RESISTENCIA EN PSEUDOMONAS AERUGINOSA Y ACINETOBACTER BAUMANNII

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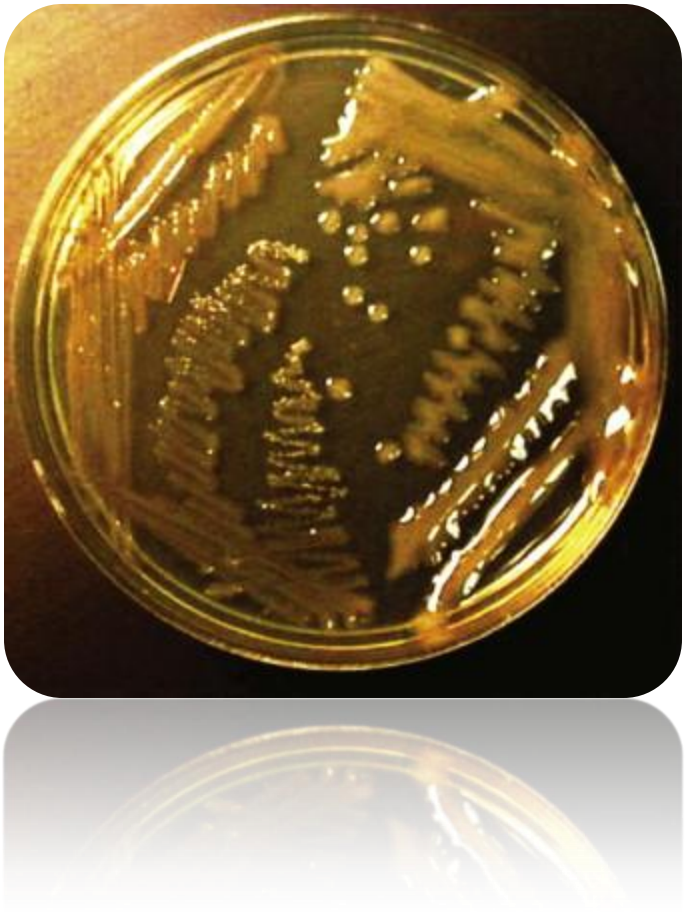
P. aeruginosa

- Bacilo gram negativo no fermentador oxidasa positivo.
- Mínimos requerimientos nutricionales
- Capacidad de sobrevivir en variedad de superficies y medios acuosos.



Owens R. Antimicrobial resistence. 2008
Mandel Infectious Diseases 2010.

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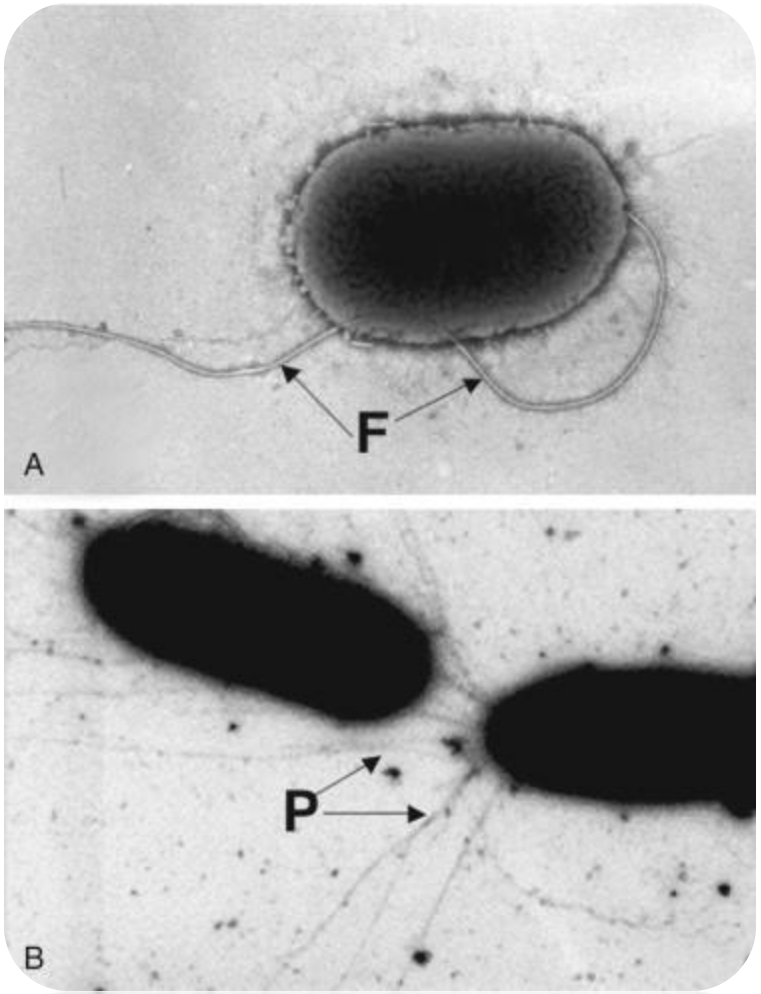

Owens R. Antimicrobial resistence. 2008
Mandel Infectious Diseases 2010.

Epidemiología

- Colonización del TGI, periné y axila
  - 7-20% de personas sanas
- Patógeno nosocomial
  - 1960 (inmunosuprimidos y pacientes con fibrosis quística)
  - Neumonía nosocomial, ITU, infección de Hda Qx, y bacteriemia
- Comunitario?
  - Infecciones asociadas al cuidado de la salud
  - Pacientes con fibrosis quística
  - Infección por HIV
  - Neumonía en pacientes con uso crónico de esteroides, o patología pulmonar estructural severa.

Owens R. Antimicrobial resistence. 2008
Mandel Infectious Diseases 2010.

En EUA

- Patógeno gram negativo mas frecuentemente aislado en UCI, independiente del tipo de infección.
  - 7,5% de los aislamientos
- Microorganismo gram negativo mas frecuentemente aislado como causante de neumonía
- MDR o Panresistencia (Resistencia medicamentos antipseudomonas) 4-14%

Owens R. Antimicrobial resistence. 2008

Patogénesis

- Tasa de mutación 1 por 10^8 células.
- Cepas hipermutantes 1000v mas.
  - Carecen de capacidad para corregir errores en el DNA o mecanismos de reparación o utilizan DNA polimerasa con reducida fidelidad de copia.
  - Sitio de mutación: *mutS*

Owens R. Antimicrobial resistence. 2008

Factores de virulencia

Location or Class	Example(s)	Activity/Effects on Host
Cell surface	Alginate	Antiphagocytic/resist opsonic killing
	LPS	Endotoxic/antiphagocytic/avoid preformed antibody to previously encountered O-antigens
	Pili	Twitching motility; biofilm formation; adherence to host tissues
	Flagella	Motility; biofilm formation; adherence to host tissues and mucin components
	Injection of type III secretion factors	PcrG, PcrV, PcrH, PopB, and PopD proteins form injection bridge for type III effectors
Outer membrane	Siderophore receptors	Provides iron for microbial growth and survival
	Efflux pumps	Remove antibiotics
Type III secretion	ExoS; ExoT; ExoU; ExoY	Intoxicates cells (ExoS/ExoT); cytotoxic (ExoU); disrupts actin cytoskeleton
Secreted proteases	LasA protease; LasB elastase; alkaline protease; protease IV	Degrades host immune effectors (antibody, complement, etc.); degrades matrix proteins
Iron acquisition	Pyoverdin; pyochelin	Scavenge iron from the host for bacterial use
Secreted toxins	Exotoxin A; leukocidin phospholipases; hemolysins; rhamnolipid	Inhibit protein synthesis; kill leukocytes; hemolysis of red blood cells; degrade host cell surface glycolipids
Secreted oxidative factors	Pyocyanin; ferripyochelin	Produces reactive oxygen species: H_2O_2; O_2 inflammatory; disrupts epithelial cell function
Quorum sensing	LasR/LasI;RhlR/RhlI PQS	Biofilm formation; regulation of virulence factor secretion

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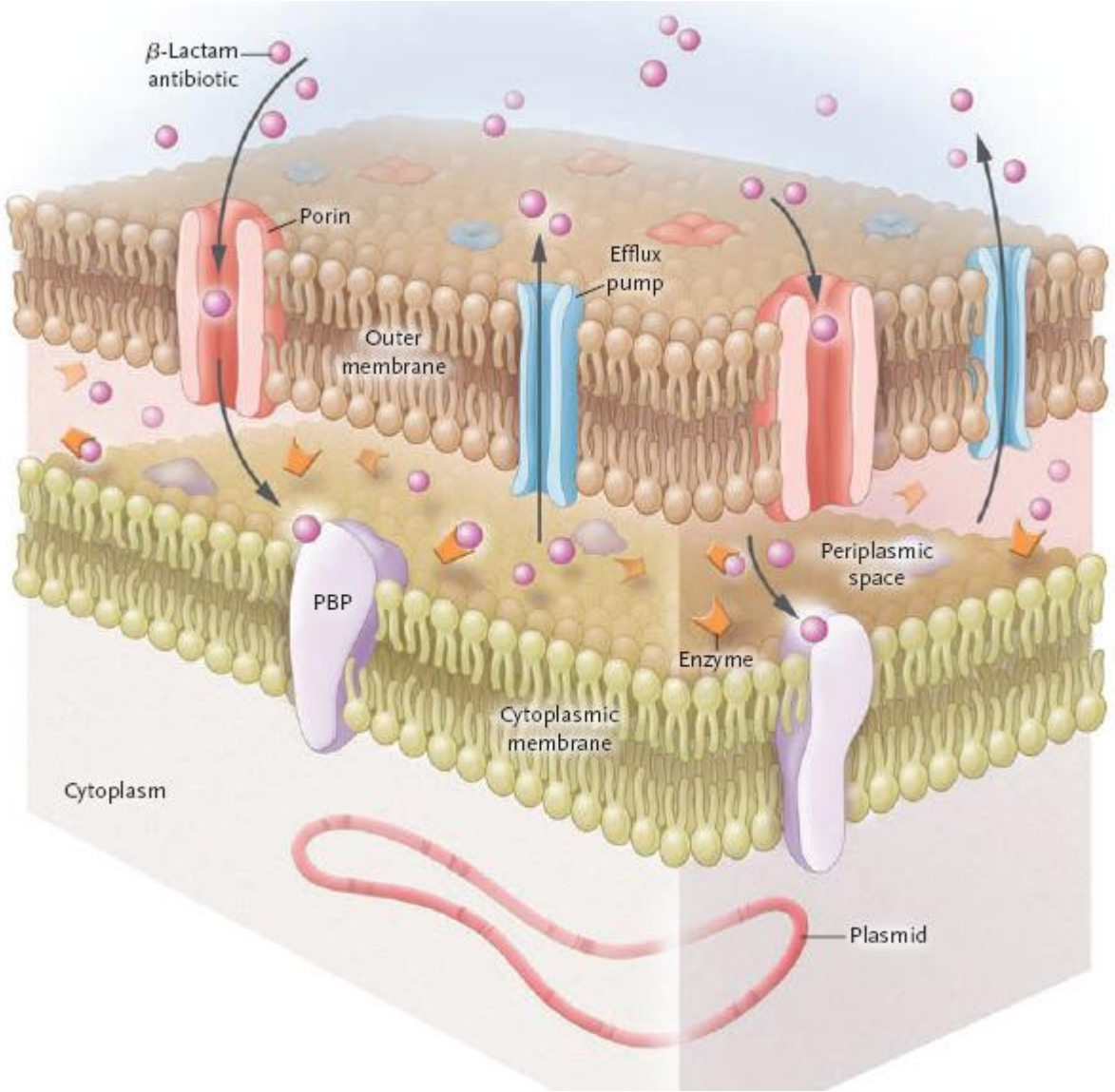

Muñoz. N Engl J Med. 2008: 358(12);1271–81

Factores predisponentes del huésped

- Neutropenia
- Alteración en barreras
  - Quimioterapia. Mucositis.
  - Quemados
- Alteración en CD4?
- Regulador de la conductancia trasmembrana de fibrosis quística (CFTR)
- Uso de esteroides

Mandel Infectious Diseases 2010.

Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America

Alison G. Freifeld,[1] Eric J. Bow,[9] Kent A. Sepkowitz,[2] Michael J. Boeckh,[4] James I. Ito,[5] Craig A. Mullen,[3] Issam I. Raad,[6] Kenneth V. Rolston,[6] Jo-Anne H. Young,[7] and John R. Wingard[8]

[1]Department of Medicine, University of Nebraska Medical Center, Omaha, Nebraska; [2]Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York; [3]Department of Pediatrics, University of Rochester Medical Center, Rochester, New York; [4]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research, Seattle, Washington; [5]Division of Infectious Diseases, City of Hope National Medical Center, Duarte, California; [6]Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas M.D. Anderson Cancer Center, Houston, Texas; [7]Department of Medicine, University of Minnesota, Minneapolis, Minnesota; [8]Division of Hematology/Oncology, University of Florida, Gainesville, Florida; and [9]Departments of Medical Microbiology and Internal Medicine, the University of Manitoba, and Infection Control Services, Cancer Care Manitoba, Winnipeg, Manitoba, Canada

CID 2011:52 (15 February).

III. In Febrile Patients With Neutropenia, What Empiric Antibiotic Therapy Is Appropriate and in What Venue?

Recommendations

General Considerations

9. High-risk patients require hospitalization for IV empirical antibiotic therapy; monotherapy with an anti-pseudomonal β-lactam agent, such as cefepime, a carbapenem (meropenem or imipenem-cilastatin), or piperacillin-tazobactam, is recommended (**A-I**). Other antimicrobials (aminoglycosides, fluoroquinolones, and/or vancomycin) may be added to the initial regimen for management of complications (eg, hypotension and pneumonia) or if antimicrobial resistance is suspected or proven (**B-III**).

CID 2011:52 (15 February).

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

Lionel A. Mandell,[1,a] Richard G. Wunderink,[2,a] Antonio Anzueto,[3,4] John G. Bartlett,[7] G. Douglas Campbell,[8] Nathan C. Dean,[9,10] Scott F. Dowell,[11] Thomas M. File, Jr.[12,13] Daniel M. Musher,[5,6] Michael S. Niederman,[14,15] Antonio Torres,[16] and Cynthia G. Whitney[11]

[1]McMaster University Medical School, Hamilton, Ontario, Canada; [2]Northwestern University Feinberg School of Medicine, Chicago, Illinois; [3]University of Texas Health Science Center and [4]South Texas Veterans Health Care System, San Antonio, and [5]Michael E. DeBakey Veterans Affairs Medical Center and [6]Baylor College of Medicine, Houston, Texas; [7]Johns Hopkins University School of Medicine, Baltimore, Maryland; [8]Division of Pulmonary, Critical Care, and Sleep Medicine, University of Mississippi School of Medicine, Jackson; [9]Division of Pulmonary and Critical Care Medicine, LDS Hospital, and [10]University of Utah, Salt Lake City, Utah; [11]Centers for Disease Control and Prevention, Atlanta, Georgia; [12]Northeastern Ohio Universities College of Medicine, Rootstown, and [13]Summa Health System, Akron, Ohio; [14]State University of New York at Stony Brook, Stony Brook, and [15]Department of Medicine, Winthrop University Hospital, Mineola, New York; and [16]Cap de Servei de Pneumologia i Allèrgia Respiratòria, Institut Clínic del Tòrax, Hospital Clínic de Barcelona, Facultat de Medicina, Universitat de Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer, CIBER CB06/06/0028, Barcelona, Spain.

during an influenza outbreak. Risks for infection with Enterobacteriaceae species and *P. aeruginosa* as etiologies for CAP are chronic oral steroid administration or severe underlying bronchopulmonary disease, alcoholism, and frequent antibiotic therapy [79, 131], whereas recent hospitalization would define cases as HCAP. Less common causes of pneumonia include, but are by no means limited to, *Streptococcus pyogenes*, *Neisseria meningitidis*, *Pasteurella multocida*, and *H. influenzae* type b.

Enferm Infecc Microbiol Clin. 2009;27(2):89–104

Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Revisión

Diagnóstico microbiológico de la colonización-infección broncopulmonar en el paciente con fibrosis quística

Antonio Oliver [a,*], Teresa Alarcón [b], Estrella Caballero [c] y Rafael Cantón [d]

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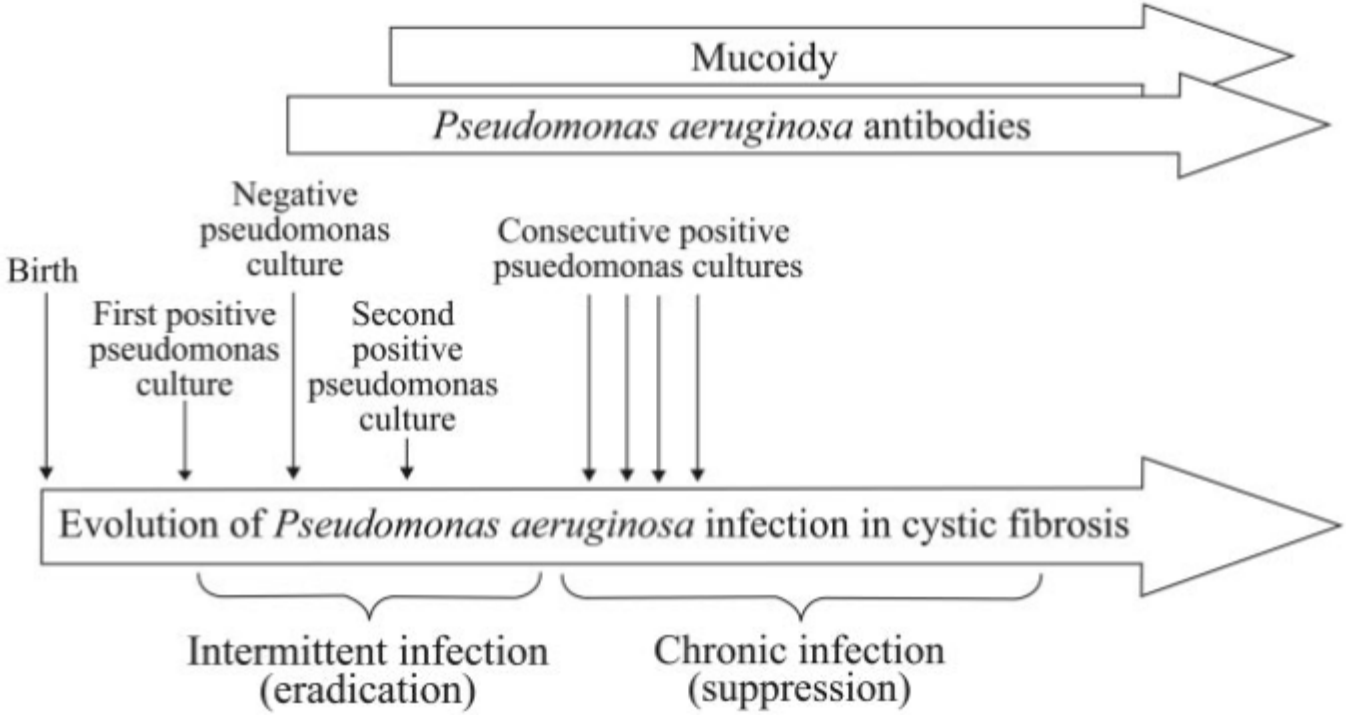
[b] *Servicio de Microbiología, Hospital de la Princesa, Madrid, España*
[c] *Servicio de Microbiología, Hospital Vall d'Hebron, Barcelona, España*
[d] *Servicio de Microbiología, Hospital Universitario Ramón y Cajal, Madrid, España*

RESPIRATORY CARE . MAY 2009 VOL 54 NO 5
Enferm Infecc Microbiol Clin. 2009; 27(2): 89–104



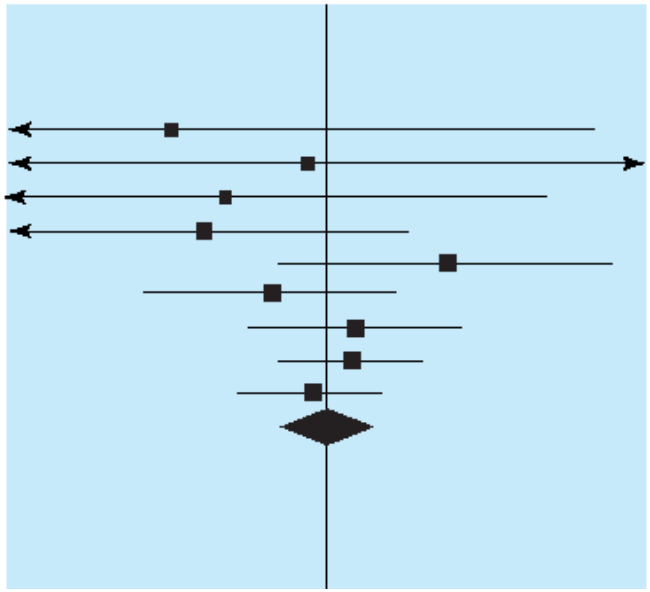
RESPIRATORY CARE . MAY 2009 VOL 54 NO 5
Enferm Infecc Microbiol Clin. 2009; 27(2): 89-104

β lactam monotherapy versus β lactam-aminoglycoside combination therapy for sepsis in immunocompetent patients: systematic review and meta-analysis of randomised trials

Mical Paul, Ishay Benuri-Silbiger, Karla Soares-Weiser, Leonard Leibovici

Study or subcategory	Monotherapy No/Total	Combination therapy No/Total	Weight (%)	Relative risk (95% CI)
01 Same β lactam				
Abrams 1979	0/12	0/12		Not estimable
Cardozo 2001	0/56	0/48		Not estimable
Sandberg 1997	0/37	0/36		Not estimable
Sculier 1982	0/10	1/10	0.28	0.33 (0.02 to 7.32)
Carbon 1987	1/25	1/22	0.37	0.88 (0.06 to 13.25)
Ribera 1996	1/45	2/45	0.48	0.50 (0.05 to 5.32)
Korzeniowski 1982	2/33	6/41	1.13	0.41 (0.09 to 1.92)
Klastersky 1973	7/22	3/23	1.76	2.44 (0.72 to 8.26)
D'Antonio 1992	7/144	10/142	2.89	0.69 (0.27 to 1.76)
Kljucar 1990	11/49	9/50	3.98	1.25 (0.57 to 2.74)
Cometta 1994	24/148	19/144	7.31	1.23 (0.70 to 2.14)
Dupont 2000	21/111	24/116	8.06	0.91 (0.54 to 1.55)
Subtotal (95% CI)	692	689	26.27	1.02 (0.76 to 1.38)

Total events: 74 (monotherapy), 75 (combination therapy)
Test for heterogeneity: χ^2=5.68, df=8, P=0.68, I^2=0%
Test for overall effect: z=0.14, P=0.89



BMJ (2 March 2004)

Table 2 All cause fatality in comparison of β lactam monotherapy *v* β lactam-aminoglycoside combination therapy for treatment of sepsis: subgroup analyses

	Same β lactam			Different β lactam		
	Studies	Patients	RR (95% CI)	Studies	Patients	RR (95% CI)
Pseudomonas aeruginosa infections	1	9	NA	2	29	1.50 (0.07 to 32.84)
Gram negative infections	3	117	0.58 (0.08 to 4.43)	5	313	1.20 (0.79 to 1.83)
Bacteraemia*	1	11	NA	5	193	1.40 (0.72 to 2.71)
Non-urinary tract infections	3	351	0.89 (0.53 to 1.49)	13	1458	0.76 (0.57 to 1.03)
Staphylococcus aureus endocarditis	3	188	0.44 (0.12 to 1.59)	0	0	—

NA=not assessed.
*Excluding studies restricted to Gram positive infections.

Table 3 Clinical failure in comparison of β lactam monotherapy *v* β lactam-aminoglycoside combination therapy for treatment of sepsis: subgroup analyses

	Same β lactam			Different β lactam		
	Studies	Patients	RR (95% CI)	Studies	Patients	RR (95% CI)
Pseudomonas aeruginosa infections	6	124	1.01 (0.68 to 1.49)	12	302	1.09 (0.65 to 1.83)
Gram negative infections	10	432	1.15 (0.82 to 1.59)	18	1403	0.88 (0.67 to 1.17)
Bacteraemia*	5	141	1.22 (0.59 to 2.52)	17	624	0.67 (0.48 to 0.93)†
Non-urinary tract infections§	10	1148	1.03 (0.66 to 1.60)	31	2945	0.71 (0.61 to 0.82)†
Gram positives/endocarditis	5	305	0.71 (0.41 to 1.22)	0	0	—

*Excluding studies restricted to Gram positive infections.
†P<0.05.
§Significant advantage for monotherapy when all studies are combined, P=0.01.

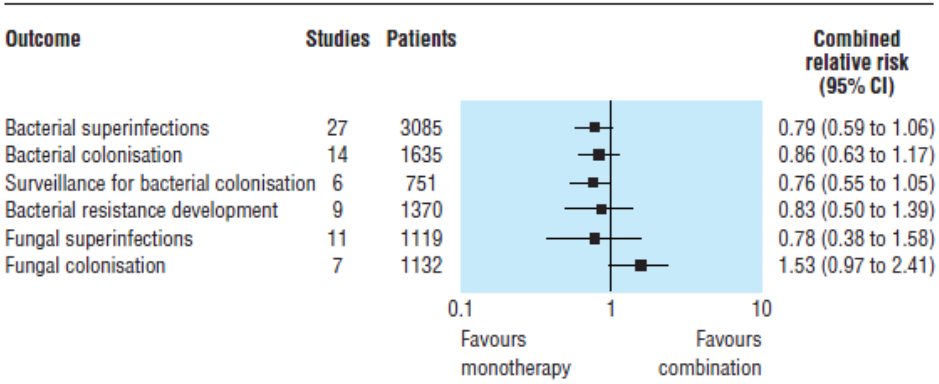


Fig 5 Summary relative risks for outcome relating to resistance development in comparison of β lactam monotherapy *v* β lactam-aminoglycoside combination therapy for treatment of sepsis. Log scale of relative risks (95% confidence intervals), random effect model. Studies ordered by weight

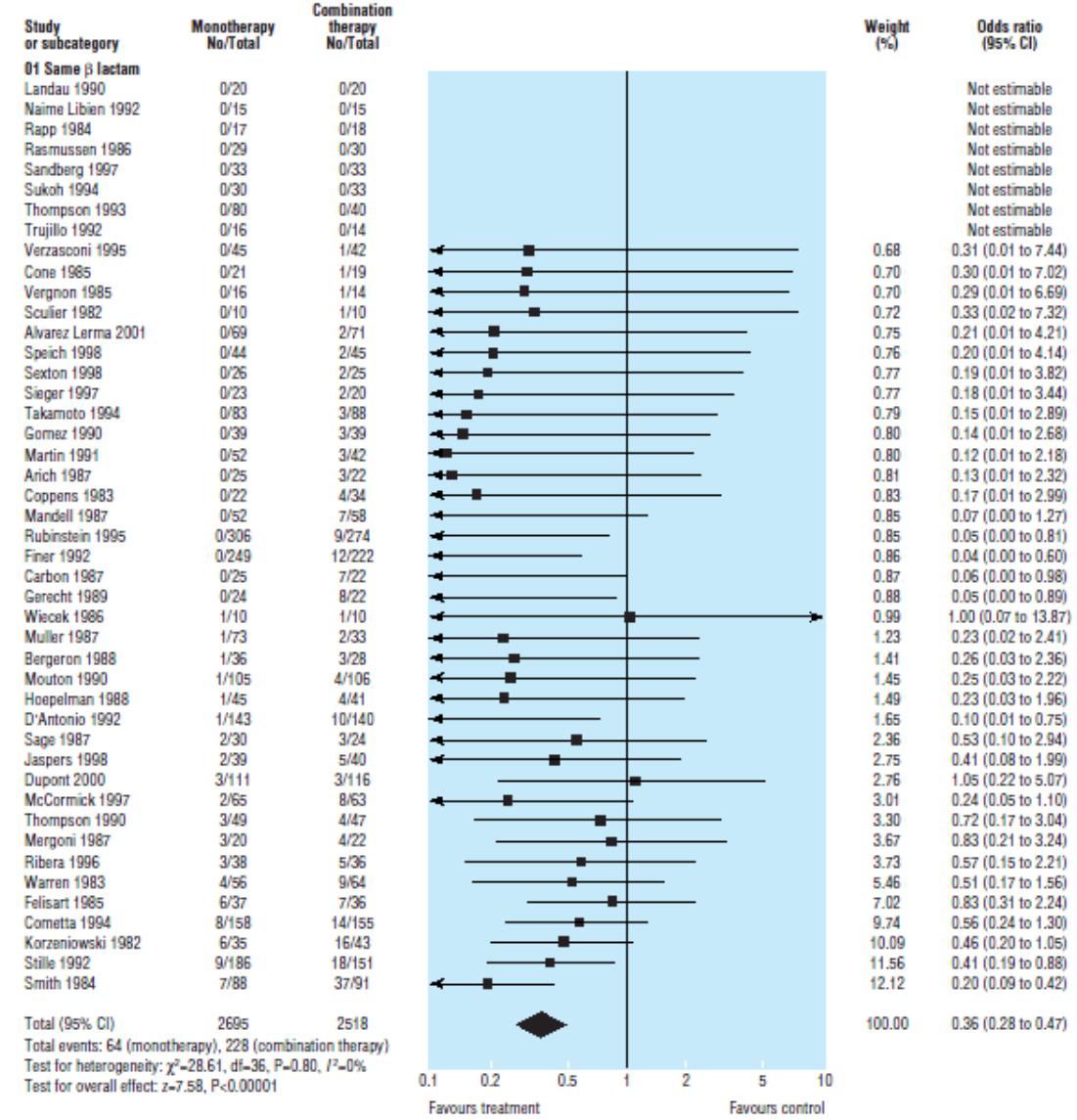


Fig 6 Adverse events: nephrotoxicity in comparison of β lactam monotherapy *v* β lactam-aminoglycoside combination therapy for treatment of sepsis. Log scale of relative risks (95% confidence intervals), random effect model. Studies ordered by weight

Beta lactam antibiotic monotherapy versus beta lactam-aminoglycoside antibiotic combination therapy for sepsis (Review)

Paul M, Grozinsky S, Soares-Weiser K, Leibovici L

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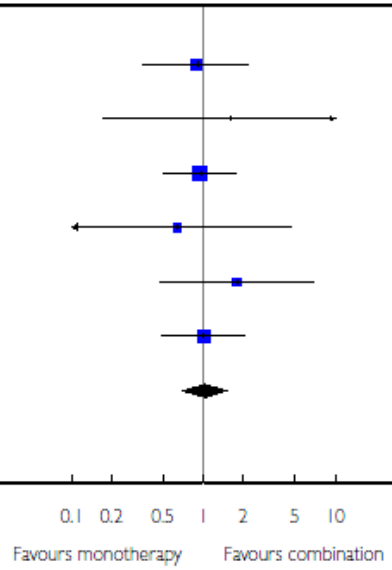
Analysis 2.7. Comparison 2 Monotherapy versus combination therapy, Outcome 7 Clinical failure (Pseudomonas aeruginosa infections).

Review: Beta lactam antibiotic monotherapy versus beta lactam-aminoglycoside antibiotic combination therapy for sepsis

Comparison: 2 Monotherapy versus combination therapy

Outcome: 7 Clinical failure (Pseudomonas aeruginosa infections)

Study or subgroup	Monotherapy n/N	Combination therapy n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Same BL				
Cometta 1994	4/9	6/12		0.89 [0.35, 2.24]
D'Antonio 1992	2/10	1/8		1.60 [0.17, 14.63]
Mergoni 1987	8/16	10/19		0.95 [0.50, 1.82]
Sculier 1982	1/4	2/5		0.63 [0.08, 4.66]
Sukoh 1994	3/5	2/6		1.80 [0.47, 6.87]
Takamoto 1994	6/12	9/18		1.00 [0.48, 2.08]
Subtotal (95% CI)	**56**	**68**		**1.02 [0.68, 1.51]**
Total events: 24 (Monotherapy), 30 (Combination therapy)				



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Review

Clinical implications of β-lactam–aminoglycoside synergism: systematic review of randomised trials

Ronit Marcus[a,1], Mical Paul[b,*,1], Heather Elphick[c], Leonard Leibovici[a]

[a] Medicine E, Rabin Medical Center, Beilinson Hospital and Sackler Faculty of Medicine, Tel-Aviv University, Israel
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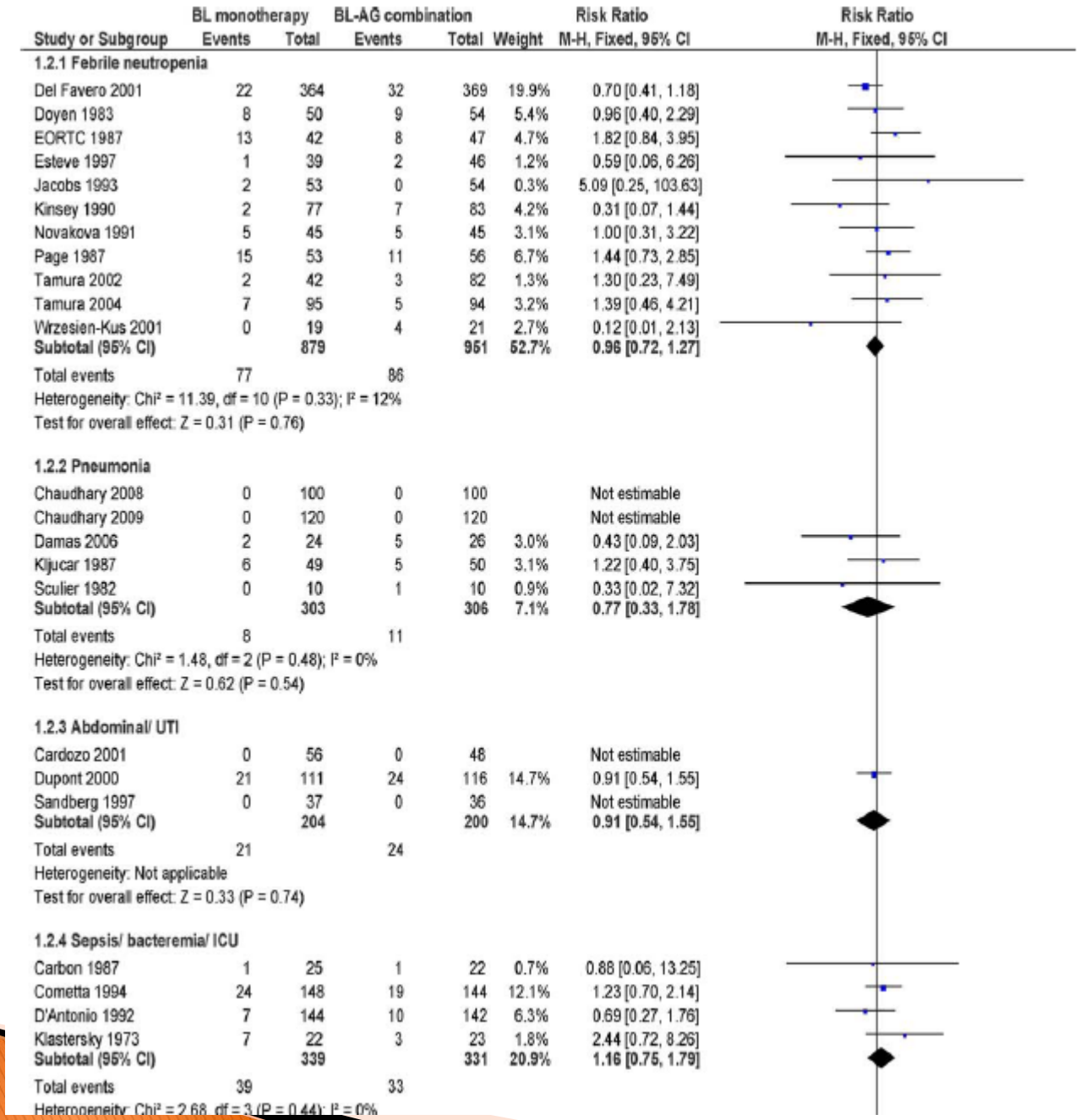
[c] Respiratory Unit, Sheffield Children's Hospital, Sheffield, UK

International Journal of Antimicrobial Agents 37 (2011) 491–503


BL monotherapy
BL-AG combination
Risk Ratio
Risk Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI
M-H, Fixed, 95% CI
1.2.1 Febrile neutropenia
Del Favero 2001 22 364 32 369 19.9% 0.70 [0.41, 1.18]
Doyen 1983 8 50 9 54 5.4% 0.96 [0.40, 2.29]
EORTC 1987 13 42 8 47 4.7% 1.82 [0.84, 3.95]
Esteve 1997 1 39 2 46 1.2% 0.59 [0.06, 6.26]
Jacobs 1993 2 53 0 54 0.3% 5.09 [0.25, 103.63]
Kinsey 1990 2 77 7 83 4.2% 0.31 [0.07, 1.44]
Novakova 1991 5 45 5 45 3.1% 1.00 [0.31, 3.22]
Page 1987 15 53 11 56 6.7% 1.44 [0.73, 2.85]
Tamura 2002 2 42 3 82 1.3% 1.30 [0.23, 7.49]
Tamura 2004 7 95 5 94 3.2% 1.39 [0.46, 4.21]
Wrzesien-Kus 2001 0 19 4 21 2.7% 0.12 [0.01, 2.13]
Subtotal (95% CI) 879 951 52.7% 0.96 [0.72, 1.27]
Total events 77 86
Heterogeneity: Chi² = 11.39, df = 10 (P = 0.33); I² = 12%
Test for overall effect: Z = 0.31 (P = 0.76)
1.2.2 Pneumonia
Chaudhary 2008 0 100 0 100 Not estimable
Chaudhary 2009 0 120 0 120 Not estimable
Damas 2006 2 24 5 26 3.0% 0.43 [0.09, 2.03]
Kijucar 1987 6 49 5 50 3.1% 1.22 [0.40, 3.75]
Sculier 1982 0 10 1 10 0.9% 0.33 [0.02, 7.32]
Subtotal (95% CI) 303 306 7.1% 0.77 [0.33, 1.78]
Total events 8 11
Heterogeneity: Chi² = 1.48, df = 2 (P = 0.48); I² = 0%
Test for overall effect: Z = 0.62 (P = 0.54)
1.2.3 Abdominal/ UTI
Cardozo 2001 0 56 0 48 Not estimable
Dupont 2000 21 111 24 116 14.7% 0.91 [0.54, 1.55]
Sandberg 1997 0 37 0 36 Not estimable
Subtotal (95% CI) 204 200 14.7% 0.91 [0.54, 1.55]
Total events 21 24
Heterogeneity: Not applicable
Test for overall effect: Z = 0.33 (P = 0.74)
1.2.4 Sepsis/ bacteremia/ ICU
Carbon 1987 1 25 1 22 0.7% 0.88 [0.06, 13.25]
Cometta 1994 24 148 19 144 12.1% 1.23 [0.70, 2.14]
D'Antonio 1992 7 144 10 142 6.3% 0.69 [0.27, 1.76]
Klastersky 1973 7 22 3 23 1.8% 2.44 [0.72, 8.26]
Subtotal (95% CI) 339 331 20.9% 1.16 [0.75, 1.79]
Total events 39 33
Heterogeneity: Chi² = 2.68, df = 3 (P = 0.44); I² = 0%

Mecanismos de resistencia

- Resistencia intrínseca y adquirida
  - Permeabilidad de membrana externa es 10-100 veces menos eficiente que en *E. coli*.
    - Membrana externa altamente impermeable
    - Expresión de sistemas de eflujo multidrogas
- Cambios mutaciónales
- Adquisición de material genético extra cromosómico

Owens R. Antimicrobial resistence. 2008

B lactamicos

- Amp C
  - Cromosómica
  - Inducible (carbapenem, clavulanato)
  - Genes reguladores: ampR, ampD o ampE
  - Resistencia a penicilinas antipseudomonas y cefalosporinas de 3 generación.
  - Cefepime y carbapenem son estables

Owens R. Antimicrobial resistence. 2008
Bonomo R. Clin Infect Dis. 2006:43(S2); 49-56

- Grupo A
  - PER-1 (Turquía, Francia e Italia) y PER-2(sur América)
  - VEB 1 y VEB 2 sureste asiático
  - GES-1, GES-2 e IBC-2: Suráfrica, Francia y Grecia.

Owens R. Antimicrobial Resistence. 2008
Jacoby G. N Engl J Med. 2005; 352(4): 380-91

OXA (grupo D)

- Enzimas basadas en serina
- Turquia y Francia
- Similares a CTX
- OXA-BLEE
- Carbapenemasas

Owens R. Antimicrobial Resistence. 2008
Jacoby G. N Engl J Med. 2005; 352(4): 380-91

Metalo β-lactamasas (grupo B)

- IMP, VIM, SPM y GIM
- Activas contra penicilinas, cefalosporinas antipseudomonas incluida cefepime y carbapenem pero sensibles a aztreonam.
- No inhibidas por inh de β-lactamasas
- Genes: *bla*$_{IMP}$ y *bla*$_{VIM}$…
- Genes trasferibles como cassettes dentro de transposones o plásmidos (Agluc)
  - Solo susceptible a polimixina, ciprofloxacina y aztreonam.

Owens R. Antimicrobial Resistence. 2008
Jacoby G. N Engl J Med. 2005; 352(4): 380-91

β-Lactamase	Examples	Substrates	Inhibition by Clavulanic Acid*	Molecular Class
Broad-spectrum	TEM-1, TEM-2, SHV-1	Benzylpenicillin (penicillin G), aminopenicillins (amoxicillin and ampicillin), carboxypenicillins (carbenicillin and ticarcillin), ureidopenicillin (piperacillin), narrow-spectrum cephalosporins (cefazolin, cephalothin, cefamandole, cefuroxime, and others)	+++	A
	OXA family	Substrates of the broad-spectrum group plus cloxacillin, methicillin, and oxacillin	+	D
Expanded-spectrum	TEM family and SHV family	Substrates of the broad-spectrum group plus oxyimino-cephalosporins (cefotaxime, cefpodoxime, ceftazidime, and ceftriaxone) and monobactam (aztreonam)	++++	A
	Others (BES-1, GES/IBC family, PER-1, PER-2, SFO-1, TLA-1, VEB-1, and VEB-2)	Same as for TEM family and SHV family	++++	A
	CTX-M family	Substrates of the expanded-spectrum group plus, for some enzymes, cefepime	++++	A
	OXA family	Same as for CTX-M family	+	D
AmpC	ACC-1, ACT-1, CFE-1, CMY family, DHA-1, DHA-2, FOX family, LAT family, MIR-1, MOX-1, and MOX-2	Substrates of expanded-spectrum group plus cephamycins (cefotetan, cefoxitin, and others)	0	C
Carbapenemase	IMP family, VIM family, GIM-1, and SPM-1	Substrates of the expanded-spectrum group plus cephamycins and carbapenems (ertapenem, imipenem, and meropenem)	0	B
	KPC-1, KPC-2, and KPC-3	Same as for IMP family, VIM family, GIM-1, and SPM-1	+++	A
	OXA-23, OXA-24, OXA-25, OXA-26, OXA-27, OXA-40, and OXA-48	Same as for IMP family, VIM family, GIM-1, and SPM-1	+	D

Jacoby G. N Engl J Med. 2005; 352(4): 380-91

Bombas de eflujo

- MexAB-OprM, MexAB-OprJ, MexEF-OprN, MexXY-OprM
  - Genes reguladores: *nalB-mexR, nalC, nfxB, nfxC - mexT*
  - Resistencia a quinolonas, penicilinas antipseudomonas y cefalosporinas antipseudomonas. Disminución en la susceptibilidad a meropenem y usualmente no compromete la susceptibilidad a imipenem.

Owens R. Antimicrobial resistence. 2008
Bonomo R. Clin Infect Dis. 2006:43(S2); 49-56

Perdida de porinas

- OprD
  - Genes reguladores: *oprD, nfxC –mexT*
  - 50% de los pacientes tratados con imipenem por mas de 1 sem
  - Solo resistencia a carbapenem

Owens R. Antimicrobial resistence. 2008
Bonomo R. Clin Infect Dis. 2006:43(S2); 49-56

Quinolonas

- Mutaciones en DNA girasa y topoisomerasa II y IV
  - Sitio de mutación: *gyrA y parC*
- Bombas de eflujo
  - Como único mecanismo no es usualmente suficiente para producir resistencia a medicamentos antipseudomonas
  - Quinolonas, penicilinas antipseudomonas, carbapenem, cloranfenicol, tetra ciclinas, aminoglucósidos.

Owens R. Antimicrobial resistence. 2008
Bonomo R. Clin Infect Dis. 2006:43(S2); 49-56

Aminoglucosidos

- Modificación enzimática
  - Acetilación, adenilación o fosforilación
  - Mediada por plásmidos o cromosomal.
- Disminución en la penetración a través de la membrana
- Bombas de eflujo
  - MexXY-OprM

Owens R. Antimicrobial resistence. 2008
Bonomo R. Clin Infect Dis. 2006:43(S2); 49-56

- Panresistencia
  - Bélgica: Sobreexpresión de AmpC y perdida de OprD.
  - Chicago: MbL + enzimas modificadoras de aminoglucosidos + hiperproducción de AmpC

Owens R. Antimicrobial resistence. 2008

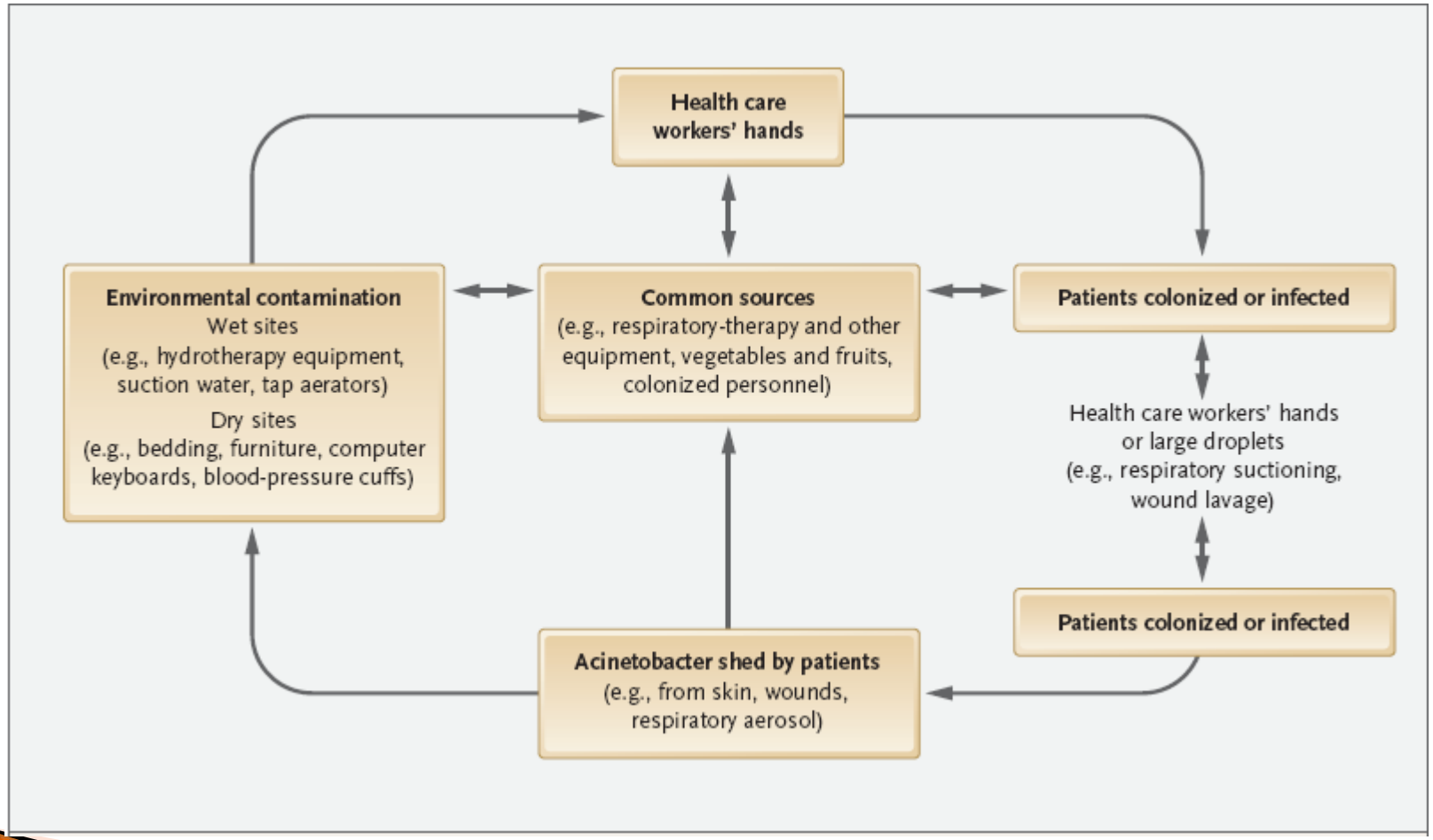
Acinetobacter

- Cocobacilo gram (–), lactosa (–).
- Resistencia intrínseca: Membrana externa impermeable. Medios sólidos y líquidos, condiciones medioambientales.
- Neumonía asociada al ventilador, Bacteriemia, Meningitis, ITU, Infección de tejidos blandos (desastres personal militar)
  - Variación estacional (verano)

Muñoz. N Engl J Med. 2008: 358(12);1271-81
Owens R. Antimicrobial resistence. 2008

- Factores de riesgo para colonización
  - Estancia hospitalaria prolongada.
  - Estancia en UCI
  - Ventilación mecánica
  - Cirugía reciente
  - Procedimientos invasivos: (CVC, IOT, traqueostomía, etc)
  - Presión de selección: uso de cef 3, FOQ, carbapenem.
  - Severidad de la enfermedad de base

Muñoz. N Engl J Med. 2008: 358(12);1271-81
Maragakis L. Clin Infec Dis. 2008;46:1254-63

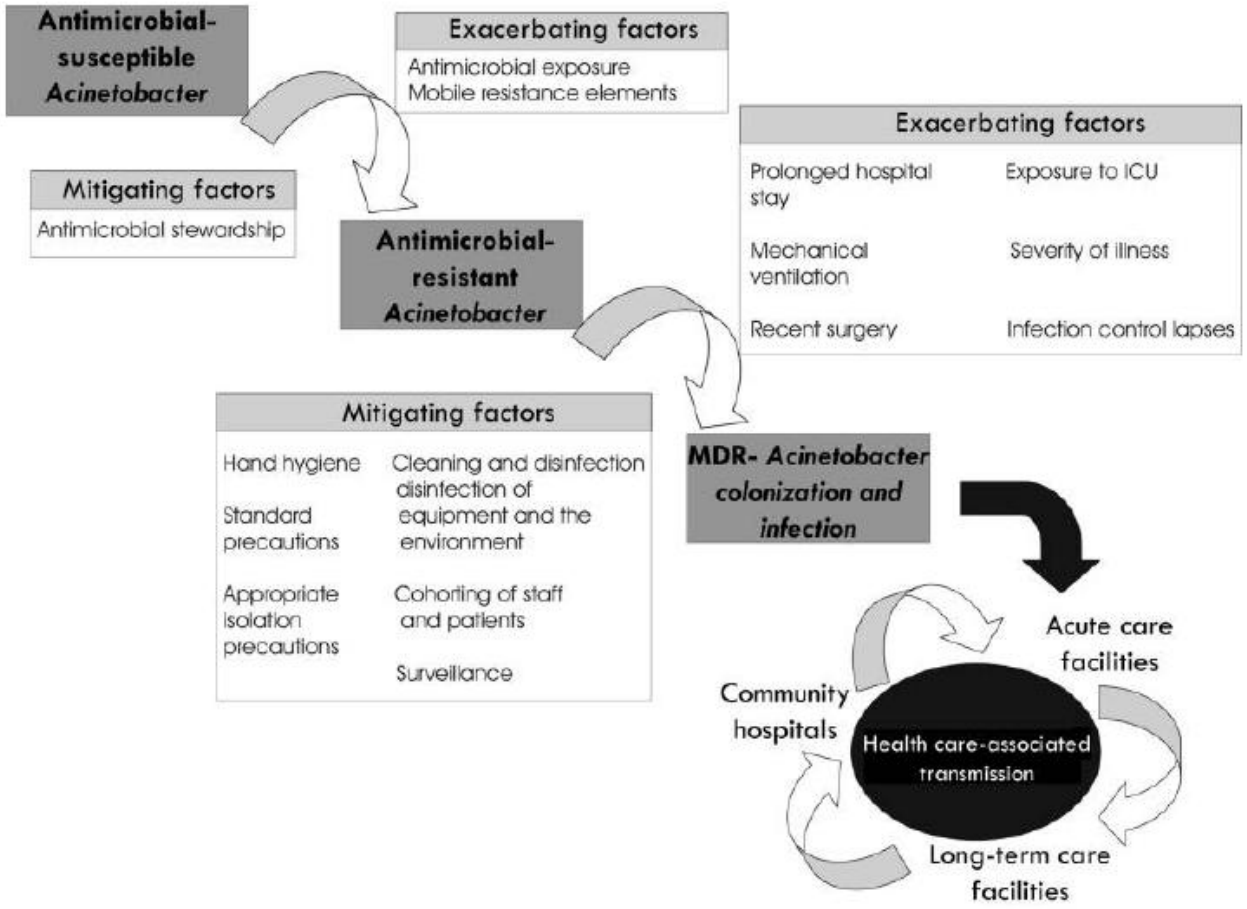


Muñoz. N Engl J Med. 2008: 358(12);1271-81

Table 1. Methods for control and prevention of multidrug-resistant *Acinetobacter* infection.

Method	Comments
Point source control	Effective in the outbreak setting when a point source is identified
Standard precautions	Includes hand hygiene, correct and consistent glove use, and appropriate use of gowns and eye protection; reported compliance among healthcare personnel is often poor
Contact barrier precautions	Includes dedicated patient care equipment and gowns and gloves for health care personnel on entry to an isolation room
Environmental cleaning and disinfection	Widespread environmental contamination is often reported in the epidemic setting, and environmental reservoirs likely play a role in the endemic setting as well
Cohorting of patients	Grouping colonized and infected patients into a designated unit or part of a unit
Cohorting of health care personnel	Designating staff to care for only patients colonized or infected with the organism
Clinical unit closure	Required in some outbreak settings to interrupt transmission and allow for thorough environmental disinfection
Antimicrobial stewardship	Programs to promote judicious antimicrobial use and prevent emergence of resistance
Surveillance	Passive or active surveillance can identify infected or colonized patients so that interventions can be implemented

Maragakis L. Clin Infec Dis. 2008;46:1254-63



Maragakis L. Clin Infec Dis. 2008;46:1254-63

- AmpC
  - Cromosomal
  - No inducible
- Oxa
  - Oxa-23 (Escocia 1985)
- Metalo b lactamasas
  - IMP y VIM (actividad depende de iones de Zn)
- Porinas y bombas de eflujo
- Quinolonas y Aminoglucosidos

Bonomo R. Clin Infect Dis. 2006:43(S2); 49-56

Mechanism	*Acinetobacter* species	*P. aeruginosa*
β-Lactamases		
AmpC cephalosporinase	+	–
Inducible	–	+
TEM	+	+
SHV	+	+
CTX-M	+	–
PER	+	+
VEB	+	+
OXA[a]	+	+
IMP	+	+
VIM	+	+
SPM	–	+
GIM	–	+
PSE	–	+
GES	–	+
IBC	–	+
OMP changes	+	+
AMEs		
Adenylating	+	+
Phosphorylating	+	+
Acetylating	+	+
Topoisomerase mutations		
gyrA	+	+
parC	+	+
Efflux pumps	+	+
Mobile genetic elements	+	+
Integrons	+	+
Membrane changes and resistance to polymyxin	–	+

Bonomo R. Clin Infect Dis. 2006:43(S2); 49–56

Conclusiones I

- Evite el uso de medicamentos con actividad anti-pseudomona a menos que el paciente presente claros FR.
- Evite la combinación de antimicrobianos a menos que desee ampliar cubrimiento en forma empírica
- Utilice tto combinado en caso de MDR confirmado… o infección por Acinetobacter spp….?

Conclusiones II

- Dosifique las dosis de antimicrobianos optimizando los parámetros PK/PD
- Insista en medidas de aislamiento de contacto y vigilancia de la prescripción y uso de antimicrobianos.