

Global Kriz: Dirençli Gram Negatifler Son Durum

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İnfeksiyon Hst.ve Kl. Mik. ABD

Alexander Fleming..

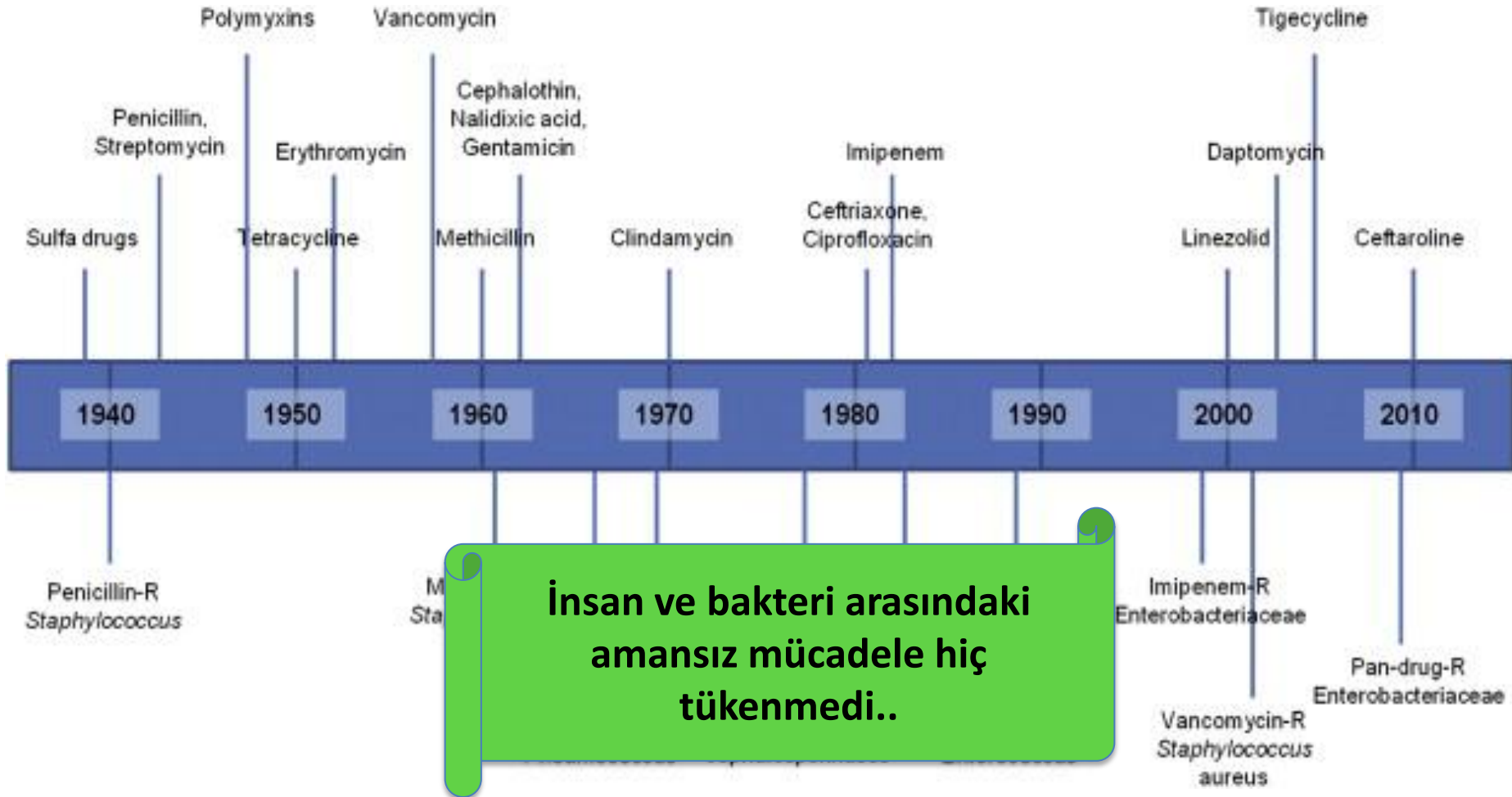


- 1928 *Penicillin*
- 1938 *Penicillin*
- Düşük konsantrasyonlarda direnç..

Tüm Antibiyotikler için geçerli olabilecek öngörü..



Antiyotik ve Direnç Gelişimi Arasındaki Amansız Takip..



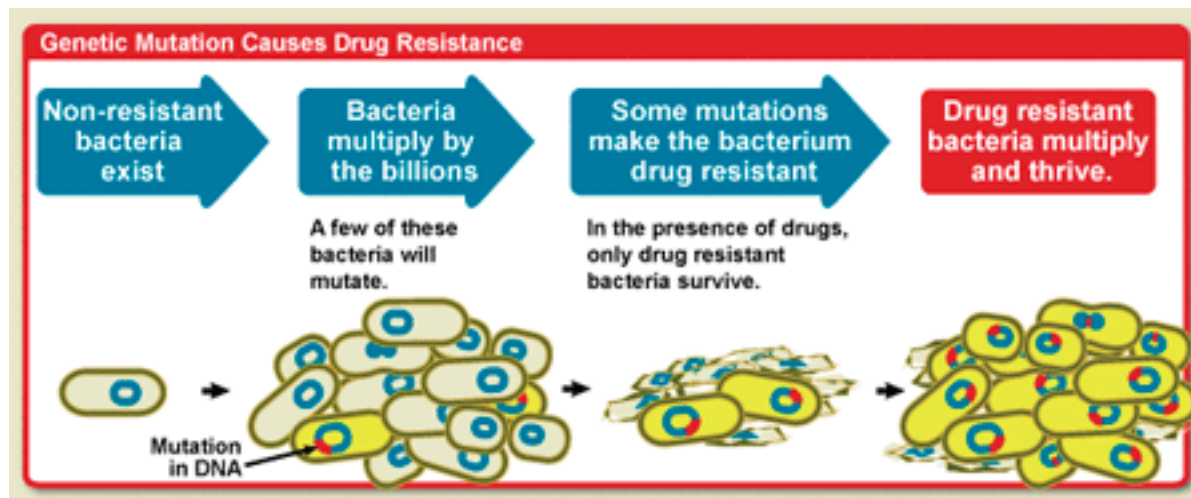
Antimikrobik Direncin Genel Mekanizmaları

Gen Mutasyonu

- Spontan gelişir
- Tek nükleotid etkilenir
- Gen başına 10^{-9} , 10^{-10}

Mobil Genetik Elemanlar

- Horizontal transfer
 - Tarsposonlar
 - İntegronlar
 - Plazmidler (Konjugasyon..)

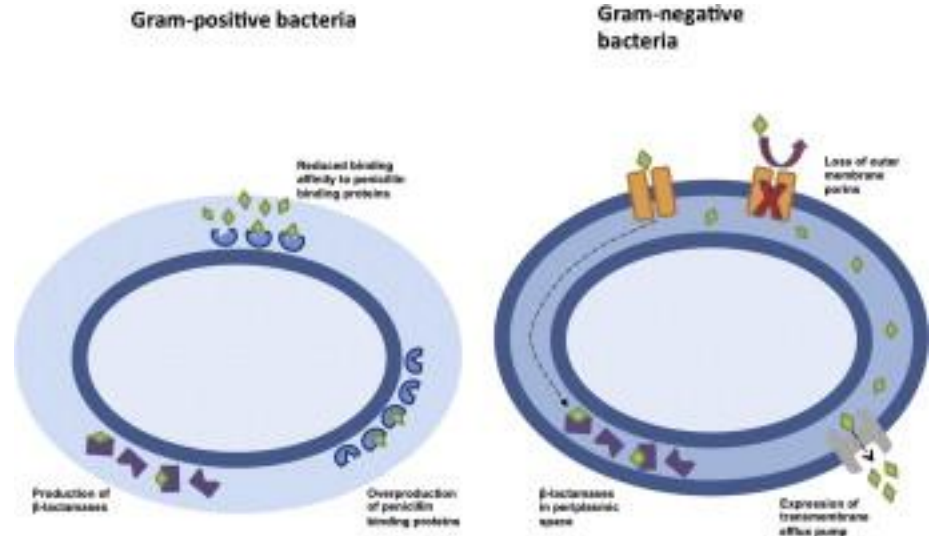


Antimikrobik Direncin Genel Mekanizmaları

İlaç Hedef Değişikliği

- AB inaktif edici enzim
- Pompa (efflux) sisteminin aktivasyonu
- Porin değişiklikleri

**“Pandrug Resistant”
bakterilerde yaygın..**



Enterobacteriaceae'larda AB Direnci

- 1940 Amp C sefalosporinazlar (*E.coli*)
- Ambler Moleküler Sınıflaması
 - Serine aktivite bölgesine göre (Class A, C, D)
 - Çinko gereksinimine göre (Class B MBL)
- Bush-Jacoby-Medeiros Fonksiyonel Sınıflaması
 - Substrat ve inhibitör özelliklerine göre
 - 1995'de tanımlandı, 2010'da düzenlendi.

Ambler	Bush-Jacoby	Özellikler	Enzim Örnekleri
A	2br	CA penisilinaza etkili	PC1
	2a	CA geniş spektrumlu enzimleri parçalar	TEM-1, 2, 13, SHV-1, 11
	2b	CA genişlemiş spektrumlu enzimi parçalar CA'ya düşük affiniteli geniş spektrumlu	TEM-3, 10, 26, SHV-2, 3, CTX-M, PER, VEB..
	2be	enzimler (İnhibitör Resistans TEMs) CA'ya rölatif dirençli GSBL	TEM 10, 31, SHV-10, 72
	2ber	CA tarafından parçalanan Carbenicillin-	TEM-50, 158
	2c	hydrolyzing enzymes	PSE-1, CARB-3
	2ce	CA tarafından parçalanan Geniş Spektrumlu Karbenisilinazlar, Sefalosporinazlar	RTG-4, CARB-10
	2e	CA tarafından parçalanan Sefalosporinazlar	CepA
	2f	Carbapenem-hydrolyzing nonmetallo-BL	KPC, SME, GES, IMI-1
B	3	Metallo-beta-lactamases	IMP, VIM, NDM-1
C	1	ACÜ-, FOX-1, MIR-1, CMY	
D	2d	Cloxacillin-hydrolyzing enzymes	OXA-1, 2, 10
	2de	CA tarafından farklı düzeyde inhibisyon	OXA-11, 15
	2df		OXA-23 51, 58
	4	CA'nın inhibe edemediği penisilinazr	B.Cepacia penisilinazları

Karbapenemler

- 1980'li yıllarda klinik kullanıma girdi
- En geniş spektrumlu antibiyotik
- ESBL ve AmpC gibi beta-laktamazların tümüne etkili
- 1980 ve 1990'lı yıllarda YBU'lerinde son tercih
- 2000 sonrası yaygın kullanım ve ESBL salgılayan suşlar da dahil GNB'lerde direnç gelişimi..
- 2010 sonrası gelişen en ciddi AB direnci..
- GLOBAL YAYILIM..

Karbapenem Kullanımı Giderek Artıyor



Karbapeneme Dirençli Enterikler (CRE)

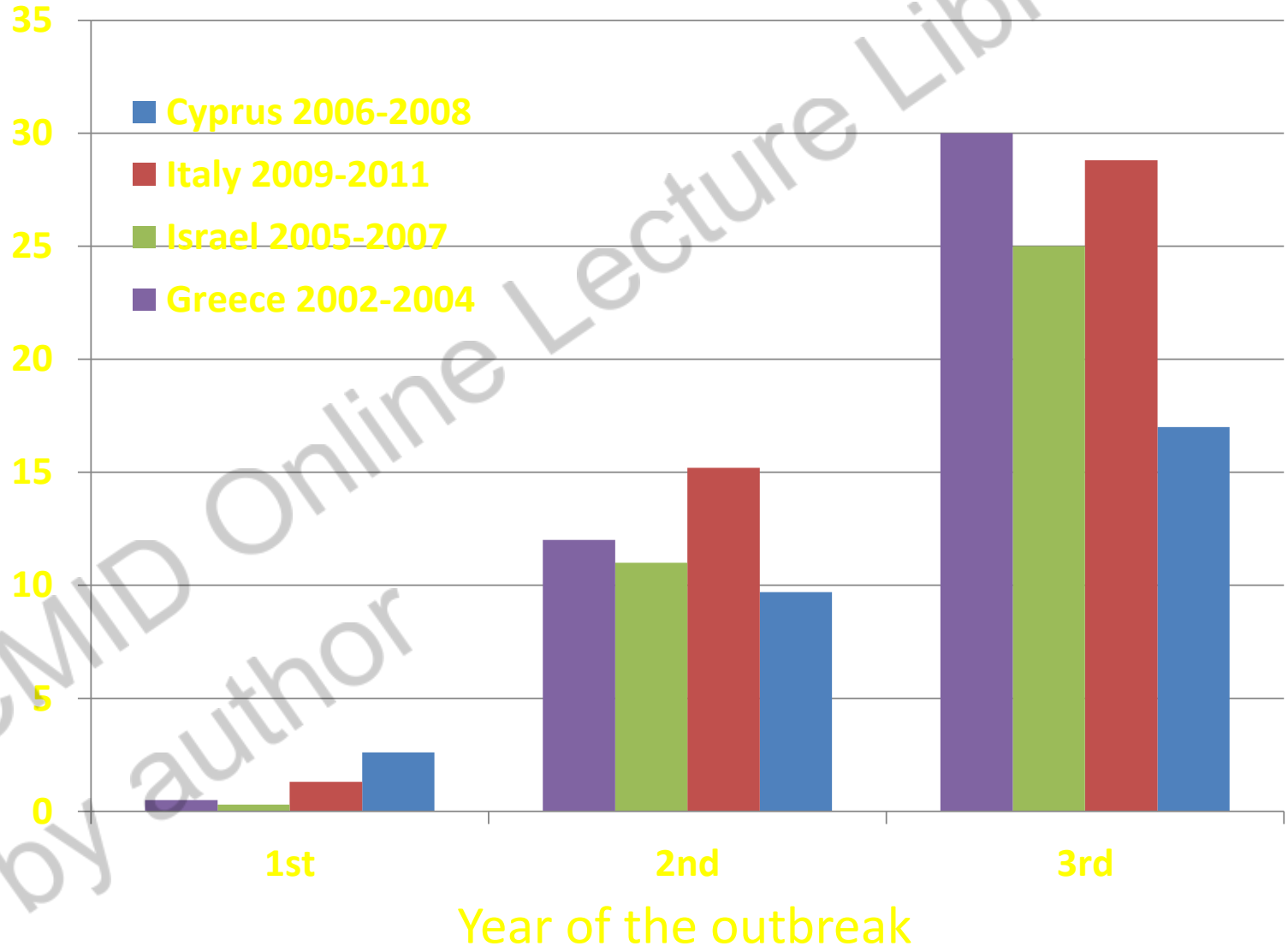
- Kolistin ve Tigesiklin dışında herşeye dirençli..
- 2013 yılında global bir sorun olduğu anlaşıldı
- 2 grup enzim bu dirençten sorumlu
 - Metalobetalaktamazlar (CA tarafından parçalanabilir)
 - Metalobetalaktamaz dışı enzim salgılayanlar
 - Sınıf A karbapenemazlar (KPC)
 - Sınıf D karbapenemazlar (OXA)

Karbapenemazlarda Antibiyotik Dirençleri

	CAZ	IMP	MER
KPC-2 (Class A)	0.001	0.15	0.25
VIM-2 (Class B)	0.9	1	0.3
OXA-40 (Class D)	0.001	0.15	0.25

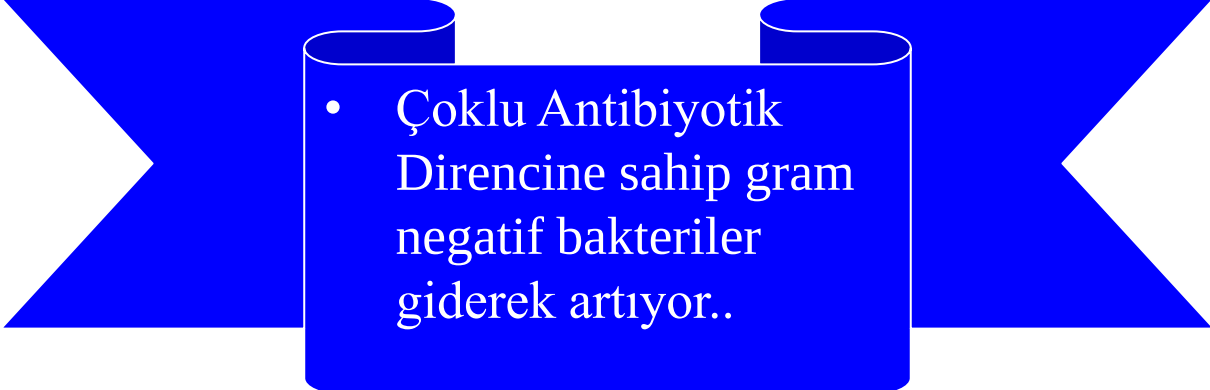
KÖTÜ HABER..
Porin kaybı (OMP) + AmpC BL
Porin kaybı (OMP) + ESBL birlikteliği

CRE Suşlarının Yayılım Süreci



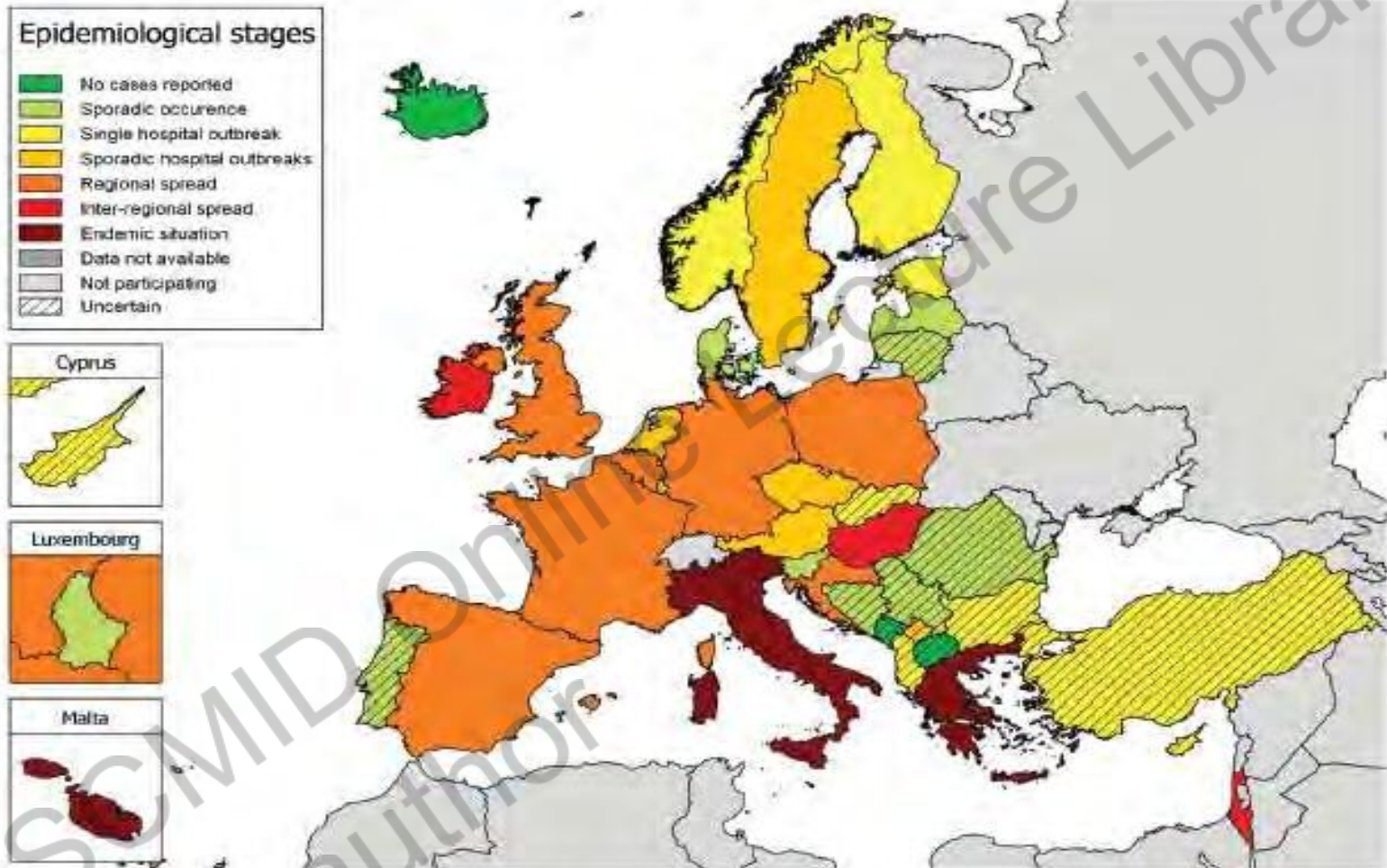
Ve bugün..

- Çoklu Antibiyotik Direncine sahip gram negatif
- Karbapeneme dirençli Enterik bakteriler
- Karbapeneme dirençli Pseudomonaslar
- Karbapeneme dirençli Acinetobacter suşları
- Panrezistan gram negatifler..

- 
- Çoklu Antibiyotik Direncine sahip gram negatif bakteriler giderek artıyor..

Avrupa'da KRE Dağılımı - 2013

Figure 3 Occurrence of carbapenemase-producing *Enterobacteriaceae* in 38 European countries based on self-assessment by the national experts, March 2013



In some countries, the epidemiological stage might not represent the exact extent of the spread of CPE as it is a subjective judgment by national experts. Results presented here reflect the uncertainty at the time of the survey.

Çoklu Antibiyotik Direnci-2014

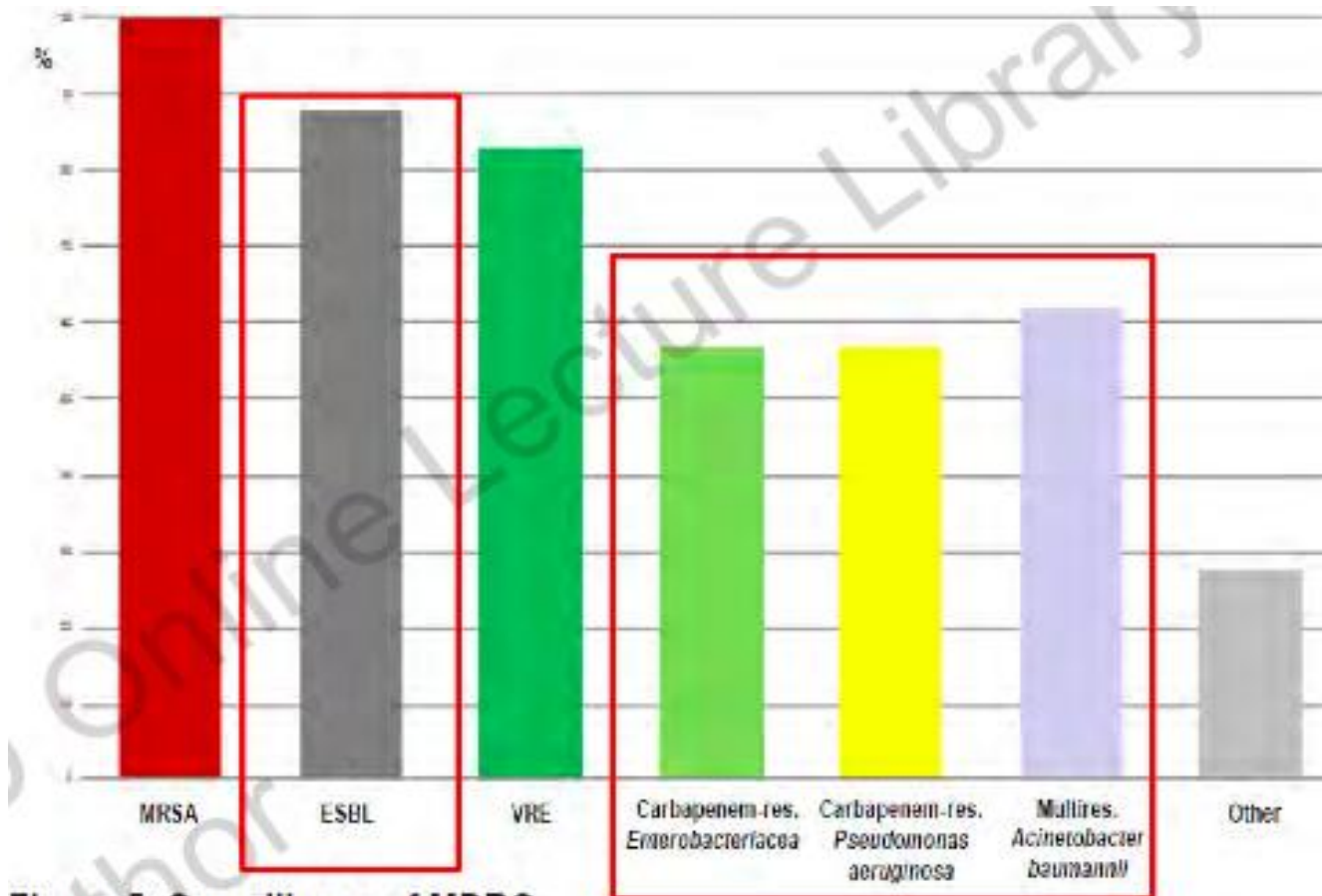


Figure 5: Surveillance of MDRO

Tuesday, Hansen ECCMID 2014

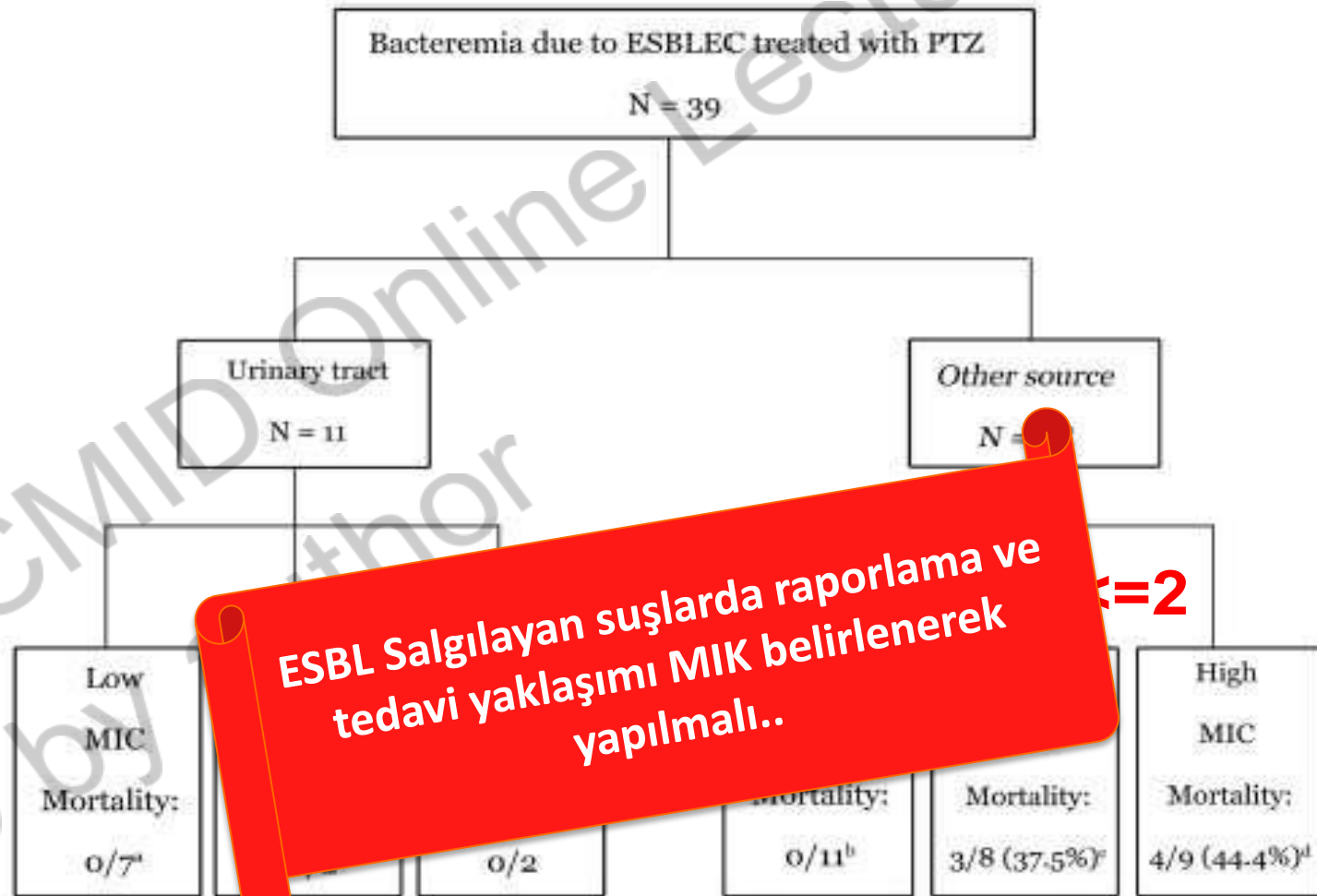
Hansen, ID Week 2012

ESBL Salgılayan Suşlarda Rasyonel Tedavi Yaklaşımı?

- ESBL salgılayan suşlarda SS kullanılmalı mı?
- Beta-laktam beta-laktamaz preparatları?
- ESBL pozitif sonuç vermek ne kadar doğru?
- Her ESBL salgılayan suş için karbapenem mi?
- İn vitro sonuçlar gerçeği yansıtmıyor mu?
- MİK değerini belirlemek daha mı doğru olur?
-
-

Impact of the MIC of Piperacillin-Tazobactam on the Outcome of Patients with Bacteremia Due to Extended-Spectrum- β -Lactamase-Producing *Escherichia coli*

Pilar Retamar,^a Lorena López-Cerero,^a Miguel Angel Muniain,^{a,b} Álvaro Pascual,^{a,c} Jesús Rodríguez-Baño,^{a,b}
the ESBL-REIPI/GEIH Group



CRE İnfeksiyonları Önemli Sonuçlar Doğuruyor..

Değişken	S-KP (n=85)	ESBL-KP (n=65)	CRKP (n=42)	P
Hastane mortalitesi (%)	20 (24)	25 (39)	29 (69)	<0.001
İnfeksiyonla ilişkili mortalite (%)	14 (17)	14 (22)	20 (48)	0.001
İnf.sonrası hastanede yatış süresi, median gün (OR)	9 (16)	16 (34)	8 (22)	0.003
Total hastanede yatış süresi, median gün (OR)	21 (36)	36 (70)	37 (31)	0.001

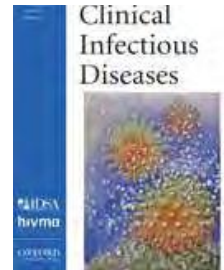
S-KP: Duyarlı *K.pneumoniae*, ESBL-KP: ESBL (+) *K.pneumoniae*, CRKP: Karbapeneme Dirençli *K.pneumoniae*

KPC (+) *K.pneumoniae* İnfeksiyonları

- Üriner sistem infeksiyonları
- İmmünosupresyon
- Yoğun Bakım Ünitesi
- Uzun süreli hastanede yatış öyküsü
- İleri yaş
- Kanser ya da kanserle ilişkili hastalık prosedürleri
- Başlangıçta birden fazla antibiyotik kullanımı

Predictors of Mortality in Bloodstream Infections Caused by *Klebsiella pneumoniae* Carbapenemase–Producing *K. pneumoniae*: Importance of Combination Therapy

Mario Tumbarello,¹ Pierluigi Viale,² Claudio Viscoli,³ Enrico Maria Trecarichi,¹ Fabio Tumietto,² Anna Marchese,⁴ Teresa Spanu,⁵ Simone Ambretti,⁶ Francesca Ginocchio,³ Francesco Cristini,² Angela Raffaella Losito,¹ Sara Tedeschi,¹ Roberto Cauda,¹ and Matteo Bassetti^{3,7}



CID 2012:55 (1 October)

Multivariate analysis of factors associated with death among patients with bloodstream infection due to KPC producing *K. pneumoniae*.

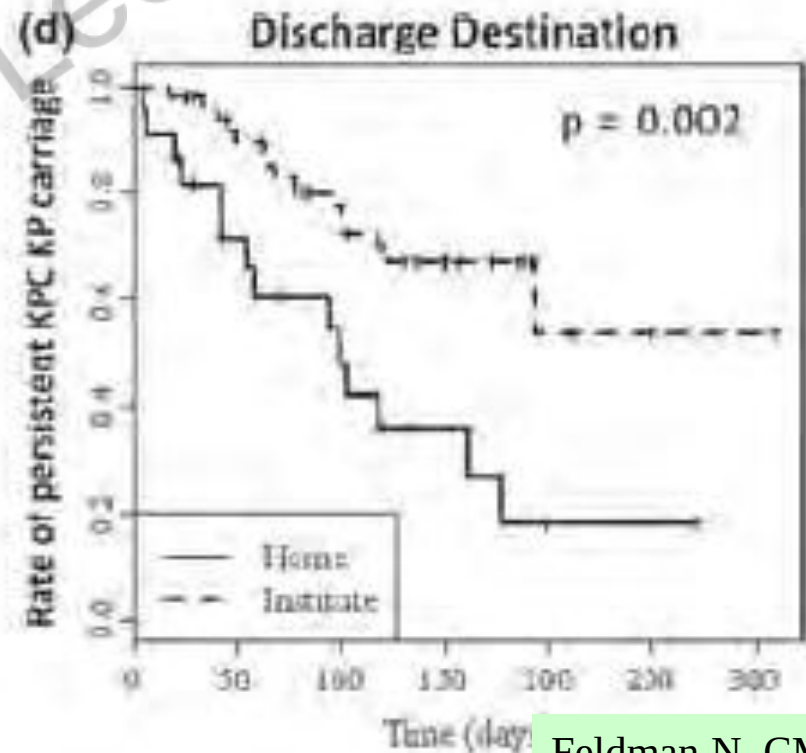
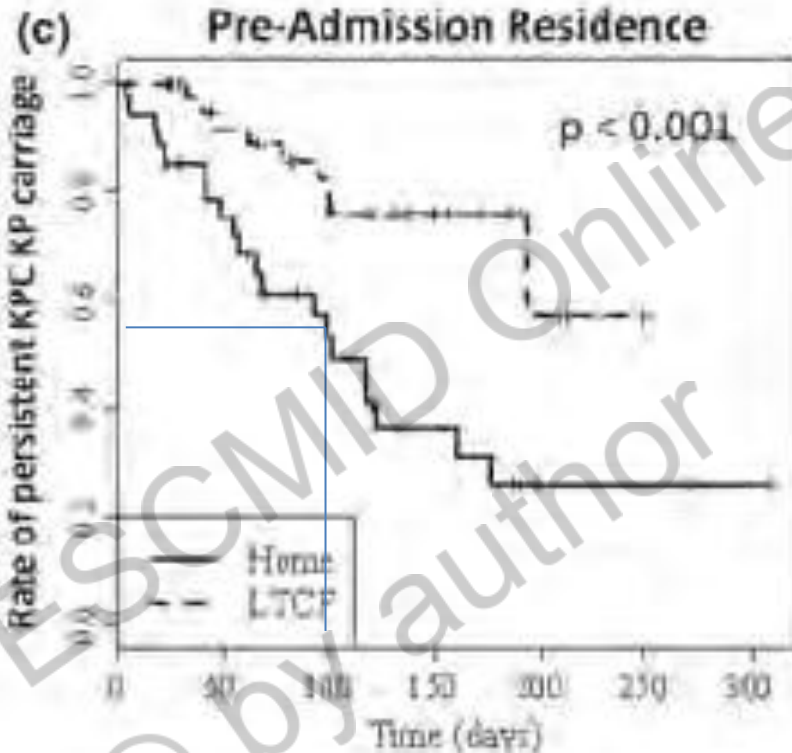
Shock	-	-	0.008	7.17 (1.65-31.03)
Inadequate initial treatment	-	-	0.003	4.17 (1.61-10.76)
APACHE III score (mean ± SD)	-	-	<0.001	1.04 (1.02-1.07)
Tigecycline & Colistin & Meropenem	-	-	0.01	0.11 (0.02-0.69)

Kolonize Hastalarda Hastane Ortamında Hızlı Yayılım ve Salgın

- Hastaneye kabul edildiğinde *KPC-K.pneumoniae* taşıyıcılığı saptanmayan bir olgunun 5 gün sonrasında ortaya çıkan tablo:
 - 4 klinik ünitesinde
 - 30 hastada kolonizasyon
 - 6 klinik infeksiyon tablosu
- Denizaşırı bir ülkeden *KPC-K.pneumoniae* suşu taşıyan ve geldiğinde saptanmayan bir olgu:
 - 9 yeni olgunun infekte olmasına neden oldu (7 gün)

KPC-Üreten *Klebsiella pneumoniae* Suşlarında Taşıyıcılık Süreci

- Hastaneden taburcu edilen hastalarda ortalama taşıyıcılık süresi:
 - Eve taburcu olanların %50'sinde 3 ay,
 - Uzun süreli bakım merkezlerine taburcu edilenlerde daha uzun süre taşıyıcılık devam ediyor..

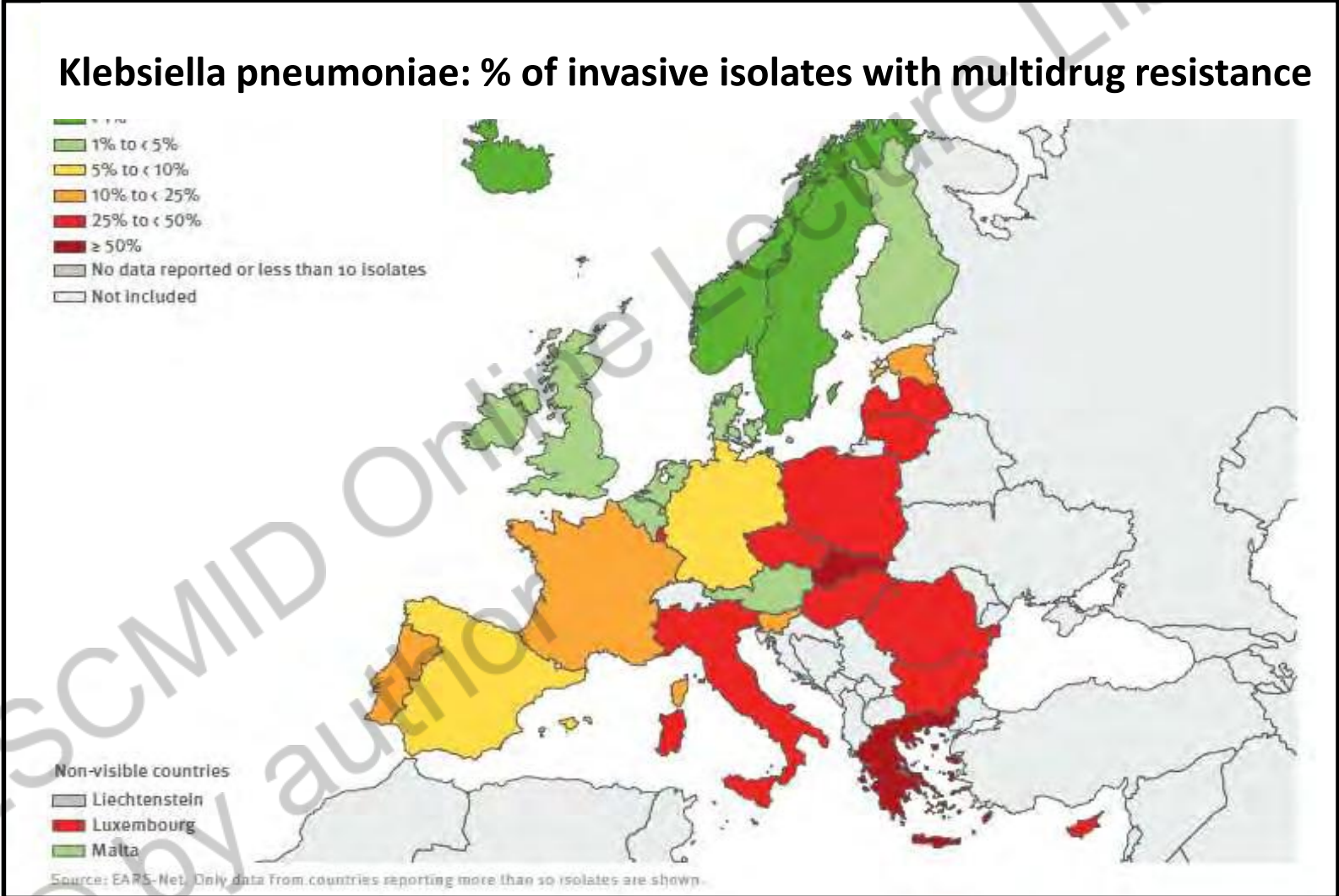


***Klebsiella pneumoniae*: % of invasive isolates resistant to carbapenem**



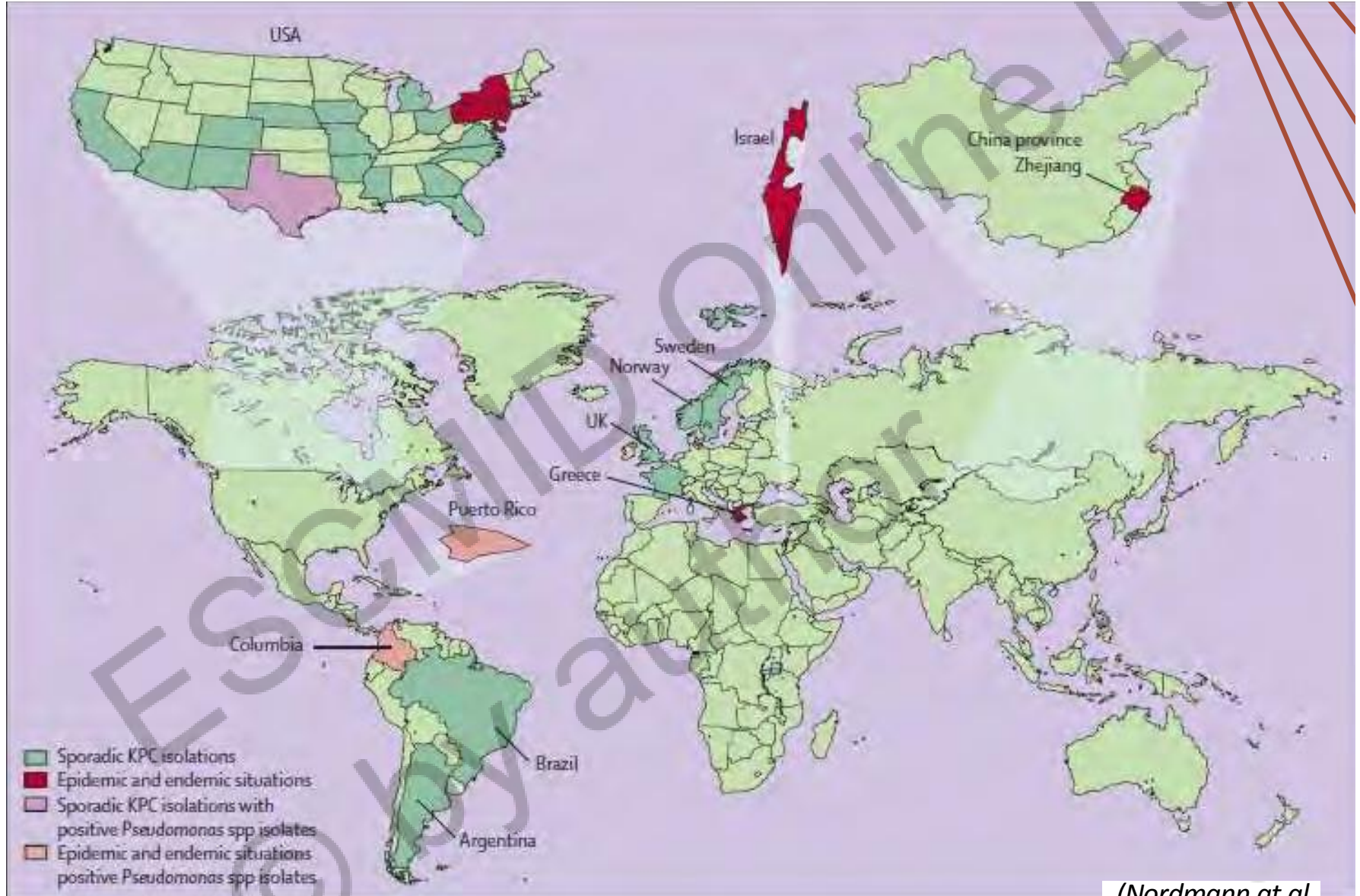
ECDC. Annual epidemiological report Reporting on 2011 surveillance data and 2012 epidemic intelligence data. <http://www.ecdc.europa.eu/en/publications/Publications/annual-epidemiological-report-2013.pdf>

MDR *K.pneumoniae* ve Avrupa



ECDC. Annual epidemiological report Reporting on 2011 surveillance data and 2012 epidemic intelligence data. <http://www.ecdc.europa.eu/en/publications/Publications/annual-epidemiological-report-2013.pdf>

Dünyada KPC Dağılımı - 2013



(Nordmann et al.,

Sınıf-D Beta-Laktamazların İn-vitro Aktiviteleri

Penisilinler	Sefalosporinler 1 ve 2. kuşak	Geniş Spektrumlu Sefalosporinler	Beta- Laktam/Beta- laktamazlar	Karbapenemler
Enzimler				
Oxacillinases				

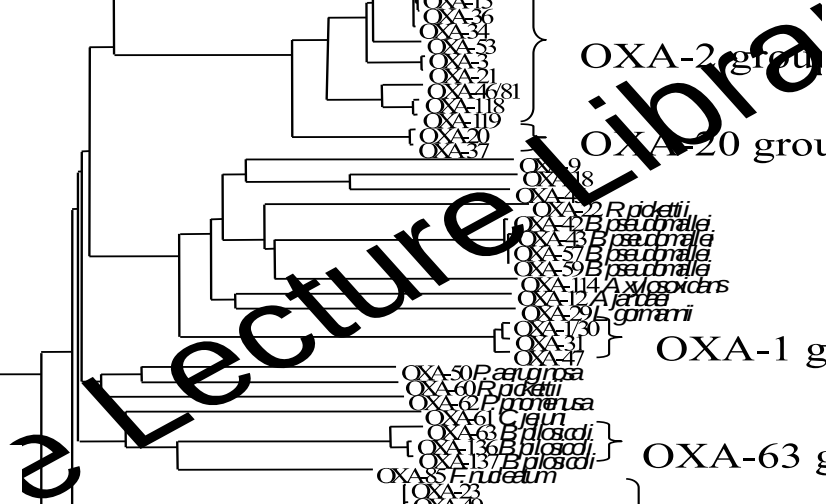
Carbapenem-Hydrolyzing class D Beta-Lactamases (CHDL)

Penisilinler	Sefalosporinler 1 ve 2. kuşak	Geniş Spektrumlu Sefalosporinler	Beta-Laktam/Beta-laktamazlar	Karbapenemler
Enzimler				
Oxacillinases				

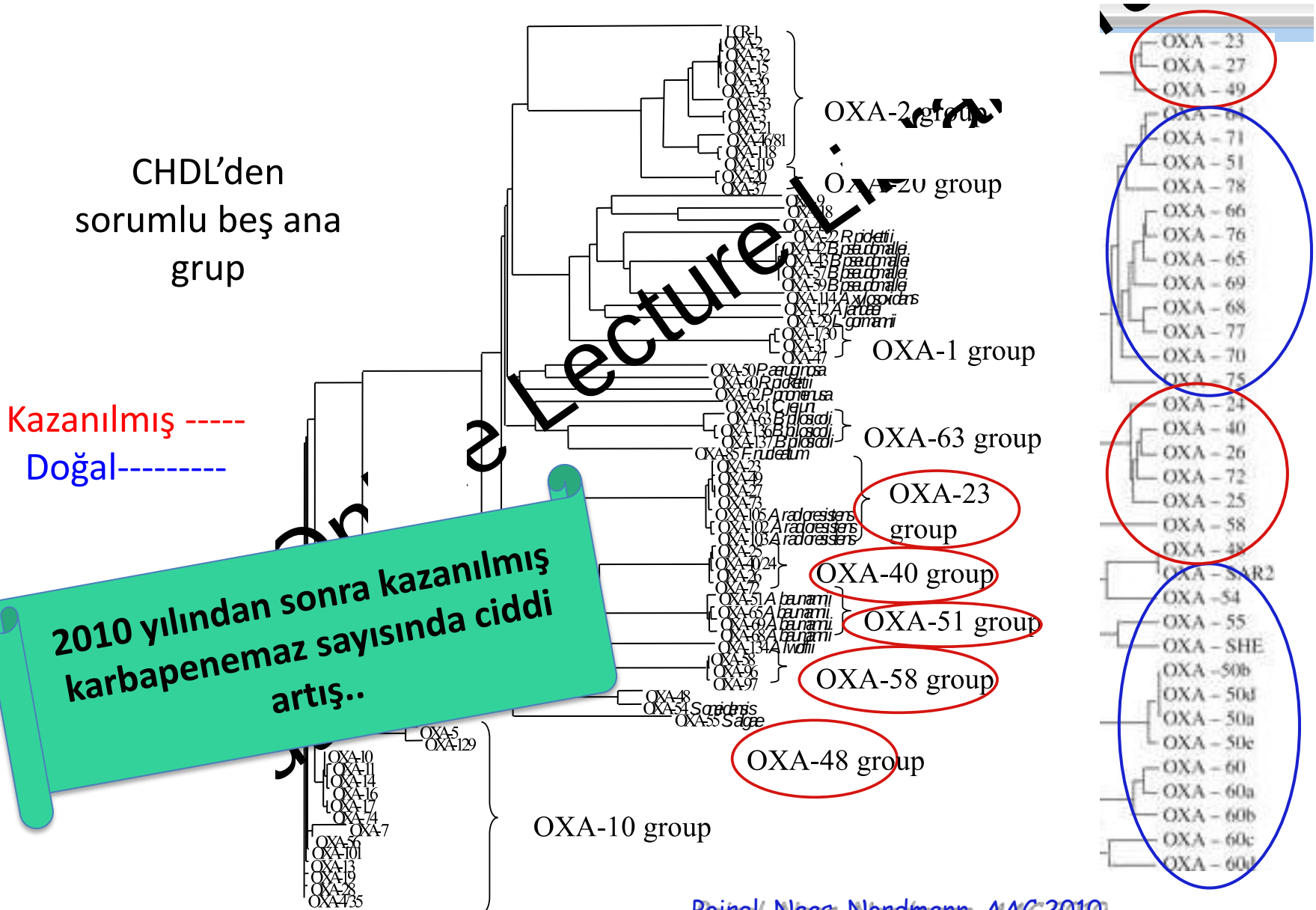
Karbapenemleri Parçalayan Sınıf D Beta-Laktamazların Yaygın Özellikleri

- Serine ile aktive olan Beta-laktamazlardır
- Klavulonik asit ile inhibe olmazlar
- NaCl ile in vitro ortamda inhibe olurlar
- Penisilinleri ve bazı Geniş spektrumlu sefalosporinleri parçalar
- Karbapenemleri düşük oranda parçalar

(>370 değişken)



Sınıf D Beta-Laktamaz Ailesi, 2014



Kazanılmış CHDLs

Snıf	Enzim	Bakteri	İlk İzolasyon Ülkesi (Zaman)
I	OXA-23	<i>A.baumannii</i>	İngiltere (1985)
I	OXA-27	<i>A.baumannii</i>	Singapur (1995-1997)
II	OXA-25	<i>A.baumannii</i>	İspanya (1995-1997)
II	OXA-26	<i>A.baumannii</i>	Belçika (1995-1997)
II	OXA-40	<i>A.baumannii</i>	Fransa, Portekiz, İspanya (2001)
III	OXA-58	<i>A.baumannii</i>	Fransa, İngiltere, Yunanistan (2005)
III	OXA-97	<i>A.baumannii</i>	Tunus (2007)
III	OXA-143	<i>A.baumannii</i>	Brezilya (2005)
III	OXA-235	<i>A.baumannii</i>	ABD, Meksika (2010)
IV	OXA-48	<i>K.pneumoniae</i>	Türkiye (2003)
V	OXA-198	<i>P.aeruginosa</i>	Belçika (2010)

Karbapenem Direncinde Önemli Rol Oynarlar

- *A.baumannii* OXA-40 (+) (Kromozomal)
- *A.baumannii* OXA-40

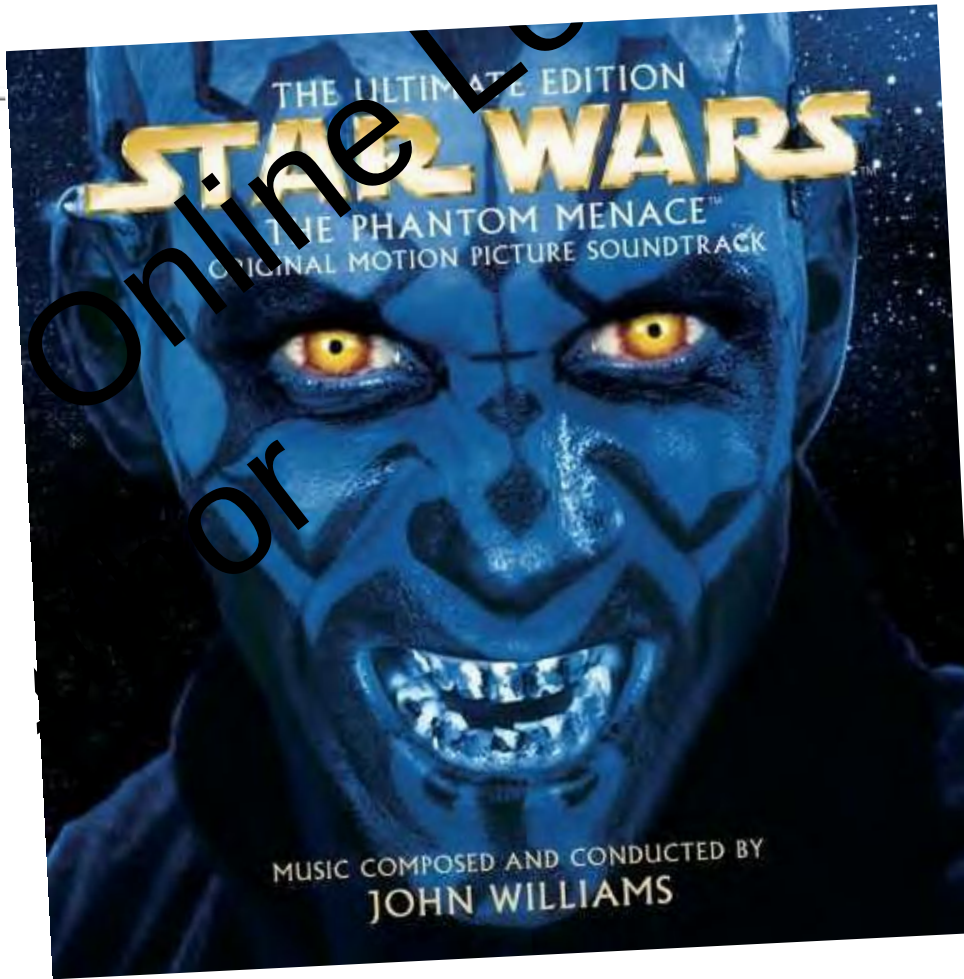


Sadece *A.baumannii* suşlarında sınırlı kalmadığı görüldü..

Enterobacteriaceae Spesifik CHDL

J Antimicrob Chemother
doi:10.1093/jac/dks121

Antimicrobial
Chemotherapy



- MDR
- XDR
- **PDR**

- OXA-48 Karbapenemazlar Önemli bir tehdit..

OXA-48

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 2004, p. 15–22
0066-4804/04/\$08.00+0 DOI: 10.1128/AAC.48.1.15–22.2004
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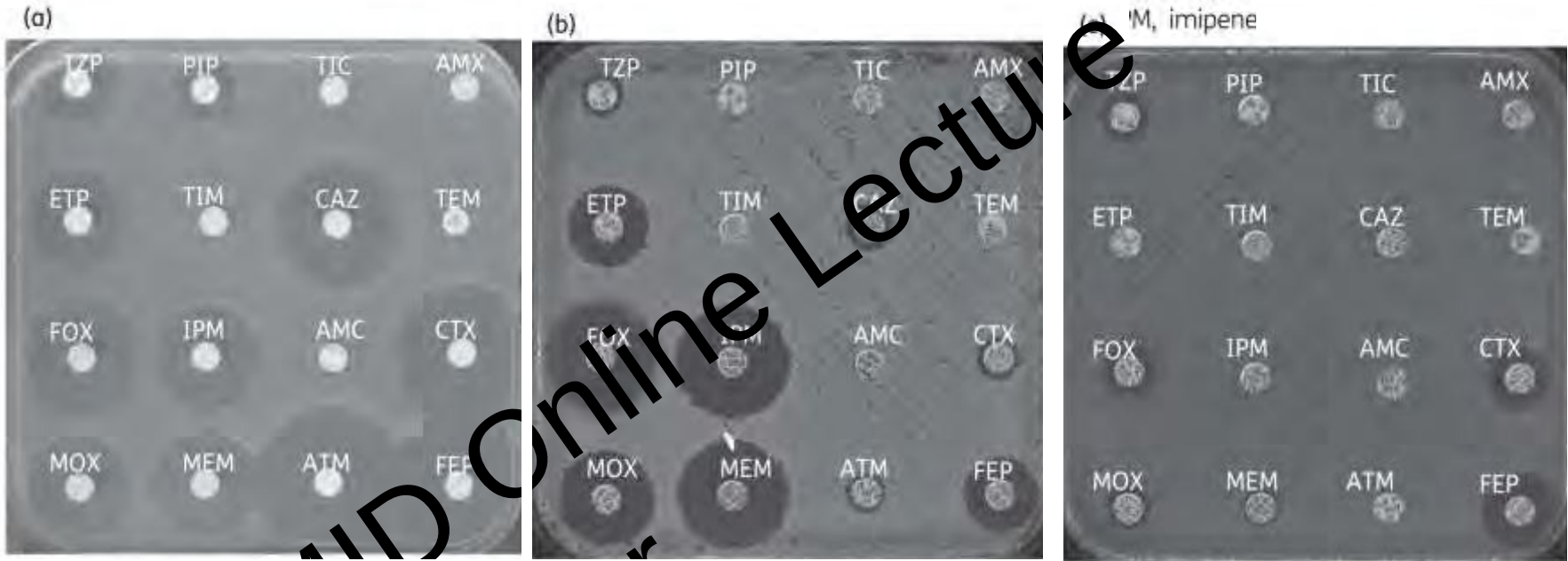
Emergence of Oxacillinase-Mediated Resistance to Imipenem in *Klebsiella pneumoniae*

Laurent Poirel,¹ Claire Héritier,¹ Venus Tolün,² and Patrice Nordmann^{1*}

Service de Bactériologie-Virologie, Université Paris XI, Hôpital de Bicêtre, Assistance Publique/Hôpitaux de Paris, Faculté de Médecine Paris-Sud, 94275 Le Kremlin-Bicêtre, France,¹ and Department of Microbiology, Istanbul Medical Faculty, Caba, Istanbul, Turkey²

- İlk olarak **Türkiye**'de *Klebsiella pneumoniae* suşlarında izole edilmiştir.
- Karbapenemazlar enterobakteri türlerinin çoğundan artık izole edilmekte..
- Direnç geni **plazmid** yerleşimli..

OXA-48 Üreten *K.pneumoniae* suşlarındaki Üç Farklı Direnç Paterni



IMP-I ve CAZ-S

IMP-S ve CAZ-R

IMP-R ve CAZ-R

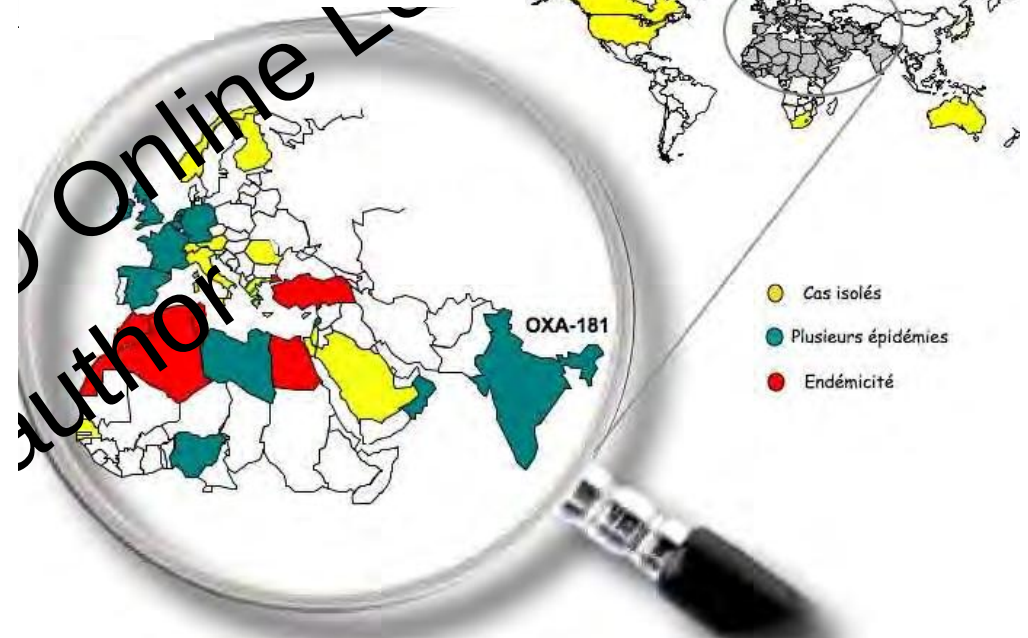
- Antibiogram sonuçları OXA-48 üreten *K.pneumoniae* suşlarında üç farklı performansı göstermektedir. Bunlar: a) Bakteri ESBL salgılamamaktadır, b) Bakteri ESBL salgılamakta ama düşük düzeyde karbapenem MİK düzeyi oluşturmaktadır. c) Bakteri ESBL salgılamakta ve yüksek düzeyde karbapenem direnci göstermektedir.

Dünya Geneline OXA-48: Son Durum

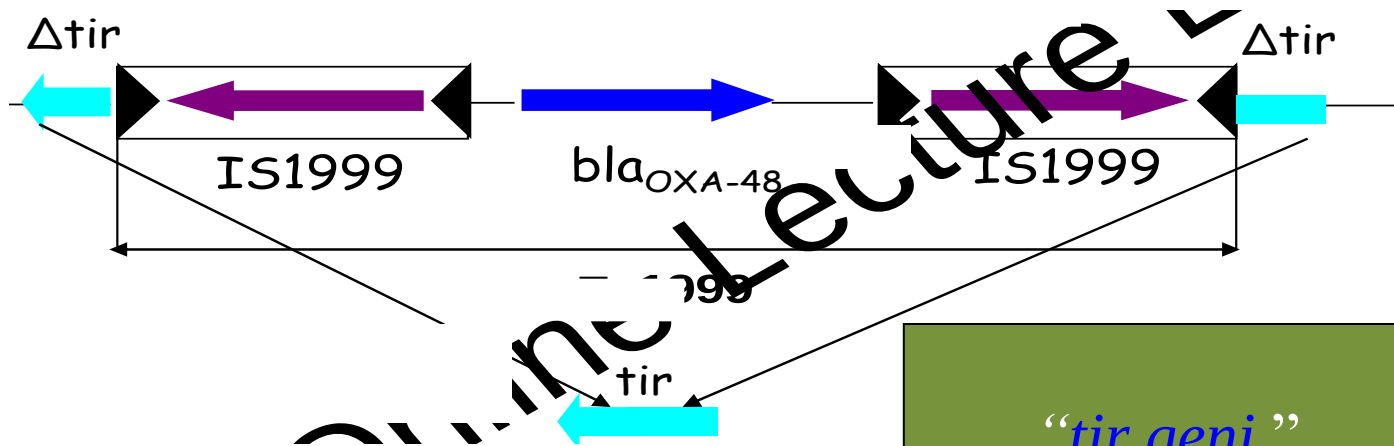
2010



2014



OXA-48 Plazmidinde Yüksek Transfer Hızı



- IncL/M plazmidinde lokalize olan *tir* geni bulunan *bla_{OXA-48}* aracılığıyla kesilir.
- *tir* geni hücreden hücreye plazmidin etkileyen bir proteini kodlar

“*tir* geni”
Tüm GNB'lere arasında
OXA-48
yayılımından
sorumlu gendir..

Derepressed Transfer Properties Leading to the Efficient Spread of the Plasmid Encoding Carbapenemase OXA-48

OXA Kaynaklı Karbapenemazlarda Son Durum

- OXA kaynaklı karbapenemazlar *Enterobacteriaceae* ve *A.baumannii*'lerde karbapenem direncinin önemli bir nedenidir.
- OXA-48 kaynaklı *Enterobacteriaceae* başta Avrupa, Kuzey Afrika ve Orta Doğu olmak üzere tüm dünyada yaygındır
- OXA-48'in kontrolünde
 - Erken saptamak amacıyla aktif sürveyans,
 - Akılcı Antibiyotik Yönetimi temel yaklaşımlardır.

Naming of NDM-1

THE LANCET



emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

© 2004 Blackwell Publishing Ltd, *Journal of Internal Medicine* 255: 105–112

community

diagnosed Gram-negative Enterobacteriaceae with resistance to cefepime isolated in New York hospitals (Antonie van Leeuwenhoek Institute) are potentially a major global health problem. We investigated the prevalence of NDM-1 in antibiotic-resistant Enterobacteriaceae in India, Pakistan, and the UK.

Isolates. Enterohaemorrhagic isolates were studied from two major sources in India—Chennai (south India), Araya (north India)—and those referred to the UK's national reference laboratory, Anitoxin susceptibility not assessed, and the presence of the enterohemorrhagic toxin gene *hly_{EHEC}* was established by PCR. Isolates were typed by pulsed-field gel electrophoresis of *Xba*I-restricted genomic DNA. Plasmids were analysed by ST nucleic probe and PCR typing. Case data for UK patients were reviewed for evidence of travel and recent admission to hospital in India or Pakistan.

Results: We identified 44 isolates with NDH-1 in Chennai, 20 in Hariana, 37 in the UK, and 27 in other sites at India or Pakistan. NDH-1 was mostly *krnA* among *Salmonella* and *Shigella* *paratyphi* (15), which were highly sensitive to all antibiotics except to tetracycline and ceftriaxone. *krnA* *paratyphi* isolates from Hariana were clonal but *NDH-1* producers from the UK and Chennai were clonally diverse. Most isolates carried the *NDH-1* gene on plasmids: one from UK and Chennai were mostly susceptible whereas those from Hariana were not susceptible. Many of the *krnA* NDH-1 positive patients had travelled to India or Pakistan within the past year, or had links with these countries.

translation. The potential of NCMs to be a worldwide public health problem is great, and co-ordinated international surveillance is needed.

volleg hergepostet. Linsen, Weizen, Hafer, und Weizen.

10. <http://www.irs.gov>

acteria that are specific and non-invasive, are entering the poultry industry as commercial products. These are currently marketed as Green-positive bacteria, although methionine-resistant *Salmonella* strains and antibiotic-resistant *Enterococcus* spp. have become major contaminants in commercially grown turkeys, raising concern that transgenic bacteria pose the greatest risk to public health. But could the increase in resistance of transgenic bacteria limit their use in *Colombophilus* strains? Will there then be fewer long and developmentally slower strains against *Green-positive bacteria* and no development of transgenic strains unaffected by tetracycline cover in 45–60 days?

The increase in resistance to Gram-negative bacteria is likely due to mobile genes or plasmids that are transferred through horizontal transmission. Horizontal transmission facilitates cross-species drug resistance, including the four types of these elements and their transmissible structures.²² Moreover, dysregulated human stress and regeneration allow bacteria plasmids and clones to be transmitted vertically between generations and

addition,^{10,11} Much of this dissemination is considered, with evidence (most verified in the animal literature) that may only be having evident since they are the source of risk species (bacteria). The CTX-M- β -lactamase spectrum literature (33 refs) included in Ref. 10, was first reported in India in the mid 1990's. The gene jumped from the chromosome of *E. coli* natural from, adaptive up to, plasmids that have subsequently spread within – colonizing CTX-M- β at the globally epidemic SBE, and its primary locus of acquired resistance is still primarily colistin-resistant in *Enterobacteriaceae*.¹²

Major streps have declined 1951 to 1980, at 30-40% in most countries in India and, although the collection might be a biased sample, they do suggest a serious problem, making the widespread use of insecticides such as organophosphorus necessary.¹⁰ Rates of organophosphorus resistance are known to also increase with the growing prevalence of 150L, probably as a result of less a greater reliance on organophosphates. Consequently, there is additional pressure for organophosphorus resistance in *Enterodactyloides*, and the emergence of a worldwide, mainly biocidal, insecticide resistance has low probability.

Dissemination of NDM-1 positive bacteria in the New Delhi environment and its implications for human health: an environmental point prevalence study

Timothy R Walsh,¹ Janis Weeks,² David M Livermore,³ Mark A Toleman¹

Summary

Background Not all patients infected with NDM-1-positive bacteria have a history of hospital admission in India, and extended-spectrum β -lactamases are known to be circulating in the Indian community. We therefore measured the prevalence of the NDM-1 gene in drinking water and seepage samples in New Delhi.

Methods Swabs absorbing about 100 μ L of seepage water (ie, water pools in streets or rivulets) and 15 mL samples of public tap water were collected from sites within a 12 km radius of central New Delhi, with each site photographed and documented. Samples were transported to the UK and tested for the presence of the NDM-1 gene, *bla*_{NDM-1}, by PCR and DNA probing. As a control group, 100 μ L sewage effluent samples were taken from the Cardiff Wastewater Treatment Works, Tremorfa, Wales. Bacteria from all samples were recovered and examined for *bla*_{NDM-1} by PCR and sequencing. We identified NDM-1-positive isolates, undertook susceptibility testing, and, where appropriate, typed the isolates. We undertook Inc typing on *bla*_{NDM-1} positive plasmids. Transconjugants were created to assess plasmid transfer frequency and its relation to temperature.

Findings From Sept 26 to Oct 10, 2010, 171 seepage samples and 50 tap water samples from New Delhi and 70 sewage effluent samples from Cardiff Wastewater Treatment Works were collected. We detected *bla*_{NDM-1} in two of 50 drinking-water samples and 51 of 171 seepage samples from New Delhi; the gene was not found in any sample from Cardiff. Bacteria with *bla*_{NDM-1} were grown from 12 of 171 seepage samples and two of 50 water samples, and included 11 species in which NDM-1 has not previously been reported, including *Shigella boydii* and *Vibrio cholerae*. Carriage by enterobacteria, aeromonads, and *V. cholera* was stable, generally transmissible, and associated with resistance patterns typical for NDM-1; carriage by non-fermenters was unstable in many cases and not associated with resistance patterns typical for NDM-1.



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April 1, 2011
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See Online Comment
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Increased Waterborne *bla*_{NDM-1} Resistance Gene Abundances Associated with Seasonal Human Pilgrimages to the Upper Ganges River

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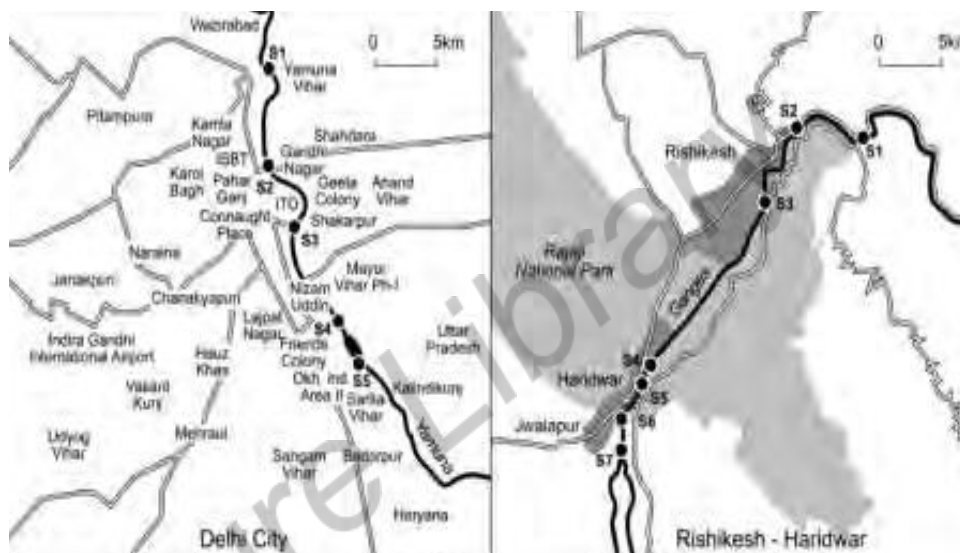
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Supporting Information

ABSTRACT Antibiotic resistance (AR) is often rooted in inappropriate antibiotic use, but poor water quality and inadequate sanitation exacerbate the problem, especially in emerging countries. An example is increasing multi-AR due to mobile carbapenemases, such as NDM-1 protein (coded by *bla*_{NDM-1} genes), which can produce extreme drug-resistant phenotypes. In 2010, NDM-1 positive isolates and *bla*_{NDM-1} genes were detected in surface waters across Delhi and have since been detected across the urban world. However, little is



NDM-1 Karbapenemazlar



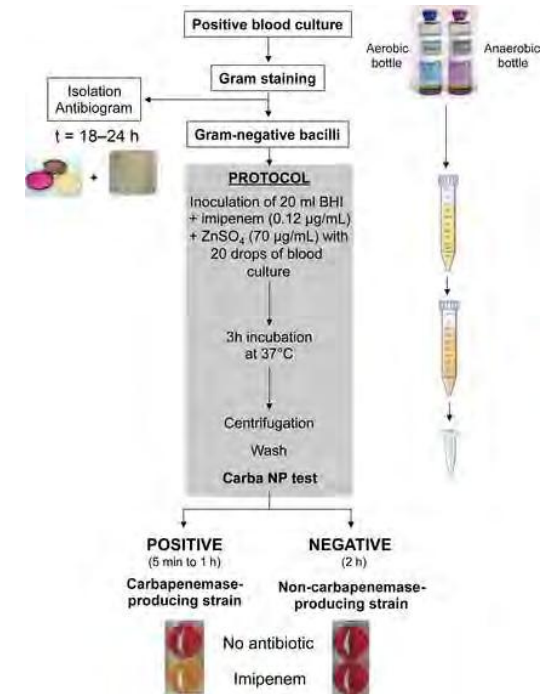
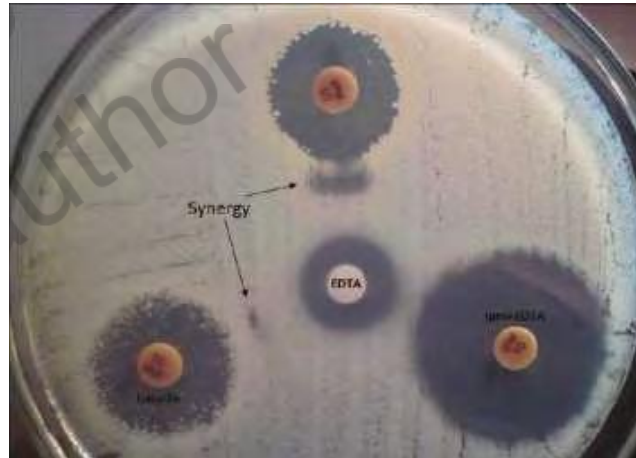
Escherichia coli NDM-1



K. Pneumoniae NDM-1

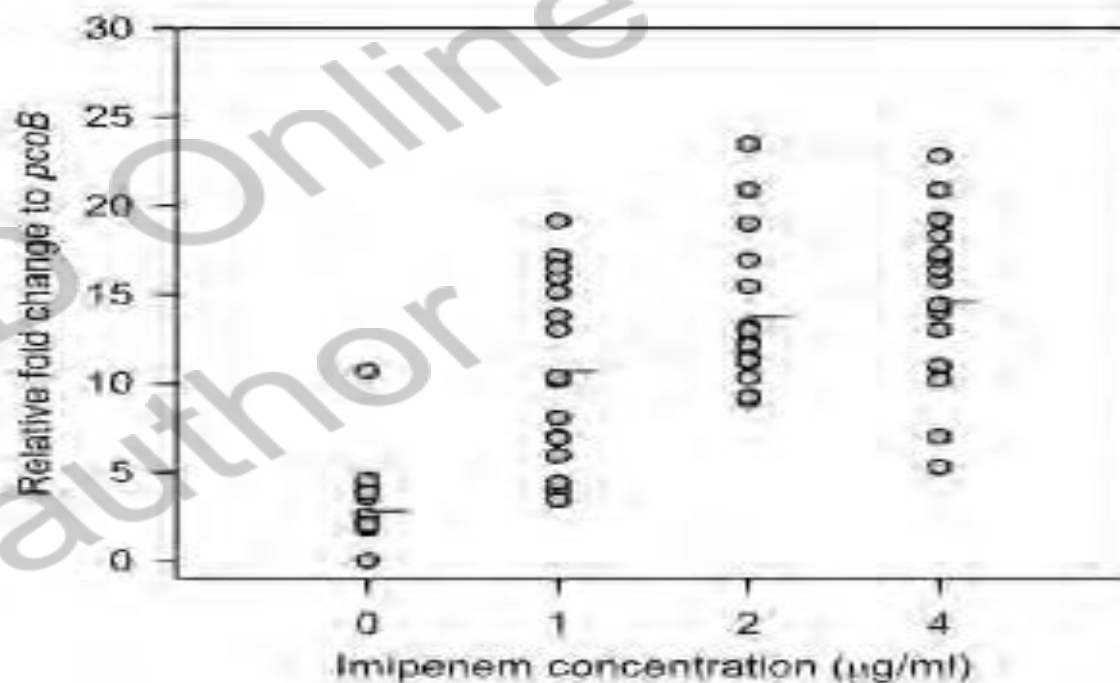
NDM-1 Karbapenemazlar

- MIK Karbapenem düzeylerinde artış
- Modified Hodge Test
- E-test / Çift disk sinerji testi
 - MBL saptanması için EDTA
- Selektif besiyeri
- Biyokimyasal testler
- Moleküler Yöntemler

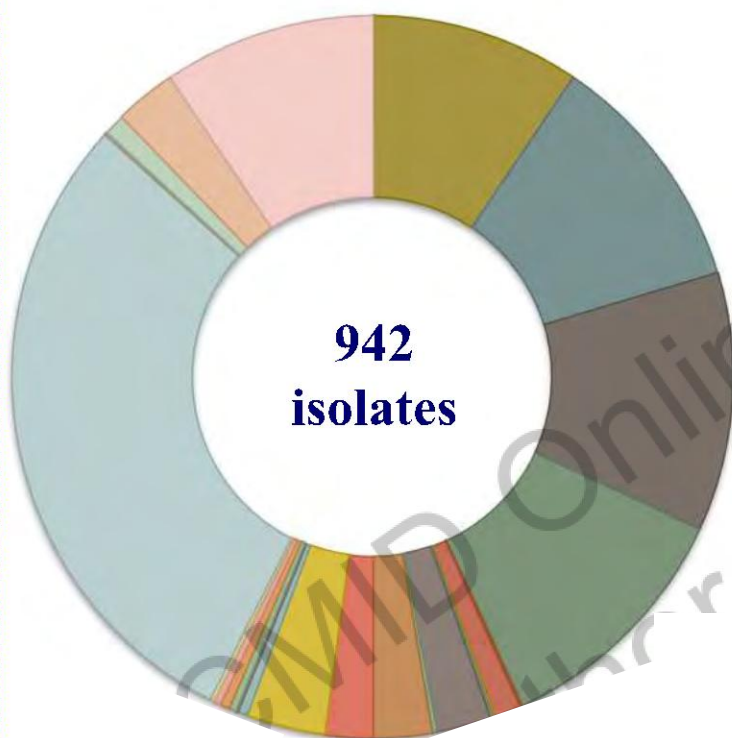


Copy Number Change of the NDM-1 Sequence in a Multidrug-Resistant *Klebsiella pneumoniae* Clinical Isolate

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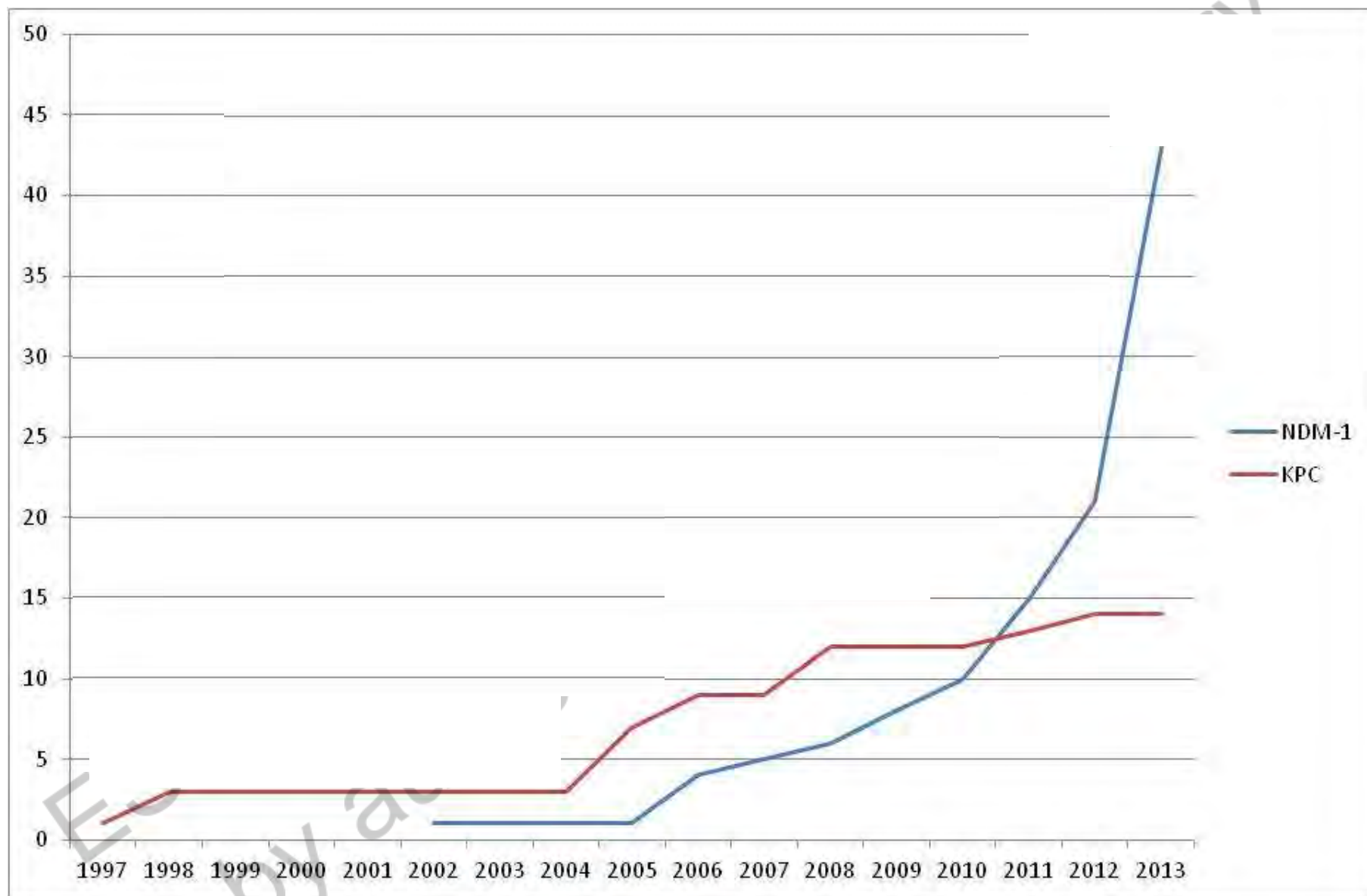
A

Identification of *bla*_{NDM}
positive isolates

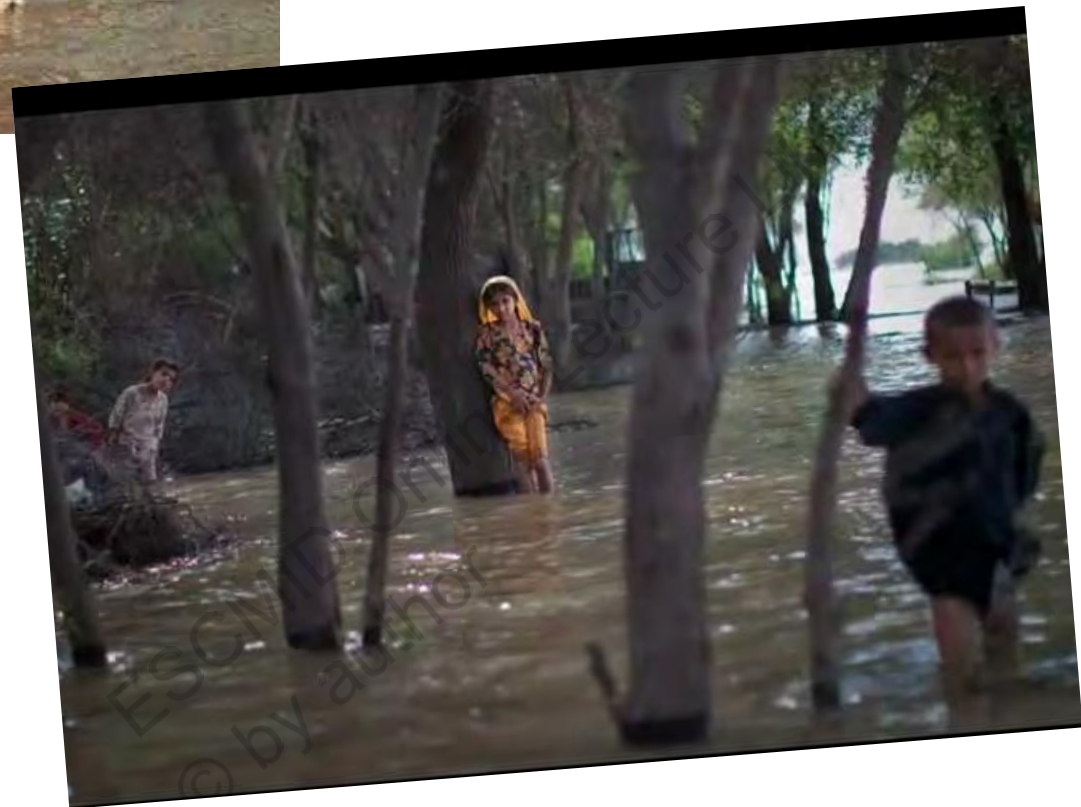


■ <i>Alishewanella</i> sp. n= 1	■ <i>Alcaligenes</i> sp. n= 33
■ <i>Citrobacter</i> sp. n= 88	■ <i>Brevundimonas</i> sp. n= 4
■ <i>Enterobacter</i> sp. n= 103	■ <i>Chryseobacterium gleum</i> n=1
■ <i>Escherichia</i> sp. n= 109	■ <i>Comamonas</i> sp. n= 3
■ <i>Klebsiella</i> sp. n= 106	■ <i>Delftia</i> sp. n=4
■ <i>Kluyvera</i> sp. n= 1	■ <i>Ochrobactrum</i> sp. n= 3
■ <i>Ledercia</i> sp. n= 11	■ <i>Pseudochrobactrum</i> sp. n= 1
■ <i>Morganella</i> sp. n= 1	■ <i>Pseudomonas</i> sp. n= 276
■ <i>Proteus</i> sp. n= 1	■ <i>Rhizobium</i> sp. n= 1
■ <i>Raoultella</i> sp. n= 23	■ <i>Shewanella</i> sp. n=9
■ <i>Achromobacter</i> sp. n= 2	■ <i>Stenotrophomonas</i> sp. n=26
■ <i>Acinetobacter</i> sp. n= 25	■ No reliable ID n=89
■ <i>Aeromonas</i> sp. n= 20	

Enterobacteriaceae







NDM-1 in China

High Rate of New Delhi Metallo- β -Lactamase 1-Producing Bacterial Infection in China

Abstract—The emergence and rise of clinical infection of *Neisseria meningitidis* serotype 1 (NMC1) has been reported in many countries and has caused serious concern worldwide [1–5]. Gambia has the largest number of meningitis cases [6–8], so intestinal carriage is a key factor in NMC14 infection epidemiology. To investigate the infection status of NMC14-producing bacteria in humans, Gambia (January to October 2013), a total of 18 273 clinical stool samples were collected from separate individuals in 12 hospitals representing 33 provinces in rural-urbanized (transformed) agricultural (LAMP) and polyethnic rural (non-LAMP) coastal districts of Gambia. A total

This result showed that the total β -lactamase activity rate of *HEtM*- β -lactamase-producing clinical isolates in clinical patients was 10.6%, for 129 (77.9%) positive samples. *HEtM*- β -lactamase-producing strains were isolated and identified. Of the 120 isolates, 12 (10.0%) were stable while the rest were unstable (the *HEtM*- β gene was lost after 7 passages). All of the 120 isolates were resistant to all antimicrobials, cephalosporins, and β -lactam inhibitors (amoxiclavams, and ampicillin) in vitro. (4). The minimum inhibitory concentrations (MIC) for impurities of most of the 120 isolates was ≤ 32 μ g/ml, but 3 isolates were ≥ 64 μ g/ml. The stable ampicillin-resistant among 13 species comprising *Acinetobacter baumannii* (10), isolated. *Escherichia parvuli* (10), *Aeromonas* group (2), *Comamonas acidovorans* (7), *Stenotrophomonas maltophilia* (2), *Acinetobacter baumannii* (2), *Aeromonas* group (2), *Aeromonas* family (2).

Staphylococcus aureus (3), *Acetivibrio* species (3), and *Acetivibrio* group (1). However no positive isolates were detected among *Escherichia coli* and *Klebsiella pneumoniae*, the results may consistent with previous research by Chen et al. (20).

[illegible]

The analysis of the putative host glycosaminoglycan profiles showed that MeMIM-1 is a tissue-specific site located in those plants only with roots approximately 30–35% to 50% *in situ* (e.g., *Jeffia*, *R. vulturis*, and *C. latifolius*) or *in vitro* (e.g., *M. myrsinifolia*, *C. verticillata*, *A. baobab*, *C. multicaulis*, *A. farnesii*, *A. capiti*, and *C. corymbi*). Transferrable MeMIM-carrying plantlets to laboratory strains of *R.* and *P.* were conducted, and the plantlets in *A. baobab* and *R. vulturis* were successfully retransferred. Interestingly, all transmissible sites were *in vivo* the transmissible plantlets only.

Although further studies are not under-

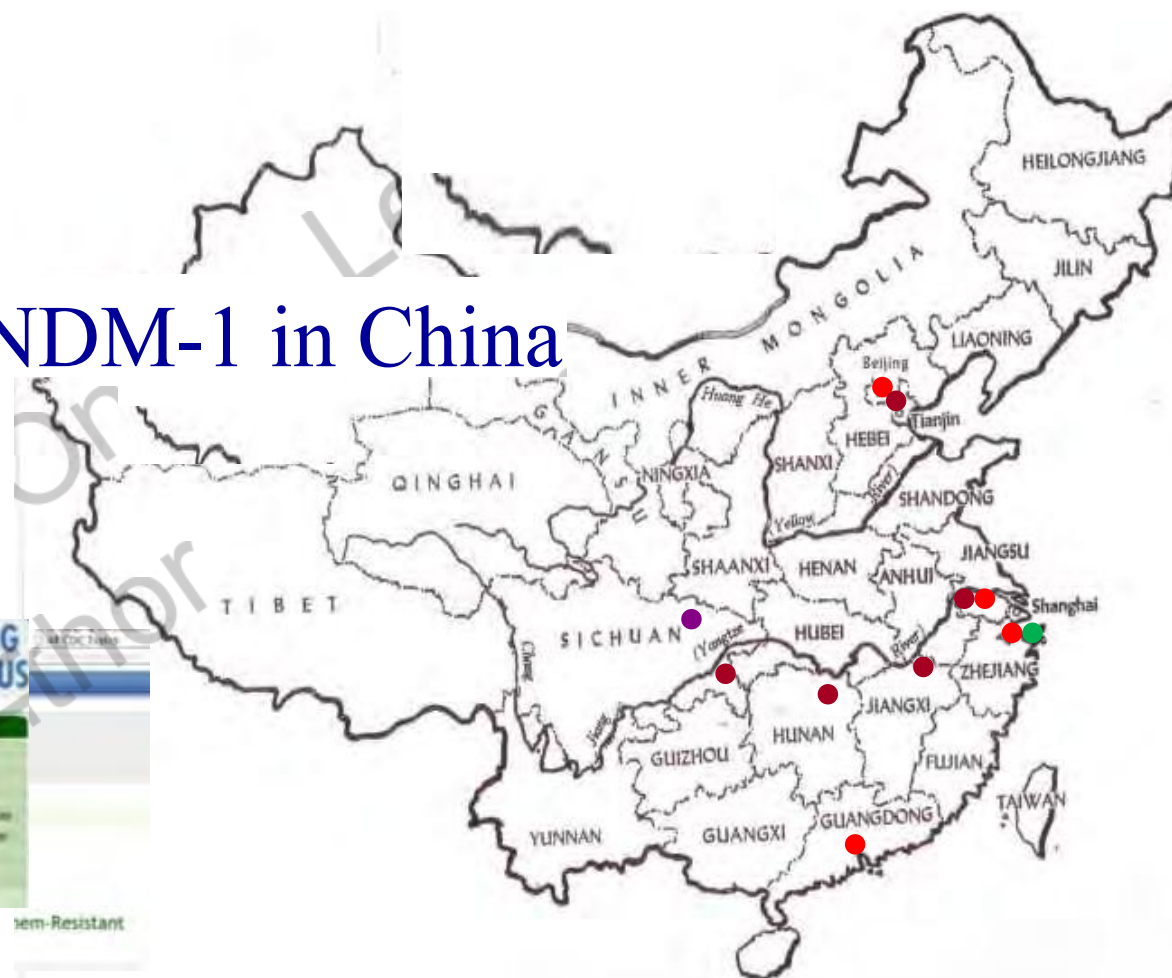
and for the spread of
planned transnational
convergence and ap-
proach. Most likely
and through the re-

Acknowledgments:—We thank Lin Bo Wang (Hubei) for financial support by the National Natural Science Foundation of China (grant numbers 81073001 and 81073002) and the Key Technology Research and Development Project (81073001).

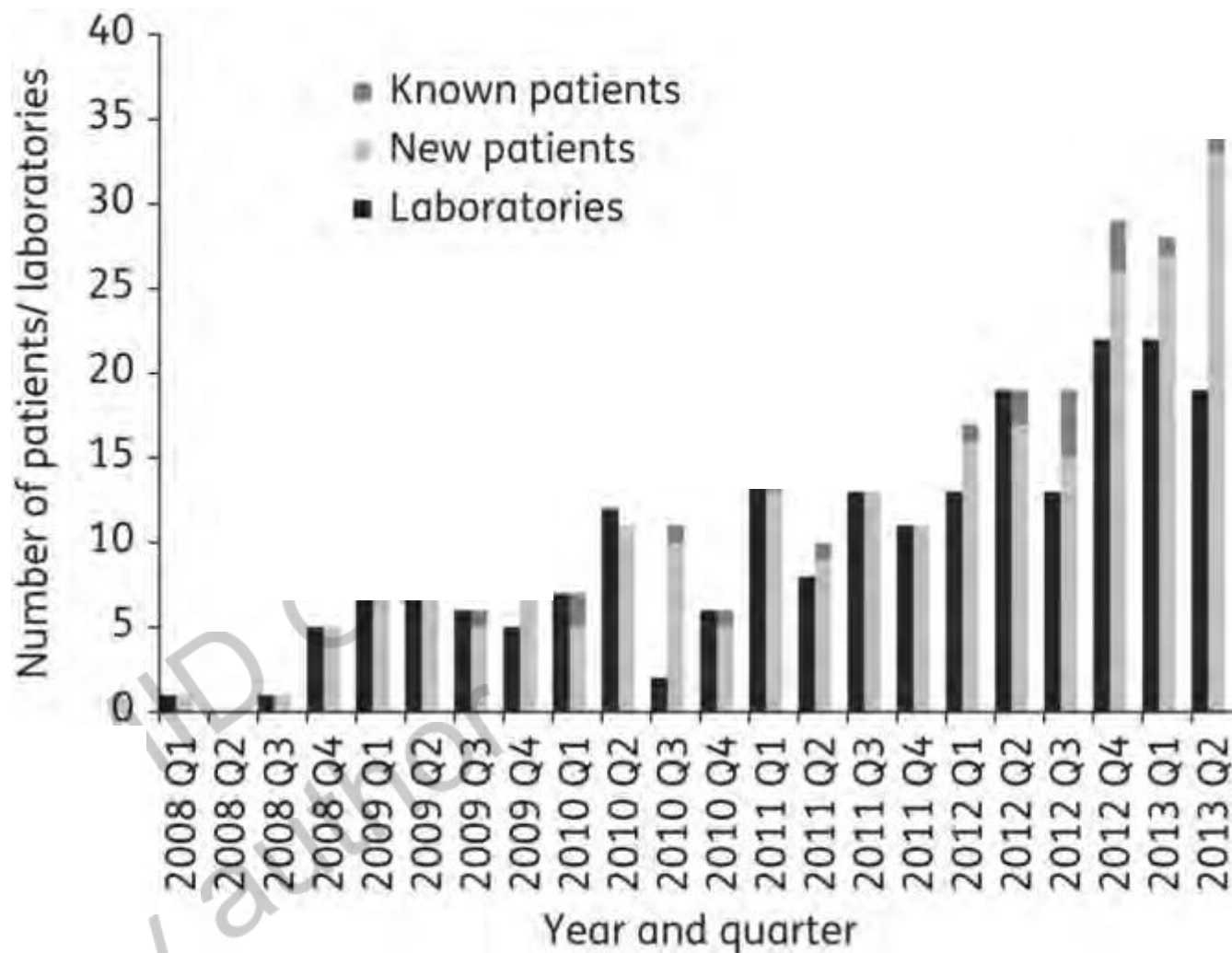
**Jimmy Wong,
Sudhanu L. Khaitwal,
Huan L. Tittel,
Geyu
Institute of Quantum Optics
and Information Technology**



Acid-Resistant

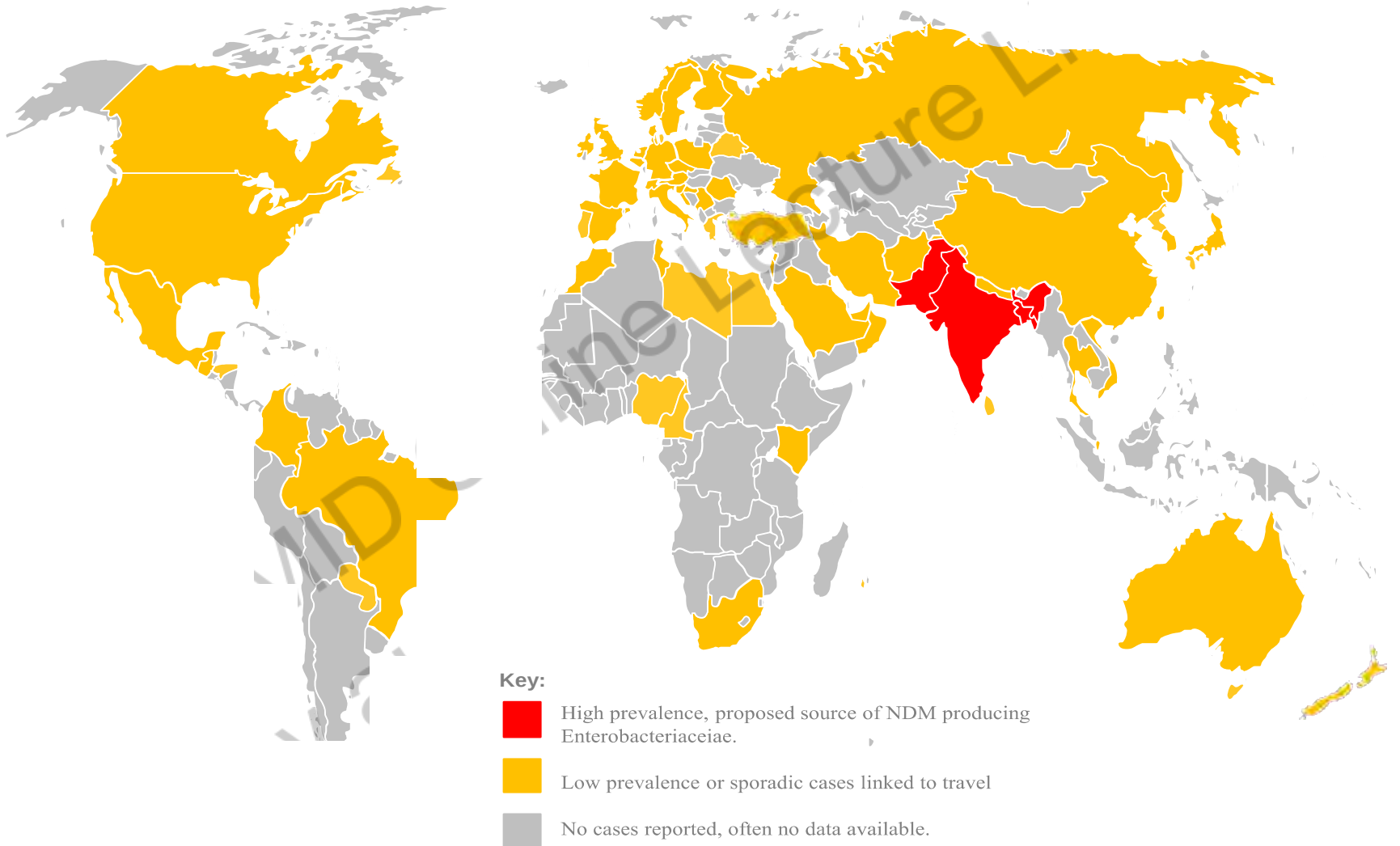


Numbers of new and known affected patients and laboratories sending NDM-positive isolates per quarter during the study period.

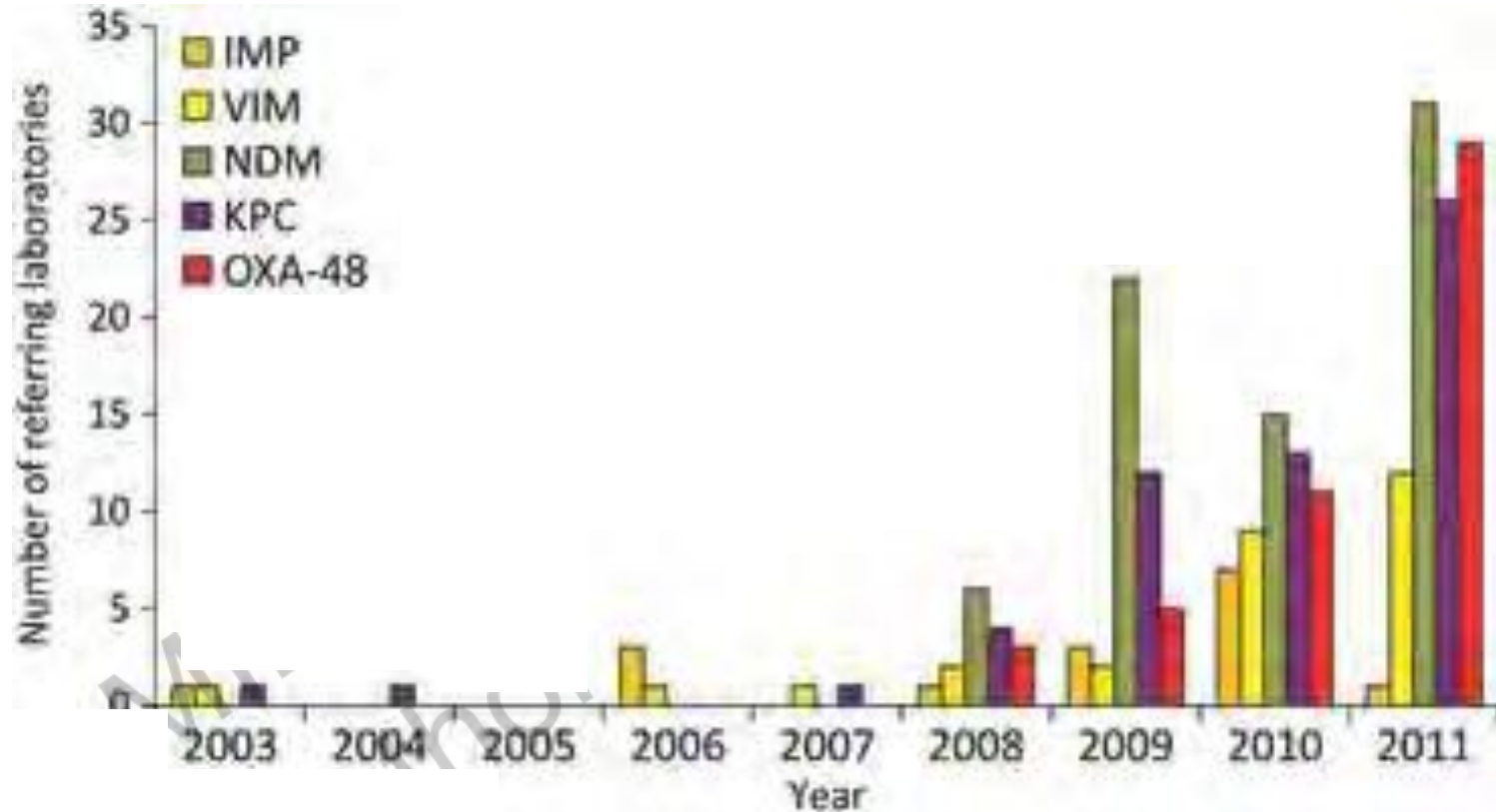


Jain A et al. J. Antimicrob. Chemother. 2014;jac.dku084

NDM-Salgılayan Enterobacteriaceae'nin Global Yayılımı



Global Bir Sorun: Gram Negatiflerde Çoklu Antibiyotik Direnci



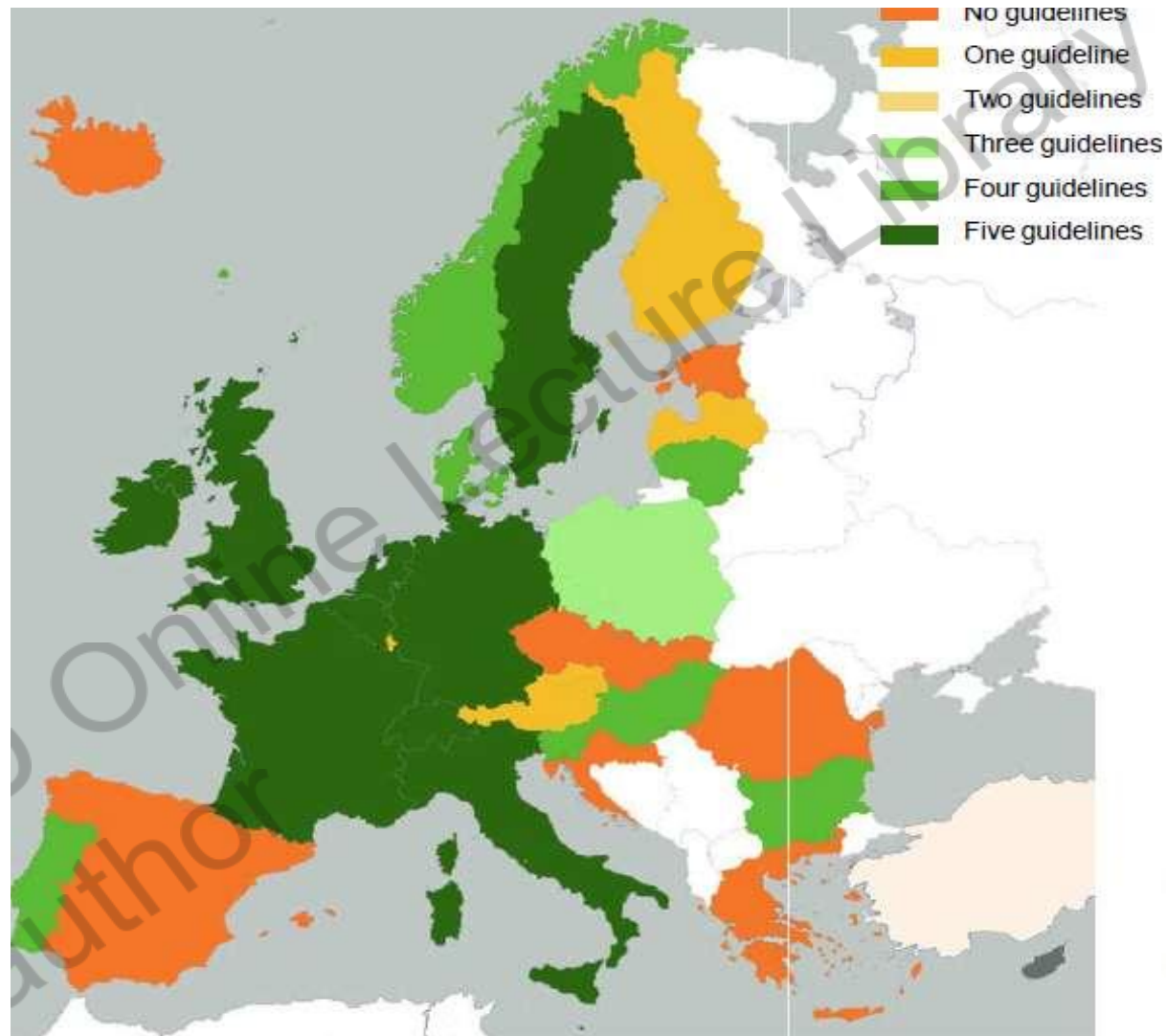
GNB'lerde Direnç Artışı Tek Kökenli Değil..



Antibakteriyel Direnç Kontrolünde Ne Yapılabilir?



Rehberler Yeterince Kullanılıyor mu?



PROHIBIT
Prevention of Hospital Infections by Intervention & Training

Avrupa Ne Yapıyor?

- **ECDC TECHNICAL REPORT.** Risk assessment on the spread of CPE, September 2011
- Guidelines for the Prevention and Control of Multi-drug resistant organisms (MDRO) excluding MRSA in the healthcare setting. **Ireland**, 2012
- Guidance document on MDR-Gram negative from Robert Koch-Institut (RKI). **Germany**, 2012
- Non-prescribing control measures to prevent cross transmission of Carbapenemase-Producing Enterobacteriaceae in acute settings. **Scotland**, 2013
- Addressing rising trends and outbreaks in carbapenemase-producing Enterobacteriaceae, NHS **England**, 2014
- Guidance document on CRE from GEIH, GEMARA de la SEIMC, **Spain** 2014

CPE Yayılımını Önleyici Yaklaşımlar

- Lokal epidemiyolojik verilerin değerlendirilmesi
 - Problemin tayini
 - Hastalar, potansiyel risk altındakiler
 - Yayılım modelinin belirlenmesi
- Girişimler
 - Taşıyıcıların erken belirlenmesi
 - Kontaminasyon kaynakları
 - Dekolonizasyon ?
 - Medikal tedavi?
- Birimler arası koordinasyon

MDR'li Olgu Saptandıktan Sonra Ne Yapılmalı?

- İnfeksiyon kaynağı ve olası bulaş yolunu belirle
 - Kurum içi olası her türlü kaynağı araştır (IA)
- Temas zincirini belirle ve izle (IA)
 - Hastanede 2-3 günlük bir gecikme, bulaşın en az 8-10 olguya olduğunu düşündürmelidir.
 - KIT, YBU gibi kritik yerlerde tüm hastalar aynı anda en yüksek bulaş riskine sahiptir
 - Temas izlemi şüpheli olgu nereye yatarsa yatsın yapılmalı, ya da hastanın tekrar hastaneye kabul edilişi ile başlatılmalıdır.
- Temas söz konusu olduğunda, geniş çaplı izlem oluştur ve negatif olguları da tekrar incele (inkübasyon periyodu) (IB)

İnfeksiyon Kontrol Yöntemleri Network Sistemi



FIGURE 1. Distribution of Society for Healthcare Epidemiology of America Research Network members responding to the survey.

Sonuç

- GNB'lerde antibiyotik direnç sorunu giderek artıyor..
- Ulusal verilerin değerlendirilmesi,
- Uluslararası veri tabanına entegrasyon
- Akılcı antibiyotik yönetim sistemi
- Ulusal ve uluslararası rehberlerin geliştirilmesi
- Kesintisiz enfeksiyon kontrol önlemlerinin uygulanması gerekmektedir..



Teşekkürler..