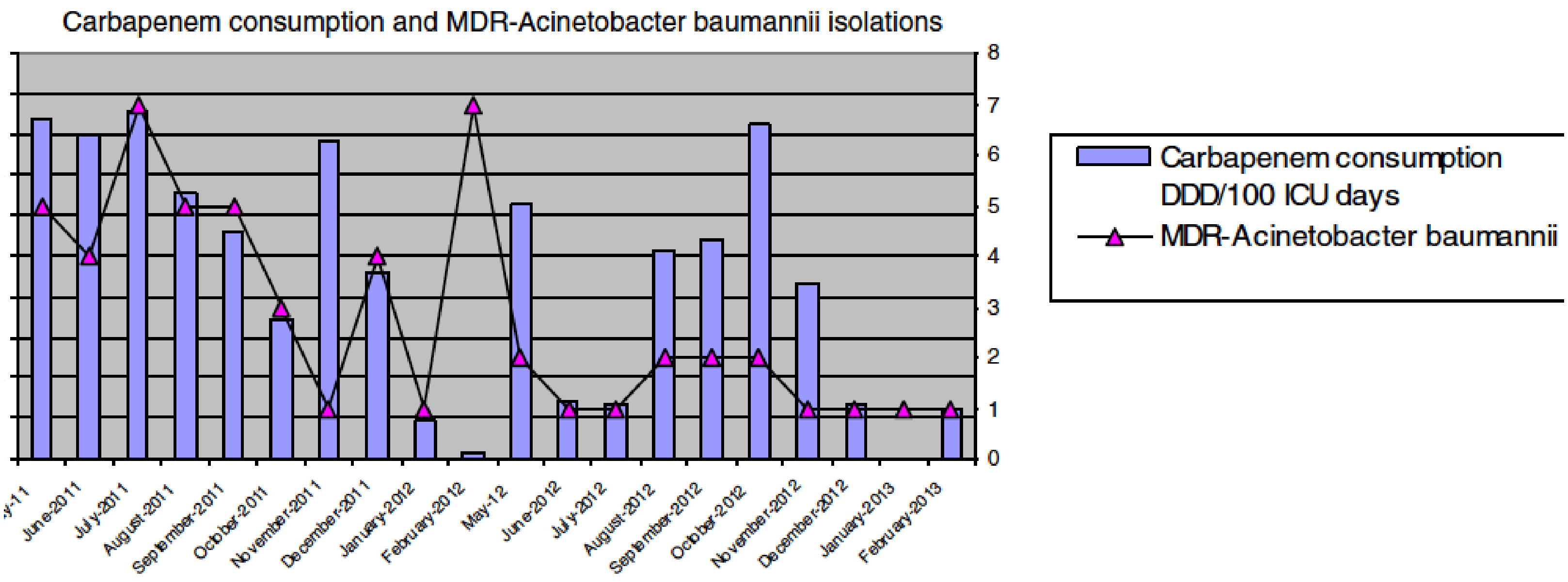
Ogutlu *et al.* *Annals of Clinical Microbiology and Antimicrobials* 2014, **13**:7
http://www.ann-clinmicrob.com/content/13/1/7

ANNALS OF CLINICAL MICROBIOLOGY AND ANTIMICROBIALS

RESEARCH **Open Access**

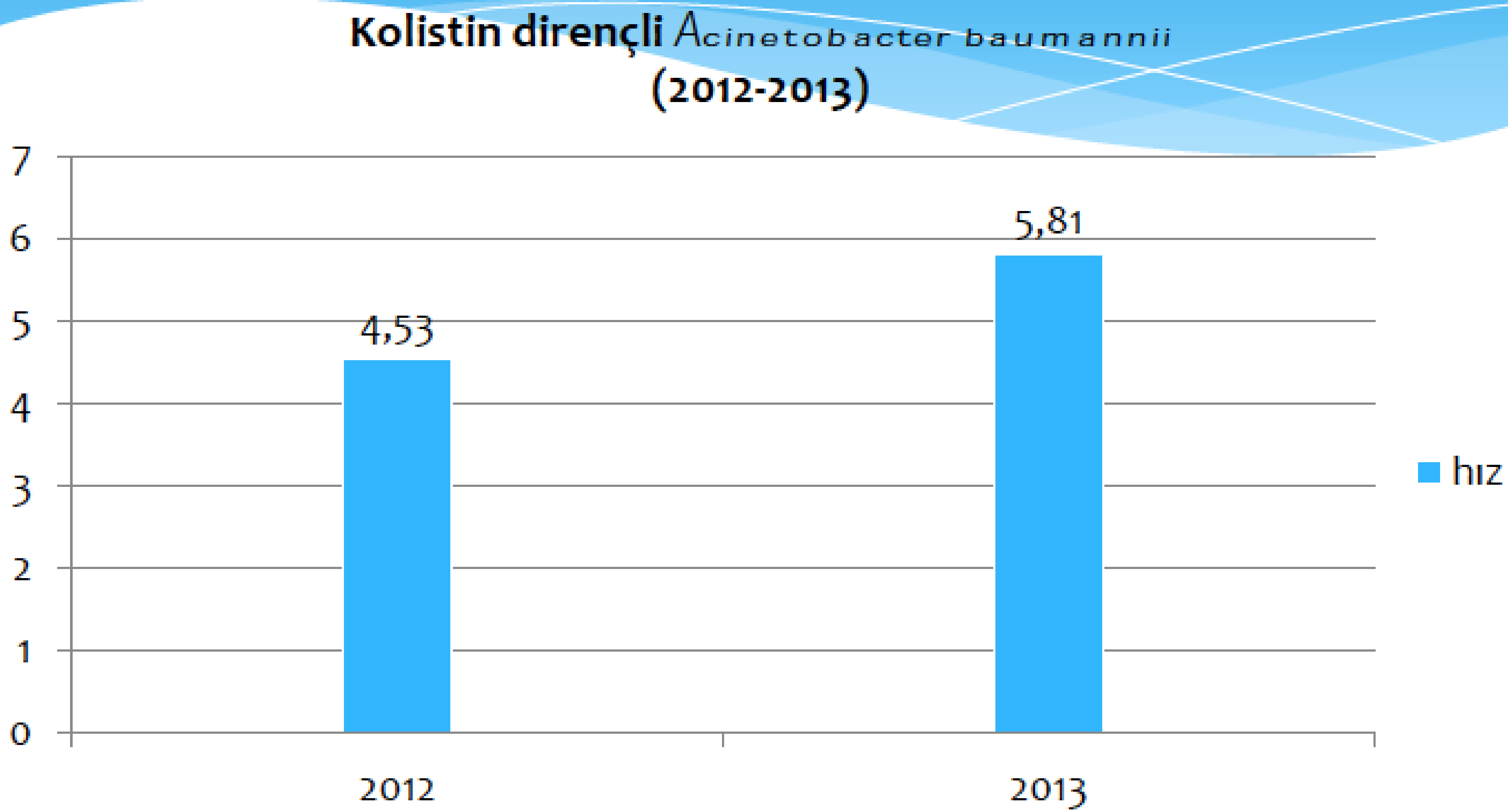
Effects of Carbapenem consumption on the prevalence of Acinetobacter infection in intensive care unit patients

Aziz Ogutlu[1,2*], Ertugrul Guclu[1,2], Oguz Karabay[1,2], Aylin Calica Utku[1], Nazan Tuna[1] and Mehmet Yahyaoglu[1]



ure 2 Carbapenem consumption and MDR-Acinetobacter baumannii isolations.

Hastane Enfeksiyonlarında



Dirençli izolatlar / Test edilen izolat sayısı X 100

Erhan Kabasakal

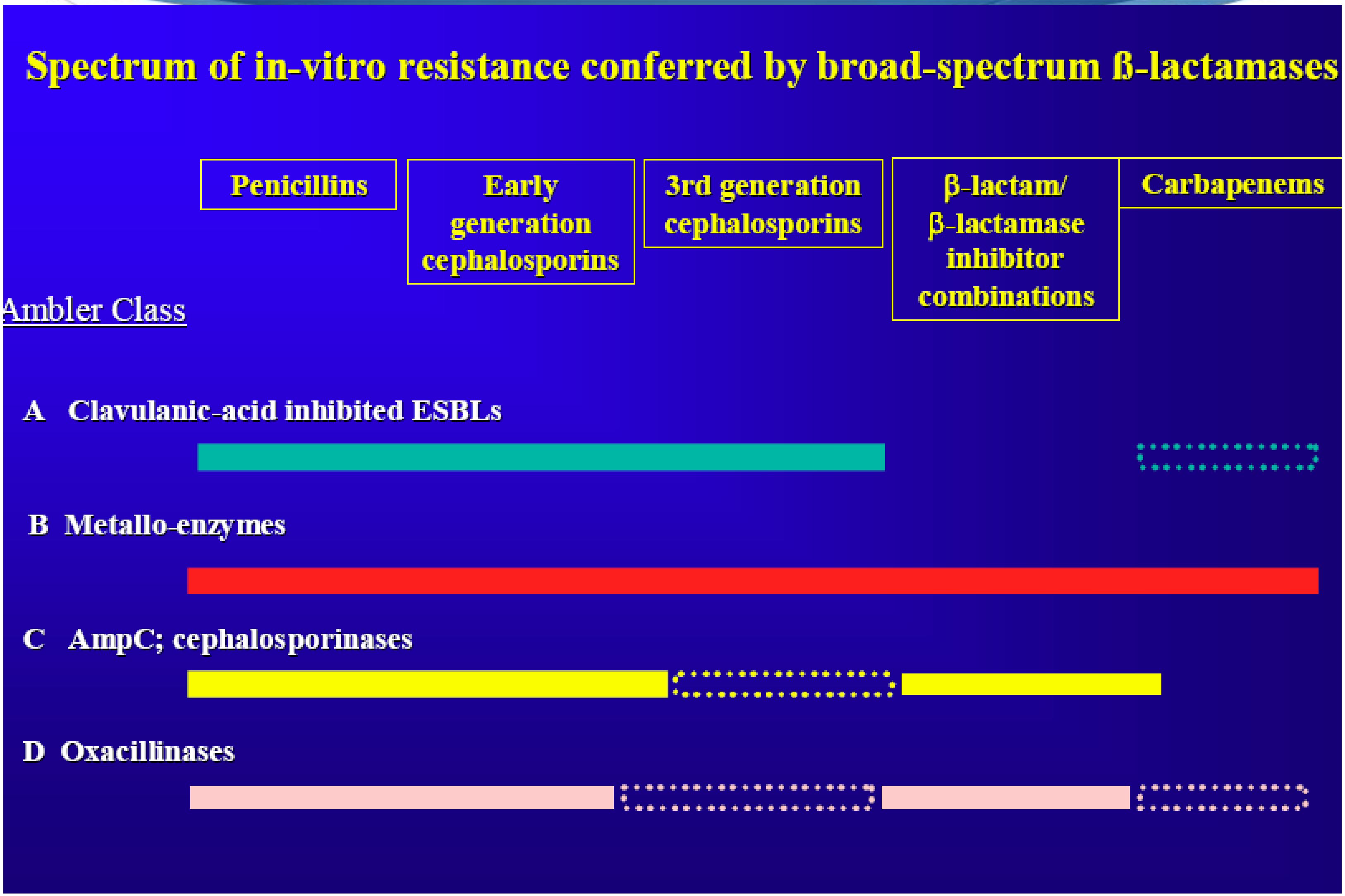
Yoğun Bakım Ünitelerinde *Acinetobacter baumannii* Kolonizasyon ve Enfeksiyon Gelişimine Yol Açan Risk Faktörleri ile Bulaşma Yolları ve Dinamiklerinin Belirlenmesi

Prof.Dr.Önder Ergönül
Prof.Dr.Lütfiye Mülazımoğlu Durmuşoğlu
Prof.Dr.Volkan Korten
Prof.Dr.Murat Akova
Prof.Dr.Yeşim Çetinkaya Şardan
Prof.Dr.Recep Öztürk
Uz. Dr. Birgül Mete
Prof.Dr.Oral Öncül
Prof. Dr. Halis Akalın
Doç.Dr.Melda Sınırtaş

Sıra	Merkez-Köken No.	OXA-51	OXA-23	OXA-24	OXA-58
1	MAR-88	+	+		
2	MAR-94	+	+		
3	MAR-97	+	+		
4	MAR-109	+			
5	MAR-111	+			+

Yoğun Bakım Öncesi Antibiyotik kullanımı			
Kinolonlar	27 (19)	35 (16)	0.392
Piperasilin-tazobaktam	10 (7)	10 (7)	0.279
Karbapenemler	21 (15)	16 (7)	0.016
3. Jenerasyon sefalosporinler	16 (11)	21 (9)	0.578
Yatış sırasında piperasilin tazobaktam kullanımı	25 (17)	37 (16)	0.761
Yatış sırasında karbapenem kullanımı	21 (15)	18 (8)	0.039

Tablo 4'e göre, ölenlerin yaş ortalaması daha yüksektir (65 vs 61, p=0.053). İnvazif mekanik ventilatör ve sonda kullanımı, apache skorunun yüksek olması ve hastaneye yatmadan önce piperasilin tazobaktam veya karbapenem kullanımı ölüm için risk oluşturmaktadır.



Spectrum of in-vitro resistance conferred by broad-spectrum ß-lactamases
Penicillins
Early generation cephalosporins
3rd generation cephalosporins
β-lactam/ β-lactamase inhibitor combinations
Carbapenems
Ambler Class
A Clavulanic-acid inhibited ESBLs
B Metallo-enzymes
C AmpC; cephalosporinases
D Oxacillinases

KORUNMA-CDC/HICPAC

- Hasta güvenliği
- Sağlık personeli eğitimi
- Uygun antibiyotik kullanımı
- Surveyans

Management of Multidrug-Resistant Organisms In Healthcare Settings, 2006
Jane D. Siegel, MD; Emily Rhinehart, RN MPH CIC; Marguerite Jackson, PhD;Linda Chiarello, R

CDC/HICPAC II

- İnfeksiyon kontrol önlemleri
- ÇD GNB-decolonizasyon önerilmez
- Kohort oluşturma
- Adanmış oda-eşya-personel

- Çoklu önlemler
- kısıtlamalar
- antibiyotik heterojenitesi,
- tedavi sürelerini kısaltmak ve daraltmak veya de-eskalasyon


Infection Control Professional
Hospital Epidemiologist
Hospital Director
Director, Information Systems
Managed Care Organization Representative
Director, Antimicrobial Management Program
Director, Clinical Microbiology
Infectious Diseases Faculty
Infectious Diseases Clinical Pharmacist
Chairman, P and T Committee
Director, Outcomes Management

Journal of Clinical Microbiology, May 2007, p. 1551–1555 Vol. 45, No. 5
0095-1137/07/$08.00+0 doi:10.1128/JCM.02424-06

Surveillance Cultures and Duration of Carriage of Multidrug-Resistant *Acinetobacter baumannii*[▽]

Dror Marchaim,[1*] Shiri Navon-Venezia,[1] David Schwartz,[2] Jalal Tarabeia,[1] Iris Fefer,[1] Mitchell J. Schwaber,[1] and Yehuda Carmeli[1]

Division of Epidemiology, Tel-Aviv Sourasky Medical Center, 6 Weizmann St., Tel-Aviv 64239, Israel,[1] and Clinical Microbiology Laboratory, Tel-Aviv Sourasky Medical Center, 6 Weizmann St., Tel-Aviv 64239, Israel[2]

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42 ay

?????:

- **Tarama**
- **Erken tanı:moleküler yöntemler?**
- **Preemptif tedavi? Empirik tedavi?**
- **Bulaş dinamikleri?**