Sorun Yaşadığımız Dirençli Mikroorganizmalarda Tedavi Yaklaşımları: Gram Negatifler

Dr. Oral ÖNCÜL
GATA Haydarpaşa Eğitim Hastanesi
Enf. Hst. Kl. Mik. Srv, Istanbul

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their corres
They cannot undertake to return, or to correspond with the writers of, rejected ma
intended for this or any other part of NATURE. *No notice is taken of anonymous commu*

IN THE PRESENT CIRCUMSTANCES, PROOFS OF "LETTERS" WILL NOT BE SUBMI
CORRESPONDENTS OUTSIDE GREAT BRITAIN.

An Enzyme from Bacteria able to Destroy Penicillin

FLEMING[1] noted that the growth of *B. coli* and a number ther bacteria belonging to the coli-typhoid g ibited by penicillin. This observati work has been dor organism

An e suspens mill of contair proper incuba extrac time. the A so was bact of e con sar cul de pu cl li t

solution its growth-inhibiting solution had retained its full streng

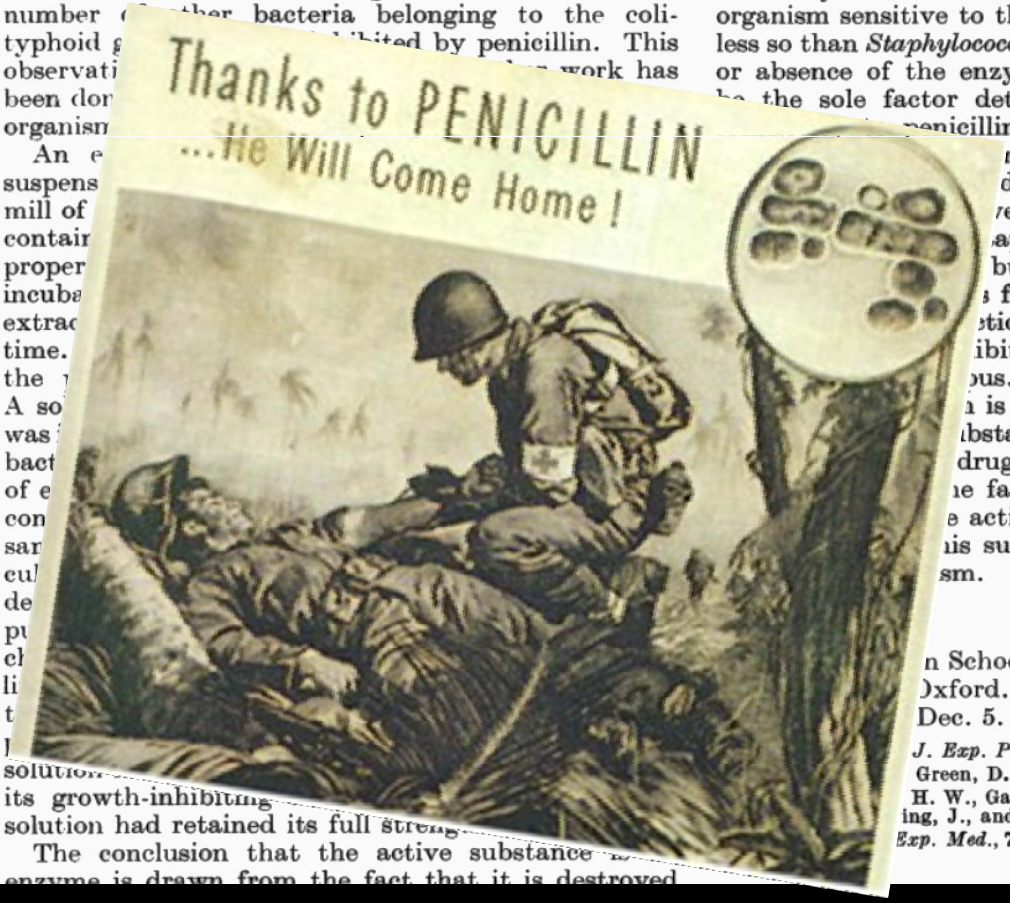
The conclusion that the active substance enzyme is drawn from the fact that it is destroyed

B. coli, it was not necessary to cru in the bacterial mill in order to ob from it; the latter appeared in t The enzyme was also found in *M.* organism sensitive to the action of p less so than *Staphylococcus aureus*. T or absence of the enzyme in a bac be the sole factor determining its penicillin.

nd tissue autol d to be without action on the ver of penicillin. Prof. A. D. aphylococcal pus to be devoid but has demonstrated a slight from a case of *B. coli* cystitis. tion of the s ibited in the pus.[4] That is not affecte bstance a defi drugs from the e fact that a e acting on peni is substance ma sm.

n School of Patho Oxford. Dec. 5.

J. Exp. Path., **10**, 226 (
Green, D. E., *Biochem.*
H. W., Gardner, A. D.,
ing, J., and Sanders, A.
Exp. Med., **72**, 217 (1940).



GSBL Evrimi

TEM-1 (1965)

1 aminoasit Penisilin ve I.kuşak SS

TEM-2 (1970)

2 aminoasit

CTX-M (1987)

Geniş spektrumlu beta-laktam

E.Coli ve K.pneumoniae'da Beta-Laktamazlar

Jacoby GA, et al. N Engl J Med, 2005; 352: 380-91

Beta-Laktamaz	Örnek	Antibiyotikler	Klavulanata yanıt	Sınıf
Geniş spektrumlu	TEM-1, TEM-2, SHV-1 OXA	Penisilinler, SS (dar spektrum) Oksasilin..	+++	A D
GSBL	TEM, SHV CTX-M OXA Diğer (BES-1, VEB-1..)	Pen, Monobaktam, SS.. Sefepim	++++ ++++ + ++++	A D A
Amp C	ACC-1, ACT-1, CFE-1, CMY..	GSBL + sefamisinler	0	C
Karbapenemaz	IMP, VIM, GIM-1, SPM-1(MBL) KPC-1, 2, 3 OXA-23, 24, 25..	GSBL + sefamisinler + karbapenem	0 +++ +	B A D

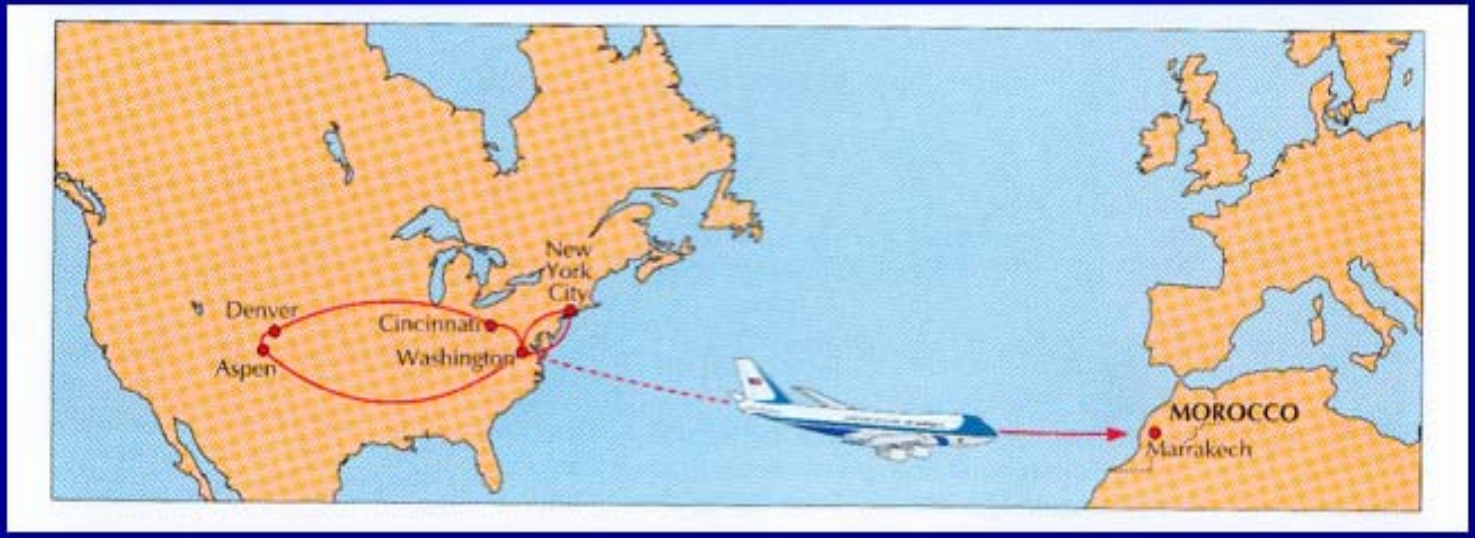
Gram Negatiflerde AB Dirençleri

- Class A
  - KPC Enzimi, 1990 North Carolina
- Class B
  - MBL (IMP-1), 1991 Japonya
  - NDM-1, 2009, New Delhi
  - VIM, 2010

Mobil
Kompleks
Önceden saptanamaz
Çoklu direnç paternine sahip

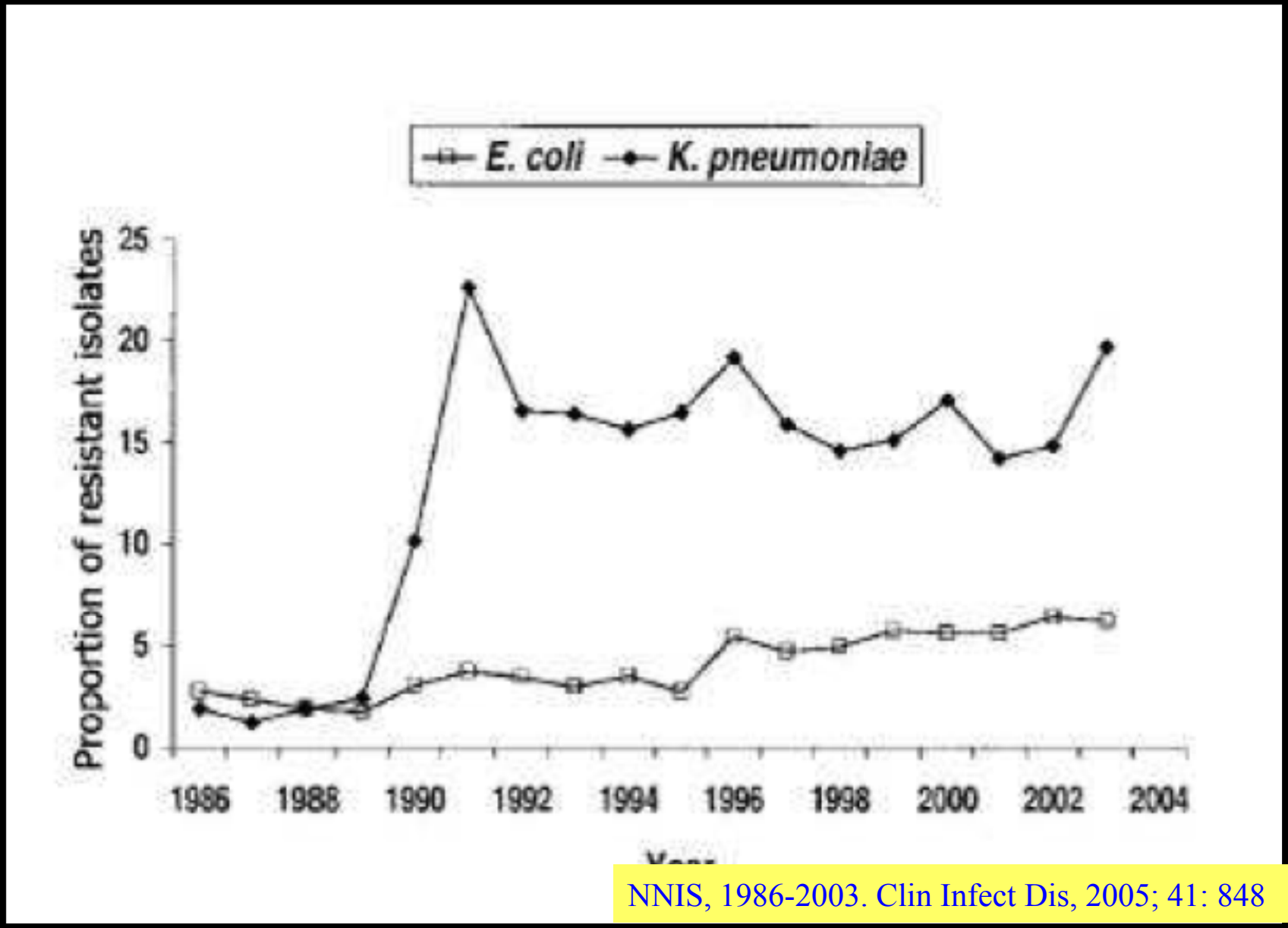
Epidemik Suşlar ve Yayılım

Transcontinental transfer of ATB resistance genes



250 millions flight a year !!!

GSBL Salgılayan E.coli ve Klebsiella Suşları



NNIS, 1986-2003. Clin Infect Dis, 2005; 41: 848

HEALTHCARE EPIDEMIOLOGY INVITED ARTICLE
Robert A. Weinstein, Section Editor

Overview of Nosocomial Infections Caused by Gram-Negative Bacilli

Robert Gaynes, Jonathan R. Edwards, and the National Nosocomial Infections Surveillance System
Division of Healthcare Quality Promotion, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

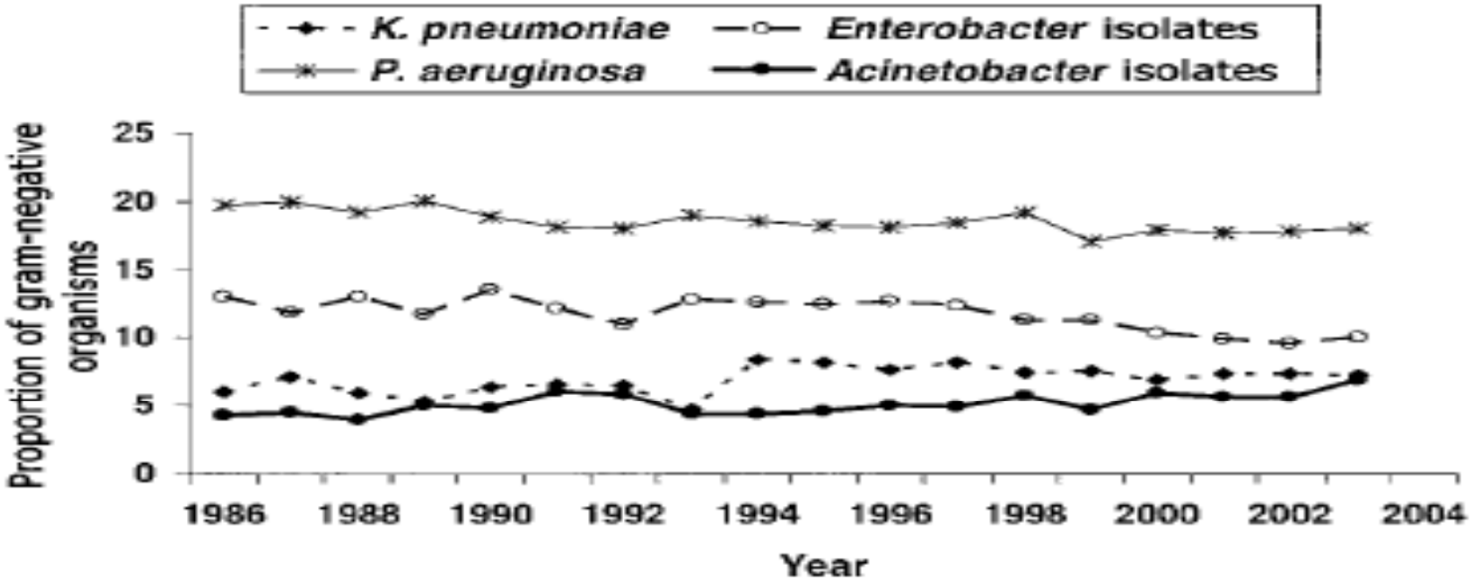


Figure 2. Results of intensive care unit surveillance for the proportion of selected gram-negative organisms reported for pneumonia from the National Nosocomial Infections Surveillance system, 1986–2003. The proportion of *Acinetobacter* species was significantly higher in 2003, compared with 1986 ($P < .001$, by the Cochran-Armitage χ^2 test for trend).

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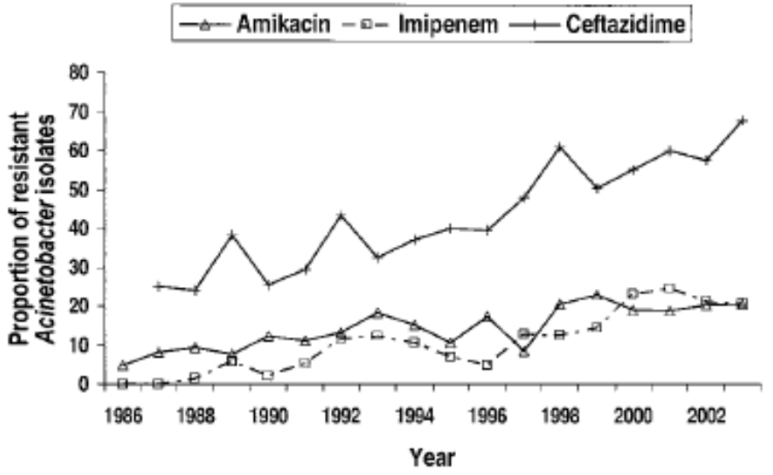
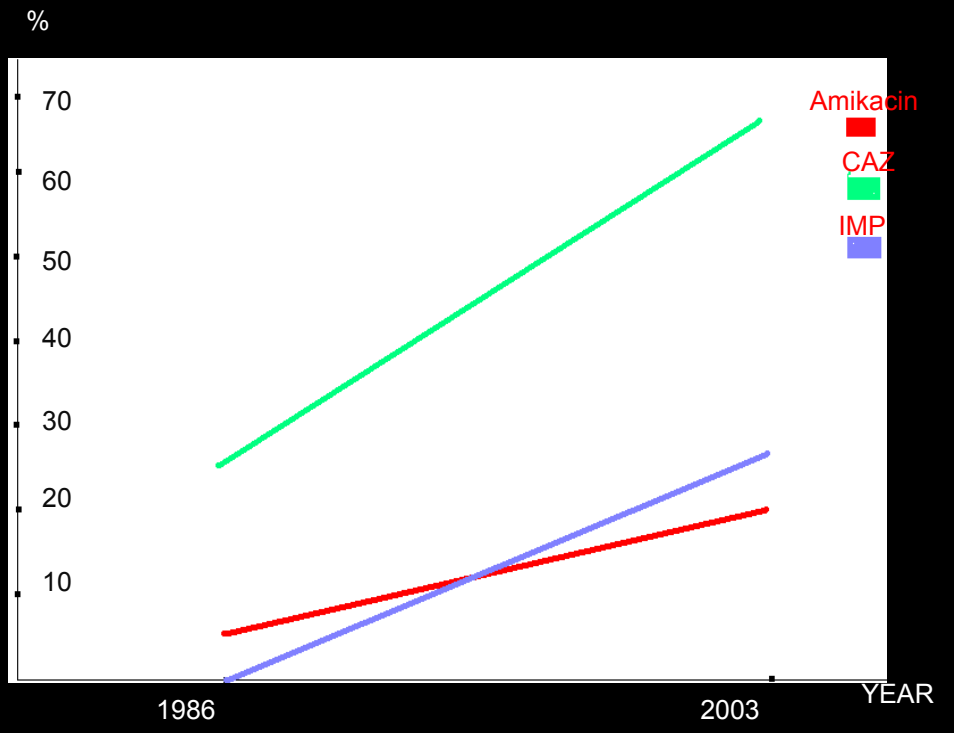
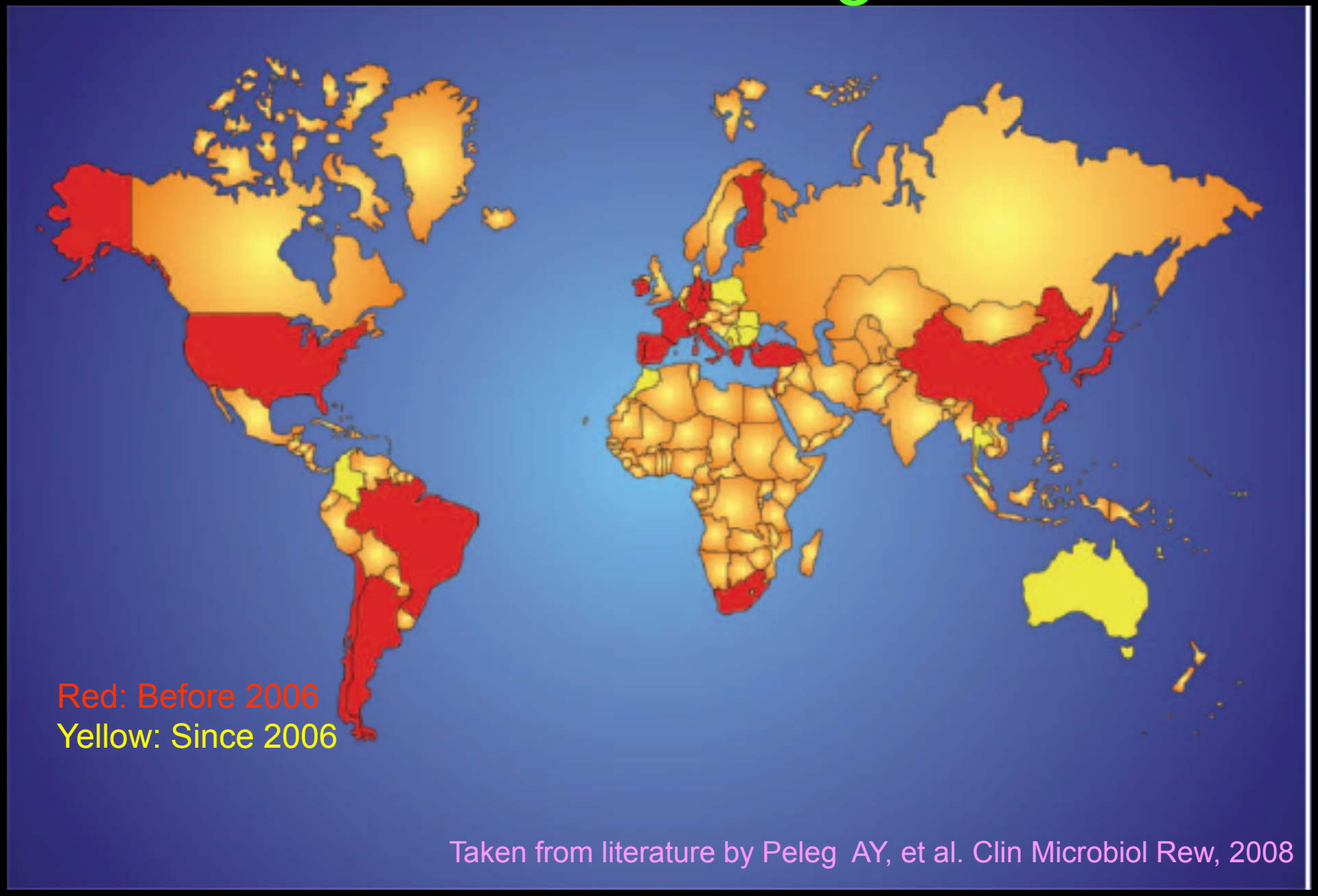


Figure 5. Results of intensive care unit surveillance revealing the proportions of *Acinetobacter* isolates that were resistant to amikacin, imipenem, and ceftazidime—National Nosocomial Infections Surveillance system, 1986–2003. In all instances, results of Cochran-Armitage χ^2 tests for trend were significant ($P < .001$).



Dünyada Karbapeneneme Dirençli *A.baumannii* Dağılımı



International Journal of Antimicrobial Agents 39 (2012) 105–114

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Review

Emergence of resistance to carbapenems in *Acinetobacter baumannii* in Europe: clinical impact and therapeutic options

Marie Kempf, Jean-Marc Rolain*

Aix-Marseille University, URMITE CNRS-IRD, UMR 6236, Faculté de Médecine et de Pharmacie, Université de la Méditerranée, 27 Bd. Jean Moulin, 13385 Marseille cedex 05, France

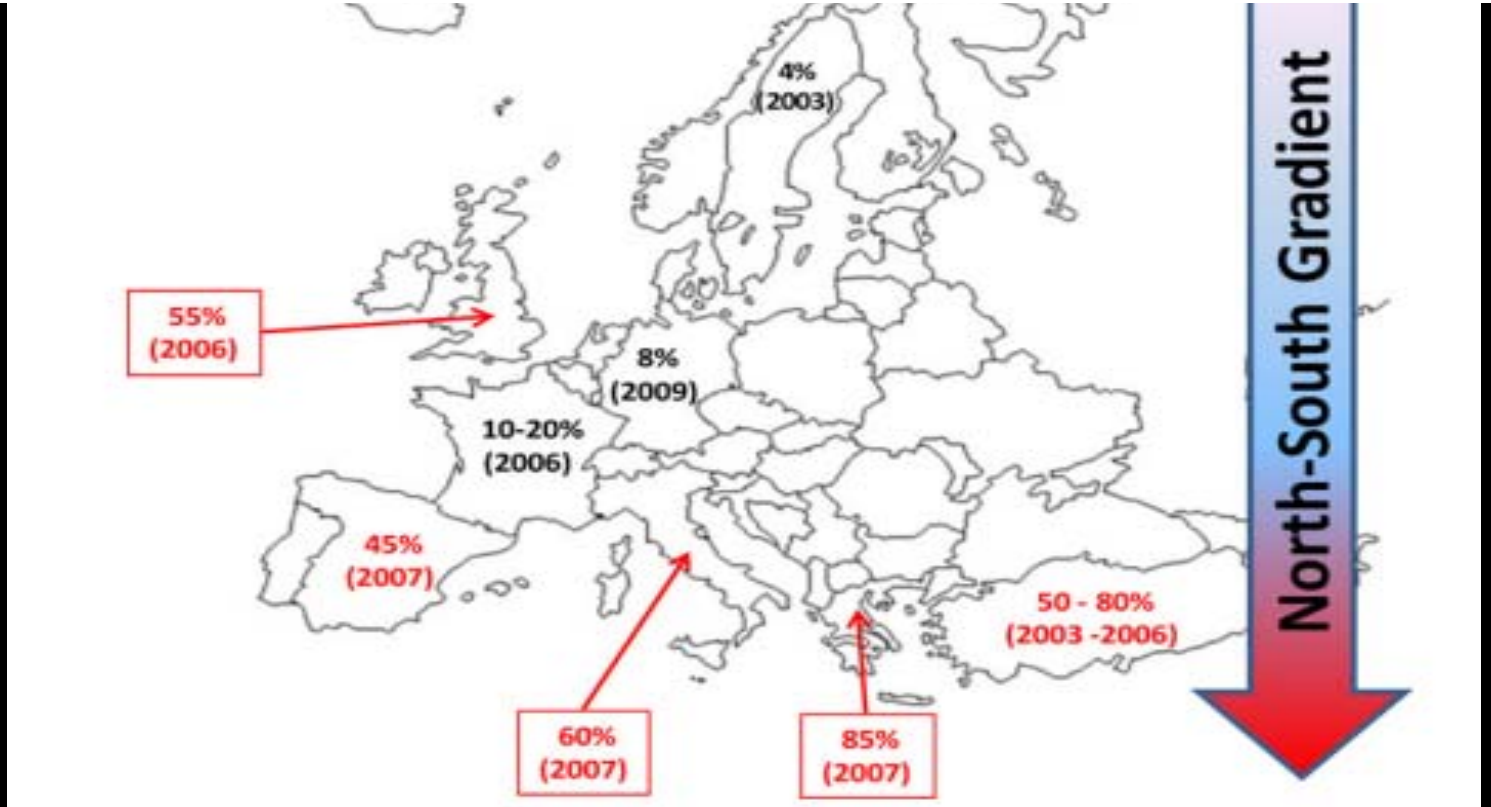


Fig. 3. The north to south gradient of prevalence of resistance to carbapenems in *Acinetobacter baumannii* in Europe (1997–2008).

Available online http://ccforum.com/content/12/S4/S4

Review

Gram-negative antibiotic resistance: there is a price to pay

Thomas G Slama

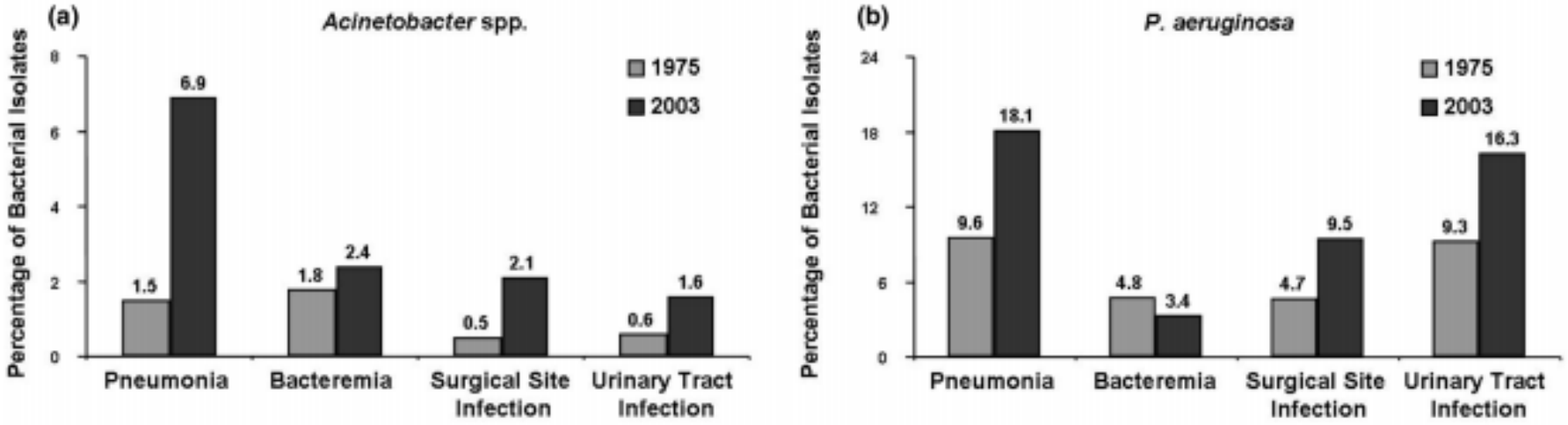
Indiana University School of Medicine, 8240 Nabb Road #300, Indianapolis, Indiana 46260, USA

Corresponding author: Thomas G Slama, slamaidi@aol.com

Published: 21 May 2008
This article is online at http://ccforum.com/content/12/S4/S4

Critical Care 2008, **12(Suppl 4)**:S4 (doi:10.1186/ccXXXX)

Figure 1



Acinetobacter spp. and *Pseudomonas aeruginosa* isolates: 1975 and 2003. Shown are the percentages of bacterial isolates associated with **(a)** *Acinetobacter* spp. and **(b)** *P. aeruginosa* by infection type in the National Nosocomial Infections Surveillance System for 1975 and 2003. Data from 1975 are from hospital-wide surveillance whereas those from 2003 are from intensive care unit surveillance [8].

Acinetobacter baumannii ile İlgili Klinik Çalışmaların Seyri

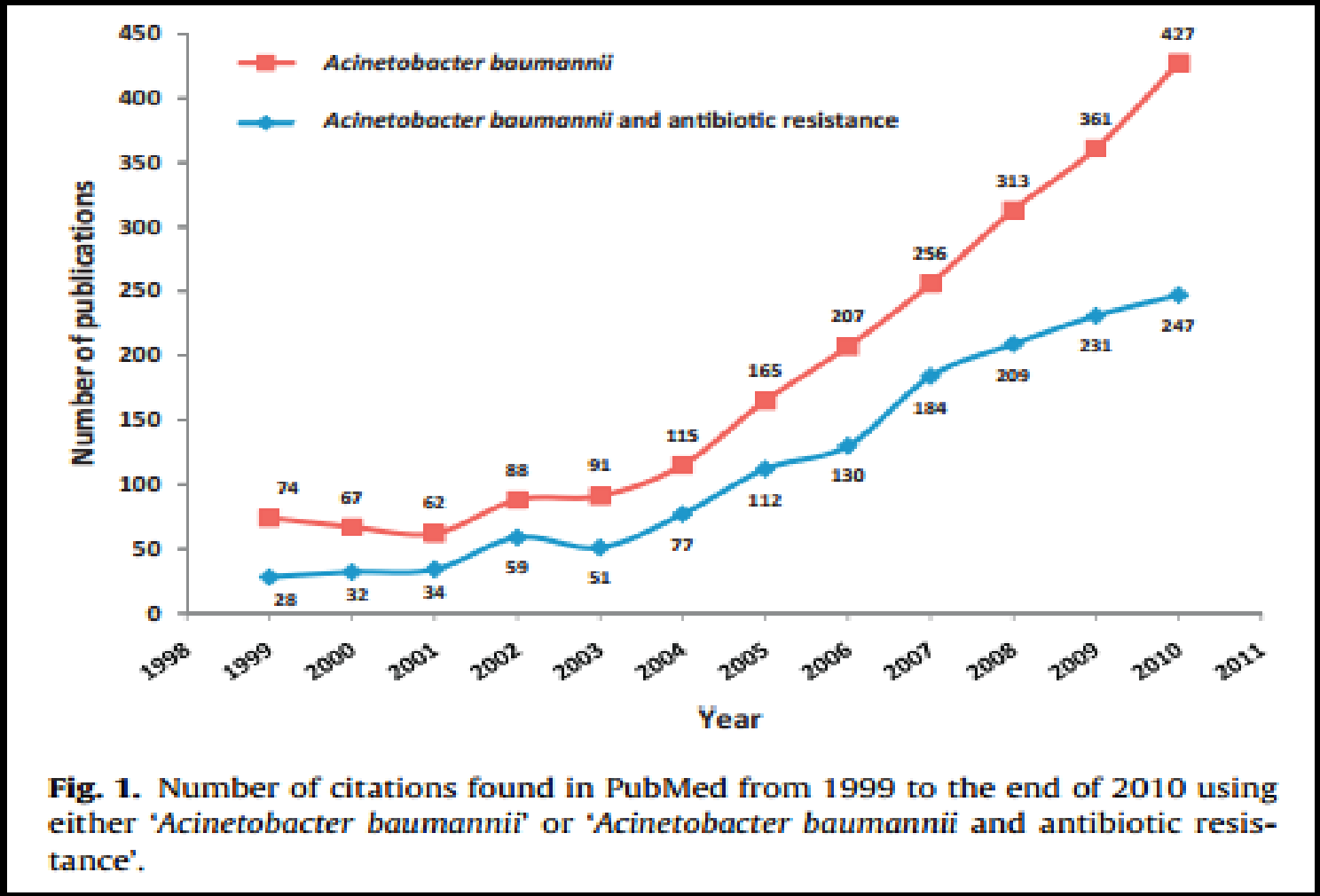
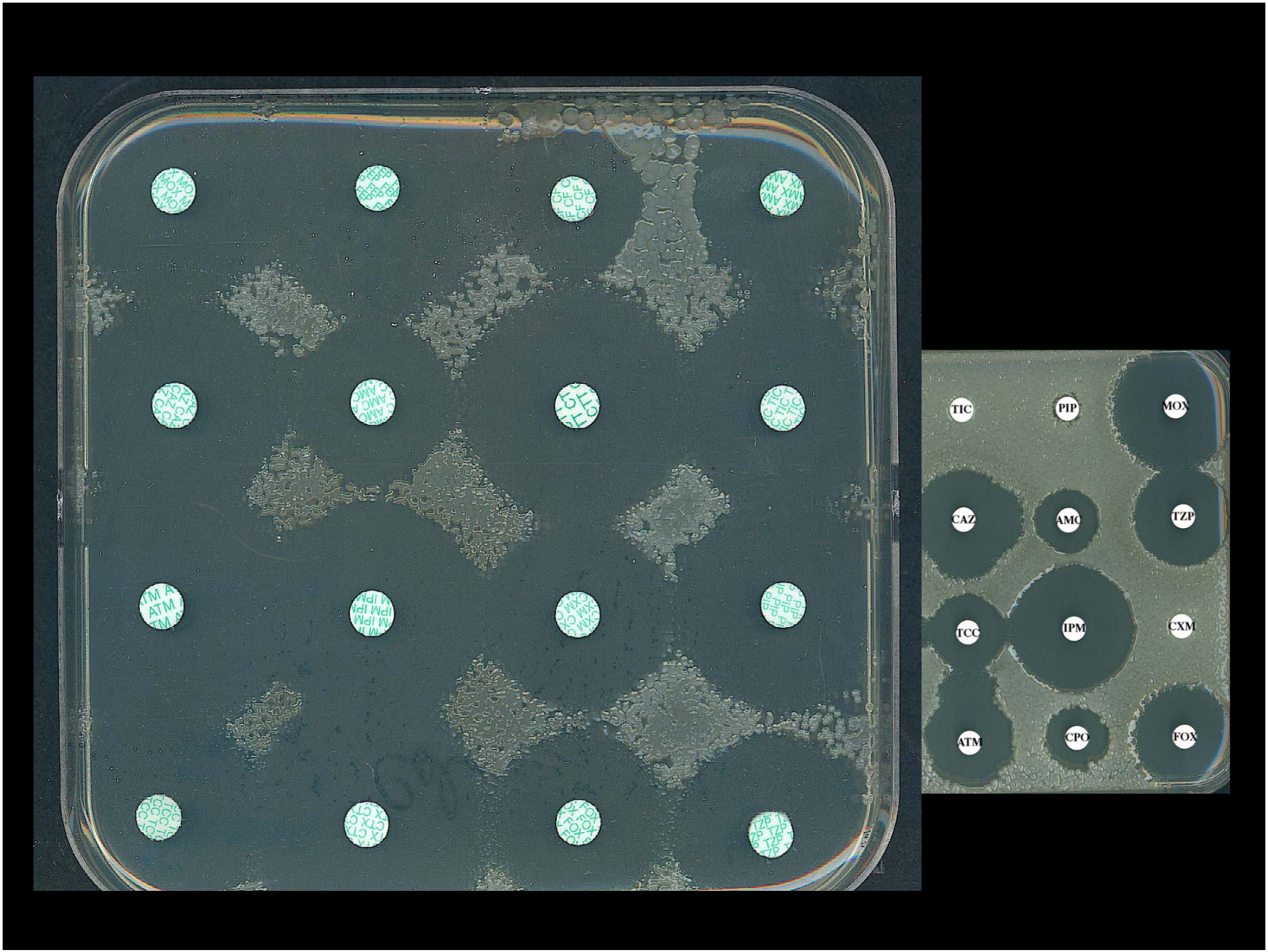


Fig. 1. Number of citations found in PubMed from 1999 to the end of 2010 using either '*Acinetobacter baumannii*' or '*Acinetobacter baumannii* and antibiotic resistance'.

Kempf M, et al. Int J Antimic Agents, 2012

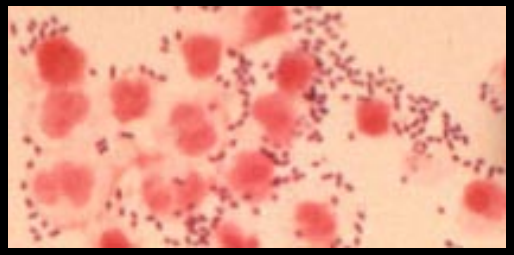

TIC
PIP
MOX
CAZ
AMC
TZP
TCC
IPM
CXM
ATM
CPO
FOX

A. baumannii

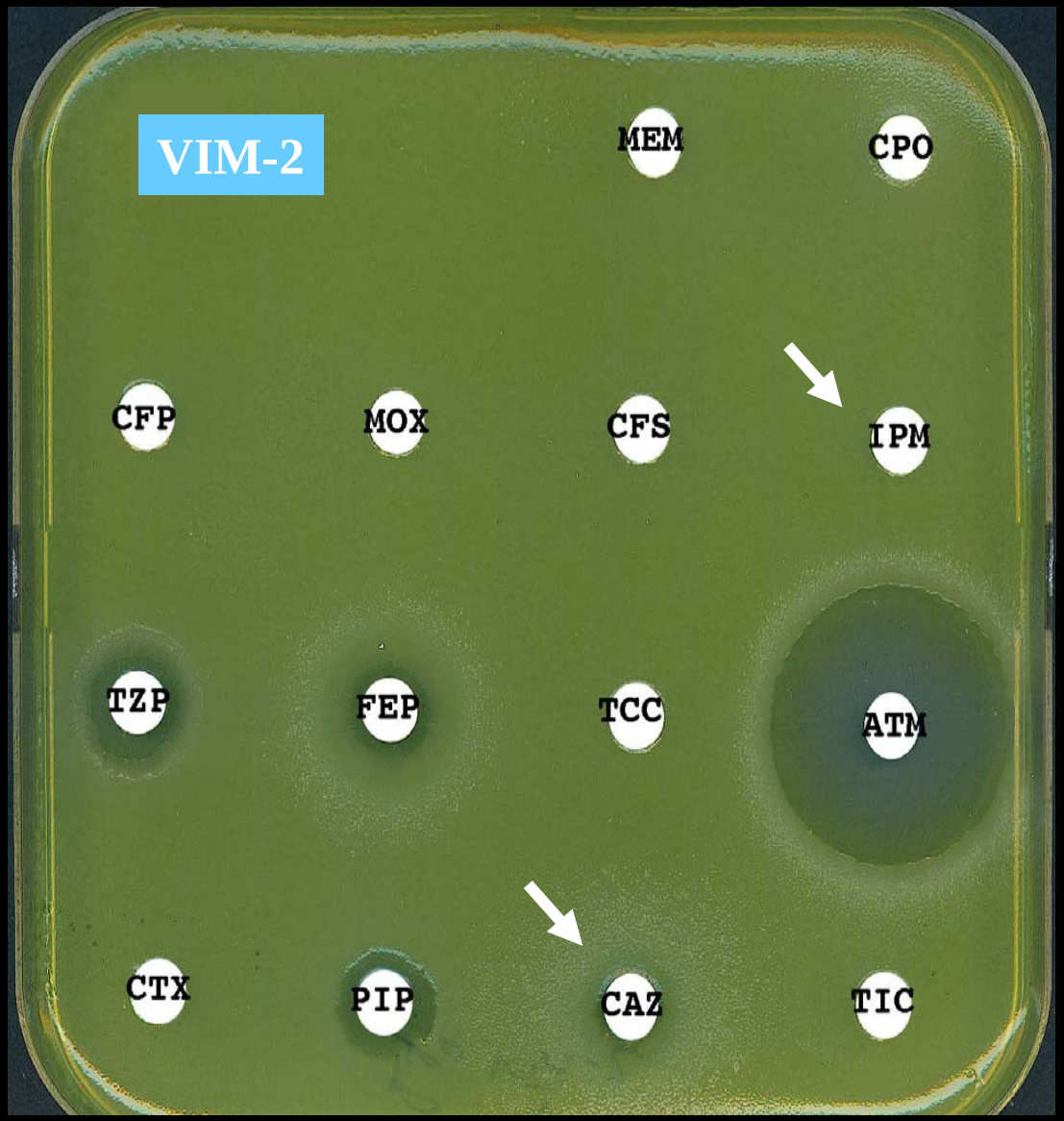
1980's

?

2000's



Metallo-ß-lactamases



- Spectrum
- Genetic background; plasmids, transposons, integrons…
- Associated resistance

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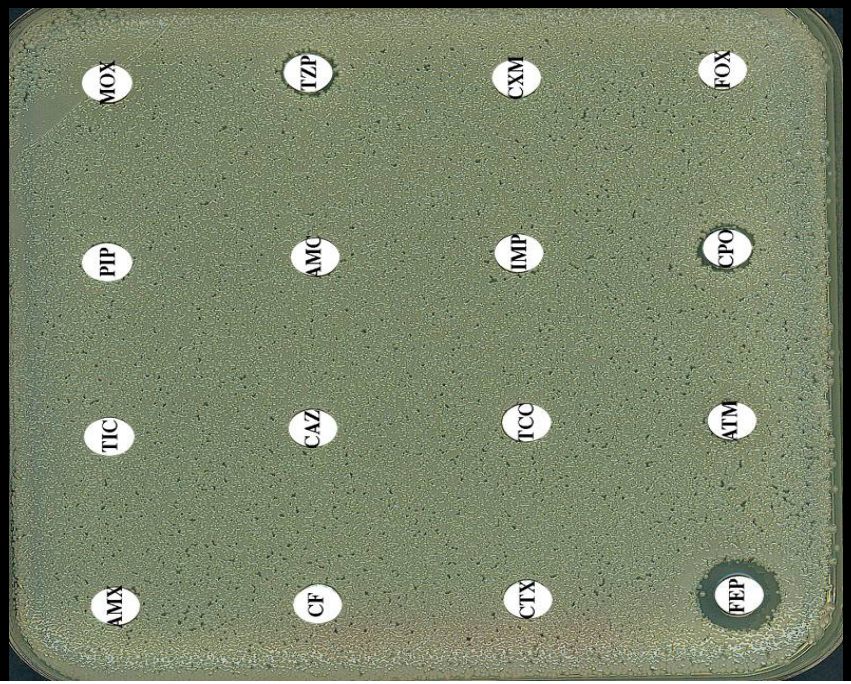
Aix-Marseille University, URMITE CNRS-IRD, UMR 6236, Faculté de Médecine et de Pharmacie, Université de la Méditerranée, 27 Bd. Jean Moulin, 13385 Marseille cedex 05, France

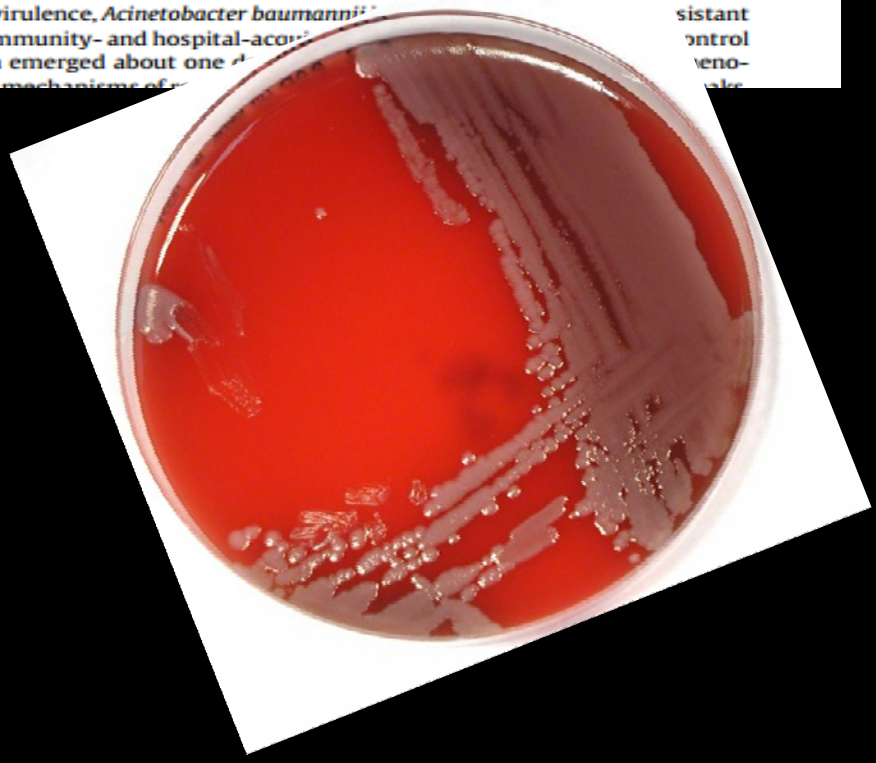
ARTICLE INFO

Keywords:
Colistin
Carbapenemase
Fitness cost

ABSTRACT

Despite having a reputation of low virulence, *Acinetobacter baumanni*
(MDR) pathogen responsible for community- and hospital-acq
and treat. Interest in this pathogen emerged about one
type, its capability of acquiring new mechanisms of r





Acinetobacter baumannii ve Direnç

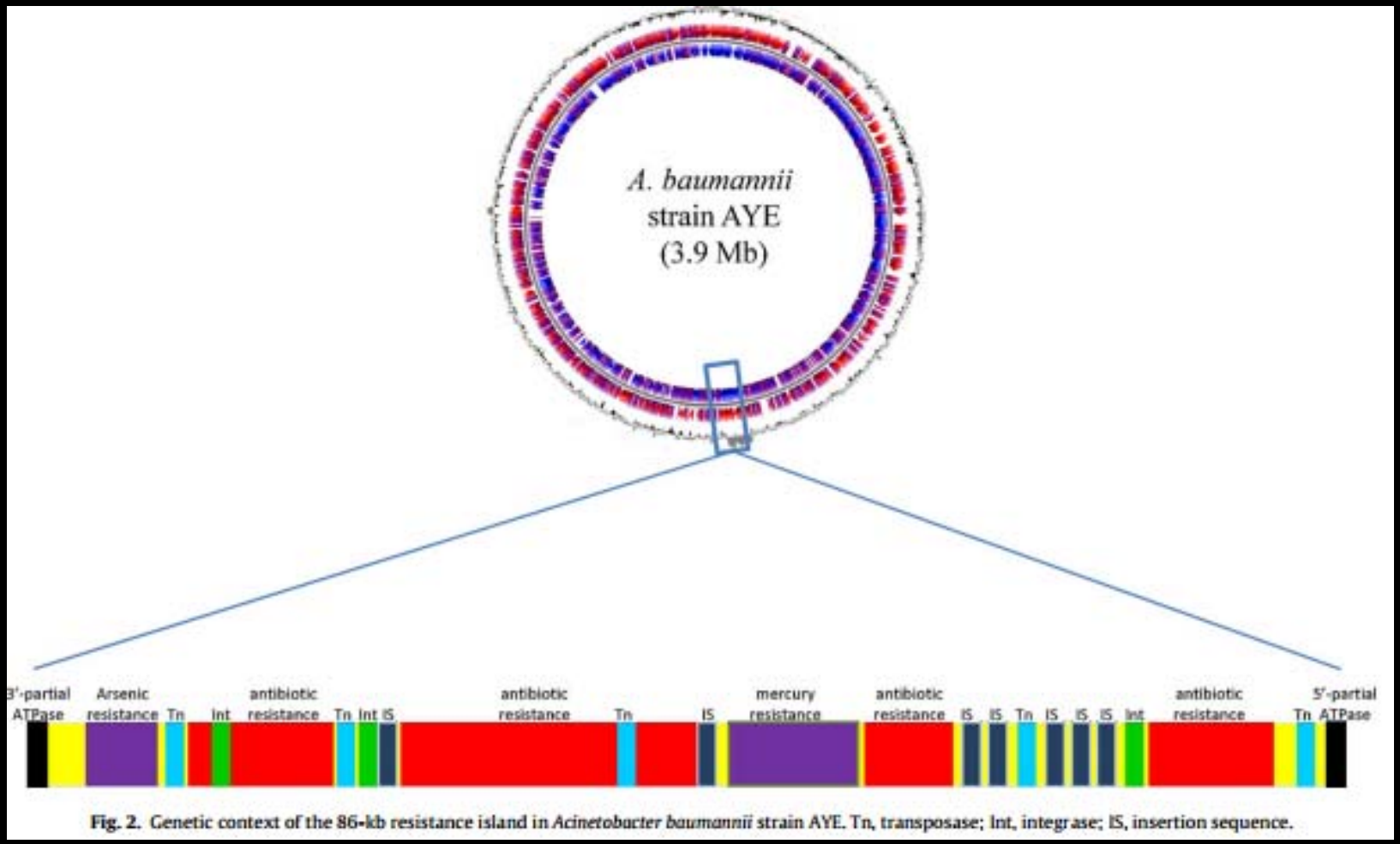
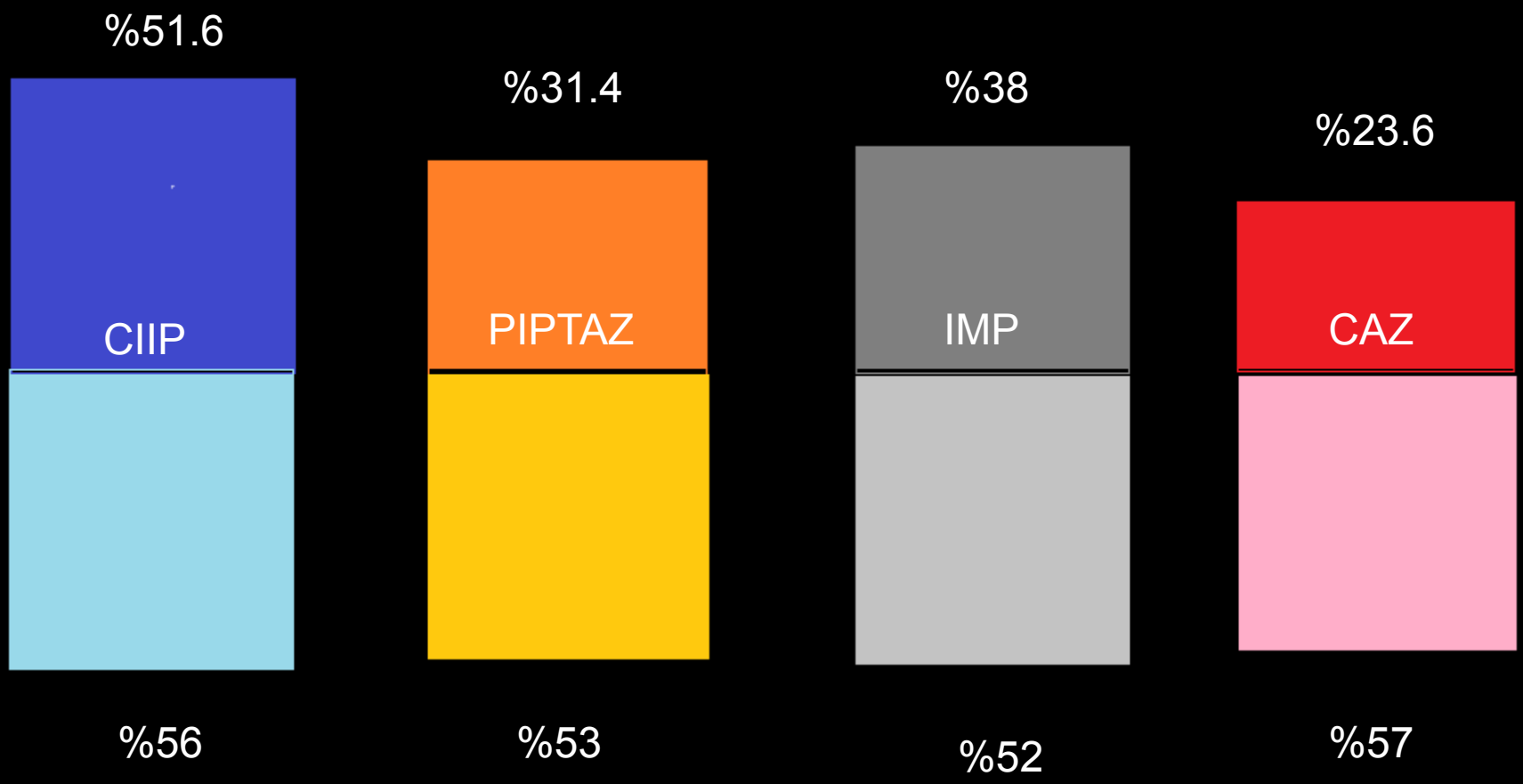


Fig. 2. Genetic context of the 86-kb resistance island in *Acinetobacter baumannii* strain AYE. Tn, transposase; Int, integrase; IS, insertion sequence.

NNIS Report (2004)

A.Baumannii Direnci (Bakterimi)



Europe (1990-1999)

Acinetobacter spp. ve Direnç Tanımı

Çoklu Direnç (Multidrug Resistant)

- ≥ 3 Sınıf Antibiyotik Direnci

- Kinolonlar
- Sefalosporinler
- Karbapenemler

Panresistant

- Tüm standart antibiyotiklere direnç

- Kolistin hariç..

Paterson DI, Clin Infect Dis, 2006

Bakteriler ve Direnç Tanımı

- ≥ 3 Sınıf Antibiyotik
- Direnci

- Kinolonlar
- Sefalosporinler
- Karbapenemler

- Tüm standart antibiyotiklere direnç

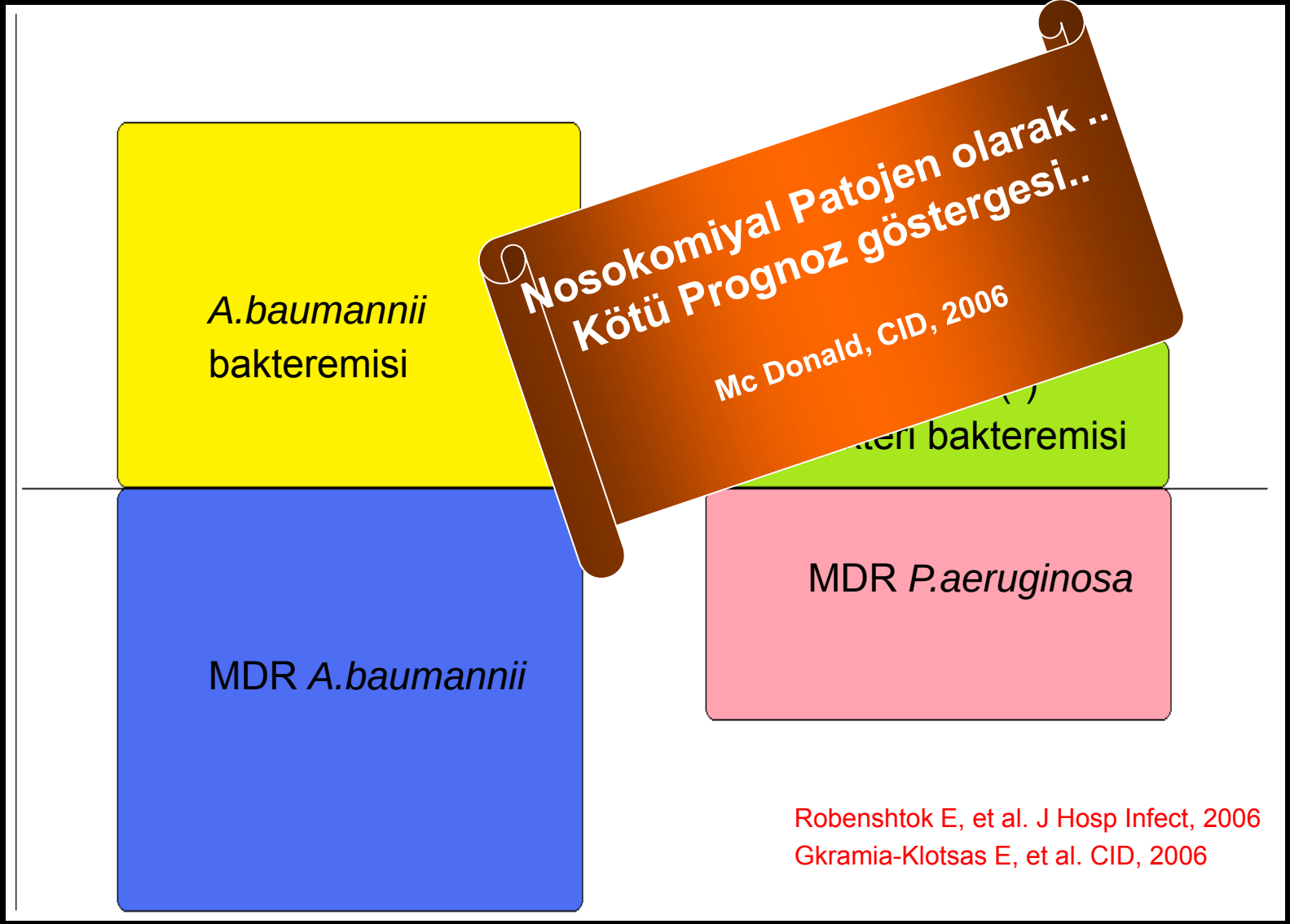
- Kolistin hariç..

Tüm standart antibiyotiklere direnç

- Kolistin dahil..

Sauli M, et al. Eurosurveillance, 2008

Acinetobacter infeksiyonları Niçin Daha Tehlikelidir?



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]

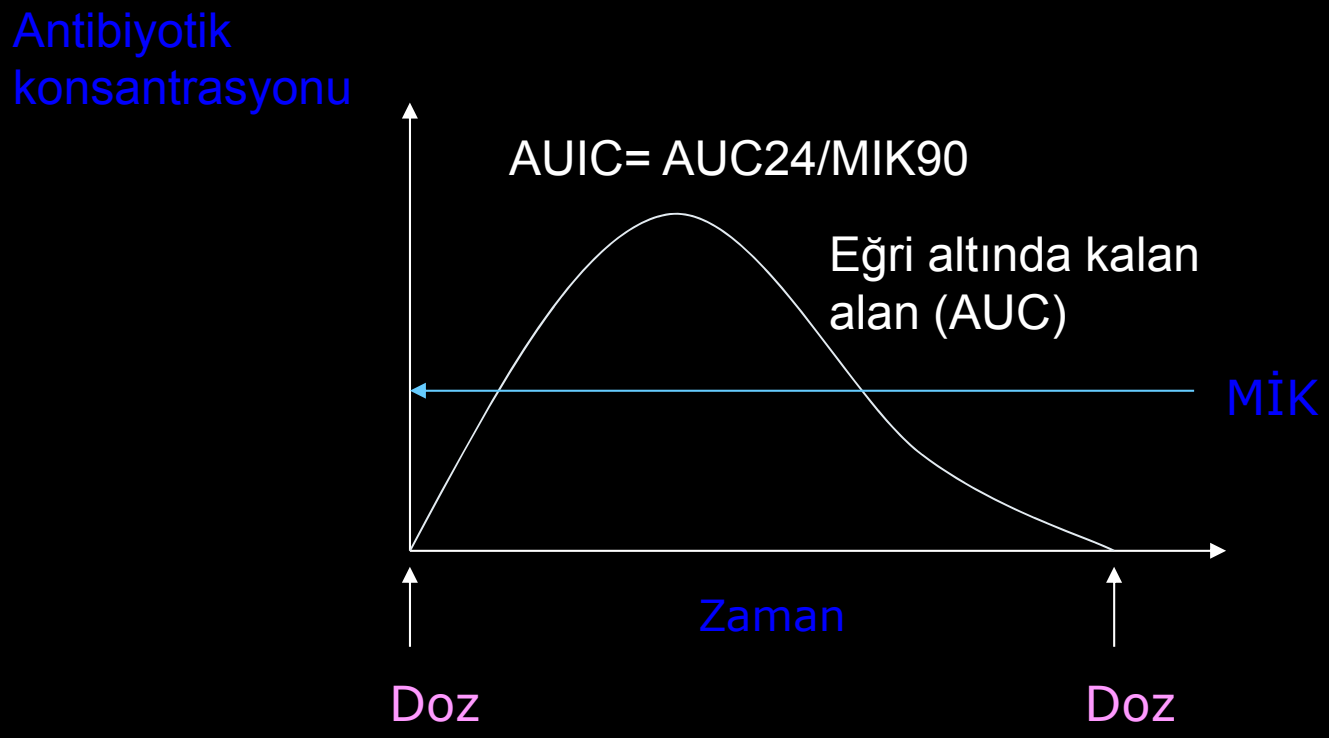
- Uzamış kolonizasyon..
- 42 ay
- Hastaların %17'si
- *Acinetobacter sp.* ENDEMİK KAREKTER


Cuba correos 5

Tedavi ile Cevap Arayan Önemli Sorular..

- Hangi antibiyotik ?
- Monoterapi mi? Kombinasyon mu?
- Parenteral mi? İnhalasyon uygulama mı?
- FK / FD profil sonucu değiştirir mi?
- Elde kalanları nasıl koruyabiliriz?
- Yeni ajanlar var mı?
- PDR patojenlerde neden mortalite az?
- Sorunlu bakteriler gerçekten bir sorun mu?

Antibiyotiklerde zamana bağımlı bakterisidal etkinlik (T>MİK)



Konsantrasyona Bağlı Etki (Cmax/MIK, AUC/MIK)

- FQ, AG, Colistin, ketolidler, azitromisin, daptomisin, metronidazol..
- Cmax/MIK ≥ (4-10)
- AUC_{24} / MIK ≥ (100-125)
- Yüksek tek doz kullanım avantajı

FK ve FD parametrelerin klinik uygulaması

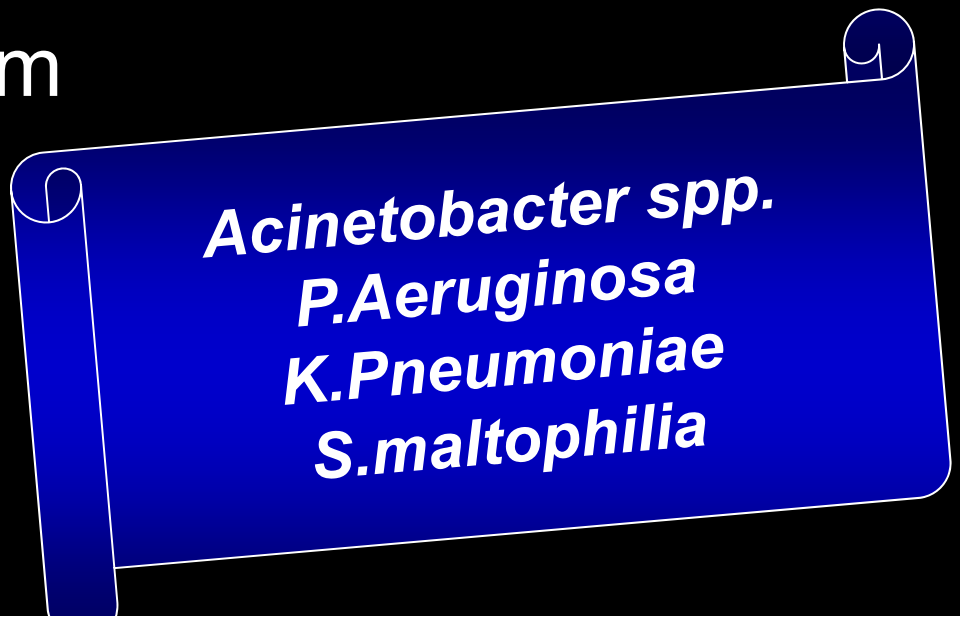
- Doz aralığında antibiyotik serum konsantrasyonunun %100 MİK'in üzerinde tutulması (T>MİK)

- Piperasilin-tazobaktam ve meropenem gibi antibiyotiklerin sürekli ya da üç saatlik infuzyonlarla verilmesi
- Maksimum öldürücü etki (4-5 x MIK)

Kuti JL et al. Diag Microbiol Infect Dis 44: 51_57, 2002.
Kuti JL et al. J Clin Pharmacol 43: 1116-1123, 2003.

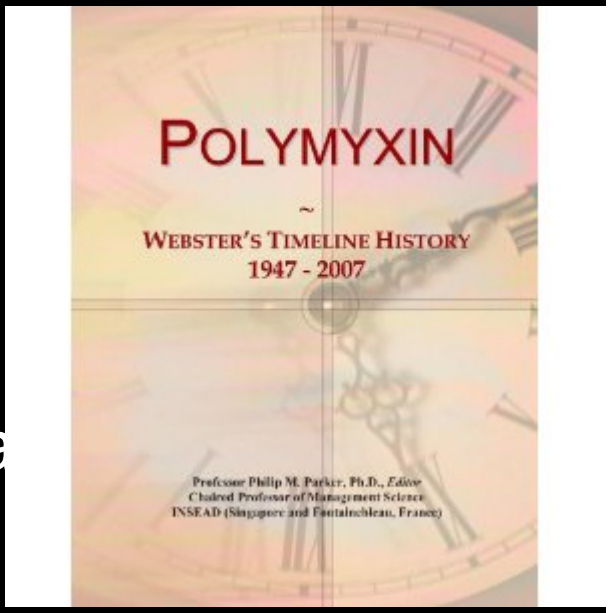
Tedavi Seçenekleri..

- Polimiksin B / E (Colistin)
- Fosfomisin
- Tigesiklin
- Doripenem
- Sulbaktam



Polimiksin

- 1947 *Bacillus polymyxa*
- Polimiksin B ve E (Colistin)
- Colistin
  - Colistin Sulfat (tablet, şurup, topika
  - Colistimethate sodium, (CMS) (Parenteral)
- Polimiksin B sulfat (ABD, Brezilya)



M100-S21
Vol. 31 No. 1
Replaces M100-S20 and M100-S20-U
Vol. 30 No. 1 and Vol. 30 No. 15

January 2011

Performance Standards for Antimicrobial Susceptibility Testing; Twenty-First Informational Supplement

Institute antimicrobial susceptibility testing standards M02-A10 and M07-A8.
An informational supplement for global application developed through the Clinical and Laboratory Standards Institute consensus process.

Test/Report Group	Antimicrobial Agent	Disk Content	Zone Diameter Breakpoints, nearest whole mm			MIC Interpretive Standard (µg/mL)			Comments
			S	I	R	S	I	R	
PENICILLINS									
B	Piperacillin	100 µg	≥ 21	18–20	≤ 17	≤ 16	32–64	≥ 128	
O	Mezlocillin	75 µg	≥ 21	18–20	≤ 17	≤ 16	32–64	≥ 128	
O	Ticarcillin	75 µg	≥ 20	15–19	≤ 14	≤ 16	32–64	≥ 128	
β-LACTAM/β-LACTAMASE INHIBITOR COMBINATIONS									
A	Ampicillin-sulbactam	10/10 µg	≥ 15	12–14	≤ 11	≤ 8/4	16/8	≥ 32/16	
B	Piperacillin-tazobactam	100/10 µg	≥ 21	18–20	≤ 17	≤ 16/4	32/4–64/4	≥ 128/4	
B	Ticarcillin-clavulanic acid	75/10 µg	≥ 20	15–19	≤ 14	≤ 16/2	32/2–64/2	≥ 128/2	
CEPHEMS (PARENTERAL) (Including cephalosporins I, II, III, and IV. Please refer to Glossary I.)									
A	Ceftazidime	30 µg	≥ 18	15–17	≤ 14	≤ 8	16	≥ 32	
B	Cefepime	30 µg	≥ 18	15–17	≤ 14	≤ 8	16	≥ 32	
B	Cefotaxime	30 µg	≥ 23	15–22	≤ 14	≤ 8	16–32	≥ 64	
B	Ceftriaxone	30 µg	≥ 21	14–20	≤ 13	≤ 8	16–32	≥ 64	
CARBAPENEMS									
A	Imipenem	10 µg	≥ 16	14–15	≤ 13	≤ 4	8	≥ 16	
A	Meropenem	10 µg	≥ 16	14–15	≤ 13	≤ 4	8	≥ 16	
LIPOPEPTIDES									
O	Polymyxin B	–	–	–	–	≤ 2	–	≥ 4	
O	Colistin		–	–	–	≤ 2	–	≥ 4	

Polimiksin MİK Değerleri

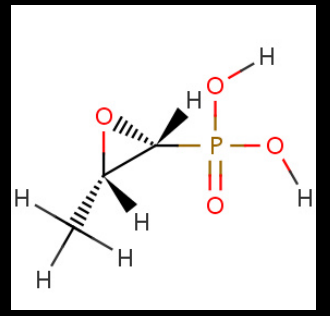
CLSI (2005)

Bakteriler	Duyarlı	Dirençli
P.aeruginosa	≤2	8≥
A.baumannii	≤2	4≥

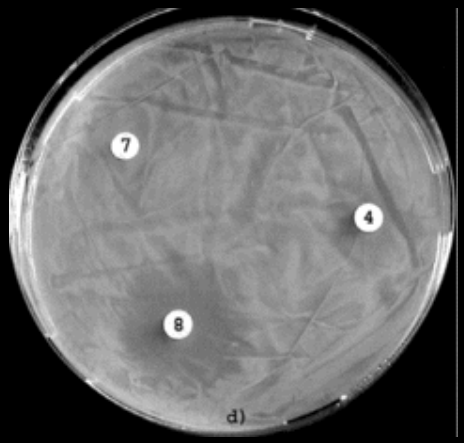
EUCAST (2009)

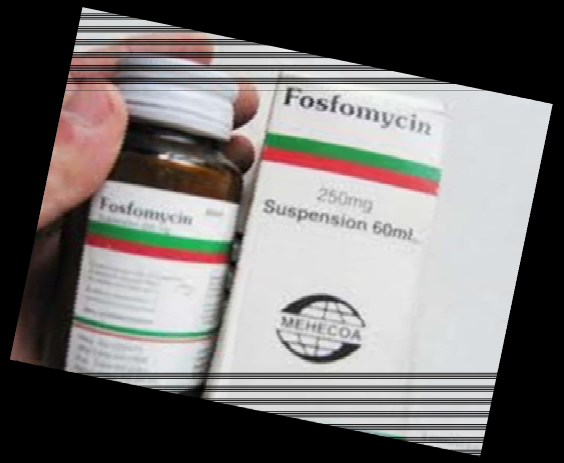
Enterobacteriaceae	≤2	4≥

Fosfomisin Tromethamine



- Fosfomisinin sentetik bir tuzu (1969)
- İn vitro aktivite
  - ESBL salgılayan Enterobacteriaceae
  - MDR/ PDR *Pseudomonas aeruginosa*
- Bilinen bir toksisitesi bulunmuyor
- Klinik deneyimler yeterli değil..





Tedavi Alanında Fosfomisin

- Fransa, Prospektif kohort çalışma
- 116 hasta ,izlem süresi >10 hafta
- Osteoartritis, ÜSİ, akciğer enf, bakteremi
  - *Pseuodomonas aeruginosa*, (%71.8 MDR)
  - MRSA
- %44 YBU takibi
- Tedavi başarısı %76.8 (76/99)

Dinh A, et al. Scand J Infect Dis. 2012 ;44(3):182-9.

Eur J Clin Microbiol Infect Dis (2012) 31:695–701
DOI 10.1007/s10096-011-1360-5

ARTICLE

Synergy of fosfomycin with carbapenems, colistin, netilmicin, and tigecycline against multidrug-resistant *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa* clinical isolates

G. Samonis · S. Maraki · D. E. Karageorgopoulos · E. K. Vouloumanou · M. E. Falagas

Sorunlu Bakterin Tedavisinde ETKİLİ..

Table 3 Synergy of fosfomycin combinations against the isol

Antibiotic in combination with fosfomycin	*Klebsiella pneumoniae*, all isolates (*N*=65)	ESBL-produc *Klebsiella pneumoniae* (*N*=	herichia	ing	MDR *Pseudomonas aeruginosa* (*N*=15)
			20)		
Isolates exhibiting synergy, *n* (%)					
Imi		(74.0)		11 (55.0)	7 (46.7)
Mer		35 (70.0)		5 (25.0)	8 (53.3)
Dor		(74.0)		6 (30.0)	11 (73.3)
Col				3 (15.0)	2 (13.3)
Net		(42.0)		5 (25.0)	2 (13.3)
Tig		15 (30.0)		5 (25.0)	2 (13.3)

Karbapenem + Fosfomisin (K.pneum)
Colistin + Tigesiklin + Fosfomisin (PDR)

Abbreviations: ESBL: extended-spectrum β-lactamase; MDR: multidrug-resistant

Colistin (CMS) Dozları

- 2.5-5.0 mg /kg doz/ gün (2-4 doz)
- 31.250-62.500 IU/kg
- 3 doz , 2 doza oranla daha başarılı

Michalopoulos and Falagas *Annals of Intensive Care* 2011, 1:30
http://www.annalsofintensivecare.com/content/1/1/30

Annals of Intensive Care
a SpringerOpen Journal

REVIEW Open Access

Colistin: recent data on pharmacodynamics properties and clinical efficacy in critically ill patients

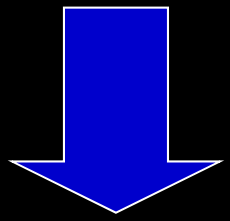
Argyris S Michalopoulos[1,2] and Matthew E Falagas[2,3,4*]

- MDR/PDR *Acinetobacter, P.aeruginosa*, Enterik bakteriler..
- Uygun olmayan
  - Uygun
  - Uygun olm
  - Uygun olm val..

Mortaliteda anlamlı Artış P=0.002

Kombinasyon ve Kolistin

- Polimiksin + IMP

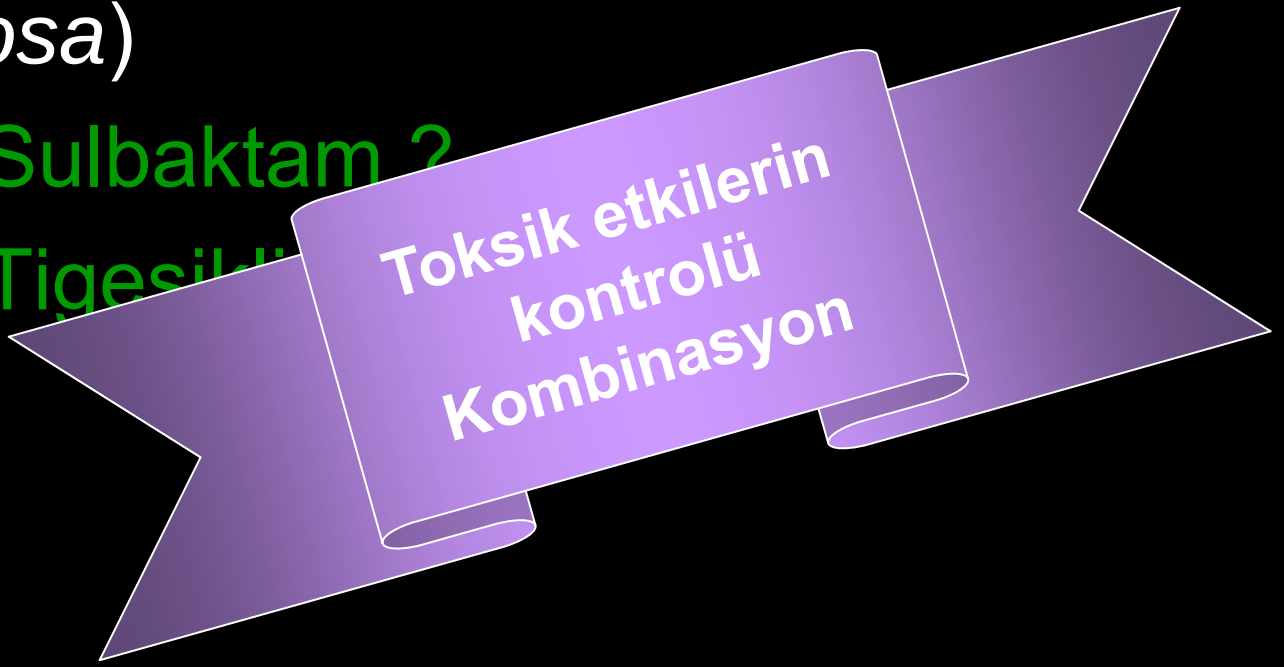


- 3 log CFU/mL azalma
- Zamana bağlı etkinlikte artış
- Direnç gelişiminde azalma
- Uygun başlangıç tedavi şansı..

Falagas MJ, Int J Antimicrob Agents, 2008

Sinerjik Etki

- Colistin + Rifampisin (MDR Acinetobacter)
- Colistin + Minosiklin (IMP-R Acinetobacter)
- Colistin + Meropenen (*A.baumannii, P.aeruginosa*)
- Colistin + Sulbaktam ?
- Colistin + Tigesiklin



Kombinasyonda Colistin

95 kanser hastası, MDR *P.aeruginosa*

- CMS (31)
- %45 nötropenik
- %52 Klinik Yanıt
- %31 mikrob.yanıt
- Relaps: %10
- %23 nefrotoksisite
- %26 mortalite

- Colistin + FO/BL(64)
- %37 nötropenik
- %48 klinik yanıt
- %41 mikrob. Yanıt
- Relaps: %11
- %22 nefrotoksisite
- %17 mortalite

Hachem RY, et al. Antimic Agent Chemother, 2007

ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Mar. 2009, p. 1295–1296 Vol. 53, No. 3
0066-4804/09/$08.00+0 doi:10.1128/AAC.01097-08

In Vitro Activities of Tigecycline, Minocycline, and Colistin-Tigecycline Combination against Multi- and Pandrug-Resistant Clinical Isolates of *Acinetobacter baumannii* Group▽

- 150 A.baumannii
- TG MİK < MİN
- Colistin + TG
- Zamana bağlı öldürücü etki

TABLE 1. Results of in vitro susceptibility testing of 150 *A. baumannii* group clinical isolates

Isolate[a]	*n*	Tigecycline[b] MIC (μg/ml)[c]			Minocycline MIC (μg/ml)[c]			% Susceptible
		Range	50%	90%	Range	50%	90%	
PDR	46	0.5–8	1	2	0.25–16	8	16	8.7
XDR	40	0.25–4	1	2	0.25–32	8	16	30
IPM-S	64	0.03–2	1	2	≤0.06–16	4	8	60.9
Total	150	0.03–8	1	2	≤0.06–32	8	16	36.6

[a] The isolates were classified according to the susceptibility to the antimicrobials listed in the text (excluding tigecycline and minocycline) as follows: PDR, resistant to all antibiotics including colistin; extensively drug resistant (XDR), only susceptible to colistin; and (for the rest of the isolates), imipenem susceptible (IPM-S), displaying variable susceptibility to the remaining agents.
[b] No susceptibility breakpoint for *Acinetobacter* has been provided by CLSI.
[c] 50% and 90%, MIC_{50} and MIC_{90}, respectively.

Journal of Antimicrobial Chemotherapy (2007) **60**, 421–423
doi:10.1093/jac/dkm178
Advance Access publication 31 May 2007

JAC

In vitro effect of minocycline and colistin combinations on imipenem-resistant *Acinetobacter baumannii* clinical isolates

Thean Yen Tan[1]*, Lily Siew Yong Ng[1], Eugene Tan[2] and Gary Huang[2]

[1]*Laboratory Medicine Services, Changi General Hospital, 2 Simei Street 3, Singapore 529889;*
[2]*Ngee Ann Polytechnic, 535 Clementi Road, Singapore 599489*

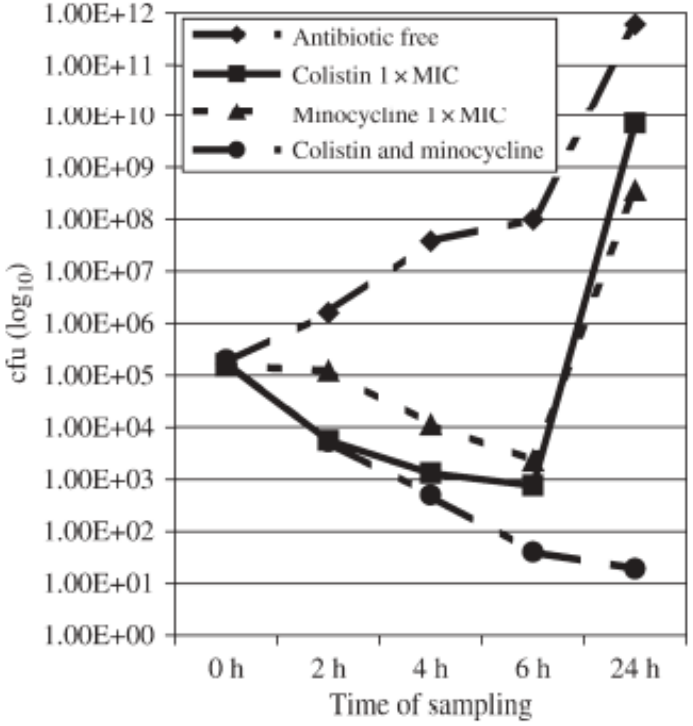


Figure 1. Time–kill curves of representative study isolate.

Table 1. Bacterial counts and synergy interpretation by time–kill methods

Antibiotic		Time of sampling after incubation			
		2 h	4 h	6 h	24 h
Colistin	average change in cfu (log_{10})	−0.7	−1.1	−1.0	+4.1
Minocycline	average change in cfu (log_{10})	−0.7	−0.7	−0.3	+3.4
Colistin and minocycline	average change in cfu (log_{10})	−2.2	−2.8	−3.1	−3.2
	no. (%) of isolates showing bactericidal activity	4 (31%)	7 (54%)	7 (54%)	9 (69%)
	no. (%) of isolates showing synergy	1 (8%)	2 (15%)	2 (15%)	12 (92%)

Kolistinin Aerosol Formu Etkili mi?

- Retrospektif çalışma..
- MDR *P.aeruginosa* ve *A.baumanni*i VAP
  - %86 klinik yanıt
  - %61 etken eradikasyonu

Kwa ALH, CID, 2005

Aerosol formun tek başına Uygun değil.. Parenteral formla birlite verilmeli..

Journal of Antimicrobial Chemotherapy (2008) **62**, 1311–1318
doi:10.1093/jac/dkn425
Advance Access publication 15 October 2008

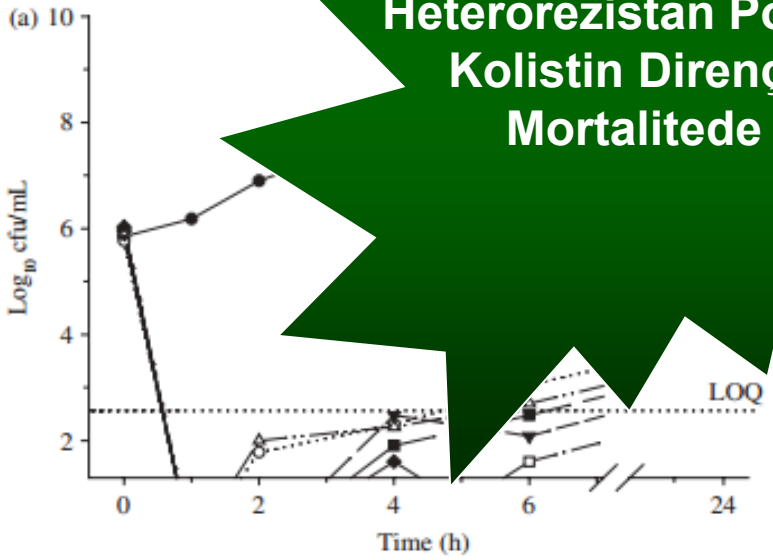
JAC

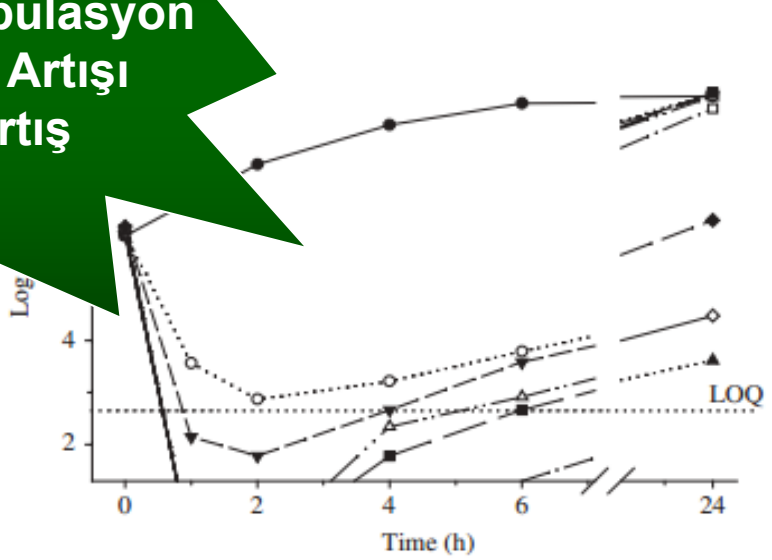
In vitro pharmacodynamics of colistin against multidrug-resistant *Klebsiella pneumoniae*

Anima Poudyal[1], Benjamin P. Howden[2], Jan M. Bell[3,4], Wei Gao[2], Roxanne J. Owen[1], John D. Turnidge[3,4], Roger L. N[illegible]on[1]† and Jian Li[1]*†

[1]Facility for Anti-infective Drug Developmen[illegible]nd Innov[illegible] Monash Institute of Pharmaceutical Sciences, Monash University, VIC, Australia; [2]Infec[illegible] Dis[illegible]l Microbi[illegible]logy Departments, Austin Health, VIC, Australia; [3]Division of [illegible]boratory M[illegible]and C[illegible]ren's Hospital, North Adelaide, SA, [illegible]lia; [4]U[illegible]de [illegible]ustralia

Heterorezistan Populasyon
Kolistin Direnç Artışı
Mortalitede artış





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[1]Facility for Anti-infective Drug Development and Innovation, Monash Institute of Pharmaceutical Sciences, Monash University, VIC, Australia; [2]Infectious Diseases and Microbiology Departments, Austin Health, VIC, Australia; [3]Division of Laboratory Medicine, Women's and Children's Hospital, North Adelaide, SA, Australia; [4]University of Adelaide, SA, Australia

- 18 YBU, Plazma Colistin doz ölçümü
- CMS yarıömrü 2.3 h, Colistin [illegible] saat
- Cmax: 0.60 mg/L (3 mily[illegible]onu)
- Cmax: 2.3 mg/L (2.d[illegible]

9 Milyon Ü Yükleme
4.5 Milyon Ü idame (12 h)

MIK (2 mg/L)'nin altında Cmax (1.doz sonu)

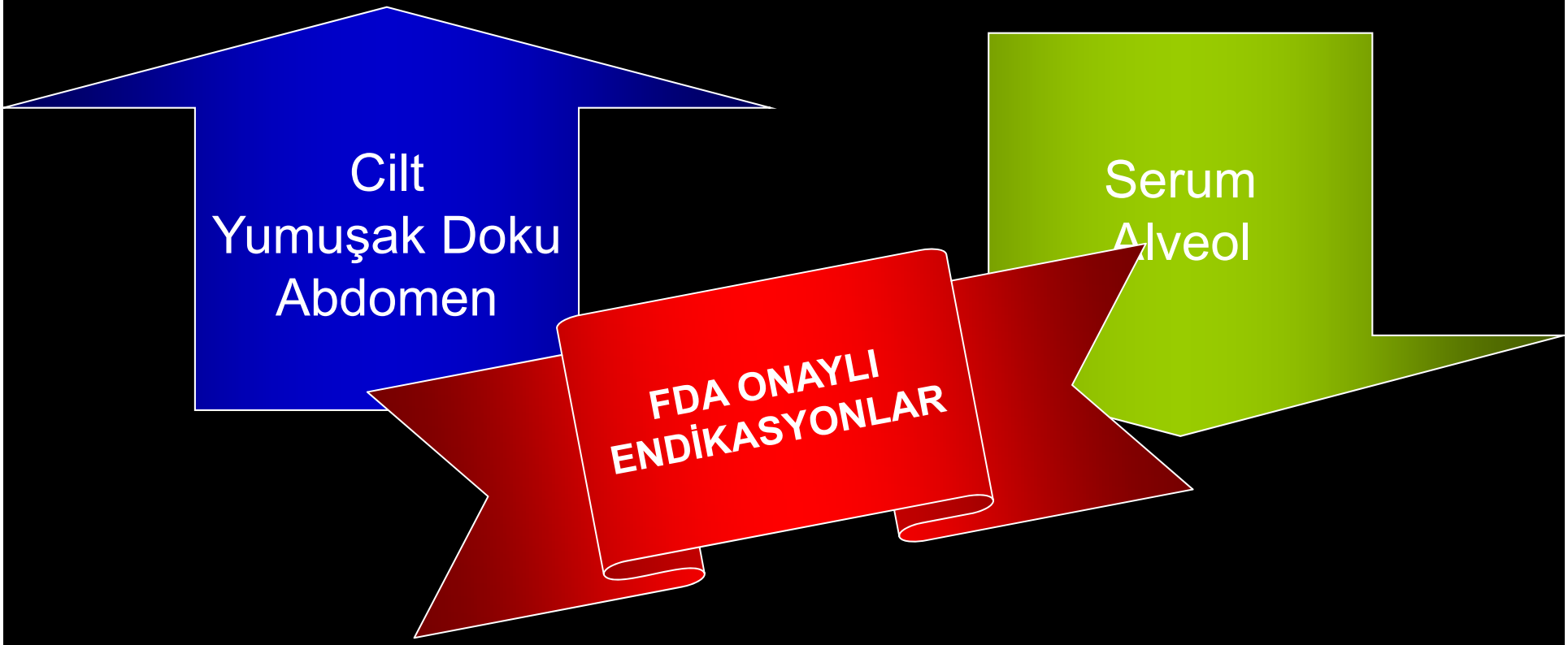
Tigesiklin

- Glisiklin türevi
- *K.pneumoniae* (ESBL, KPC, MDR..)
- *A.baumannii* in vitro etkili
- İn vivo etkinlik ?
- Colistin + Tigesiklin kombinasyonu..
- 2 mg/L MIK değeri,

Tigesiklin

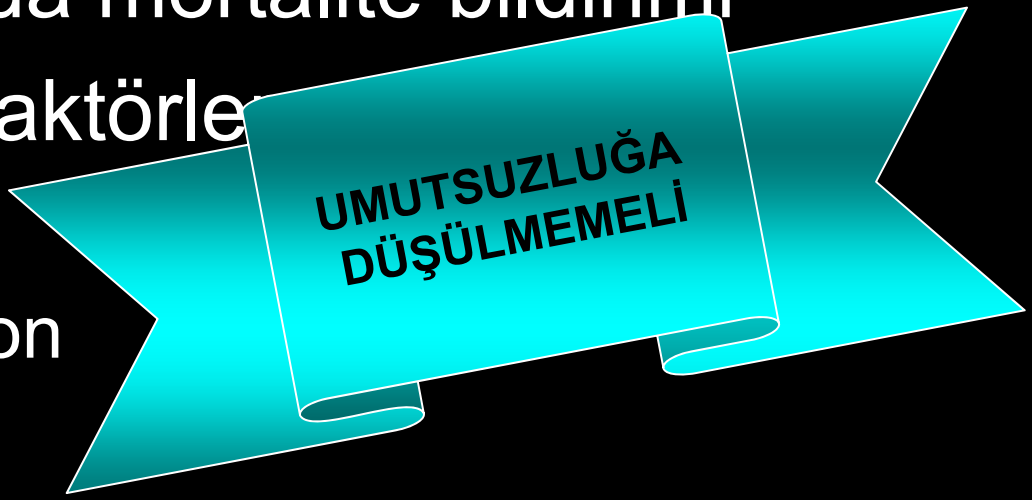
- 200 mg yükleme + 100 mg / gün IV idame
- Vmax: 3 mg/L
- *A.baumannii* MIK değeri: 2 mg/L
- Yüksek volüm dağılımı: 8 mg/L
- Solunum sekresyonunda *A.baumannii* eradikasyonu: (+)
- Bakteremi ve şiddetli enf. (-) (Cmax: 0.68)

Tigesiklin


Cilt
Yumuşak Doku
Abdomen
Serum
Alveol
FDA ONAYLI
ENDİKASYONLAR

PDR Enfeksiyonlarında Mortalite Neden Daha Yüksek Değil?

- %33-%80 arasında mortalite bildirimi
- Bakteri ile ilişkili faktörler
  - Yavaş büyüme
  - Yavaş transmisyon
  - Düşük virulans
- Antibiyotiklerin in vivo daha etkili olması
- Kombinasyon tedavilerindeki sinerjik etki



Falagas MJ, Int J Antimicrob Agents, 2008

Aerosol Antibiyotikler

- ANTİBİYOTİKLER
- Aminoglikozidler
  - Tobramisin
  - Amikasin
- Kinolonlar
  - Siprofloksasin
  - Levofloksasin
- Monobaktamlar
  - Aztreonam

- ETKİ (*P.aeruginosa*)
  - +++
  - ++
  - ++++
  - ++++
  - ++++

Dudley MN, et al. Current Opin Biotech, 2008

- Ceftaroline (Teflaro) (Astra Zeneca)
- Ceftazidim / Avibactam (ESBL)
- Cubist's-CXA-201 (*P.aeruginosa*)
- Cempra's CEM-102
- Delafloxacin
- Furiex's JNJ-Q2

Sonuç

- Uygun başlangıç tedavisi
- Kombine antibiyotik kullanımı
- Kolistinle inhaler monoterapiden kaçın
- Colistin yükleme dozu
- En başarılı tedavi enfeksiyon kontrolü..

Teşekkürler..