

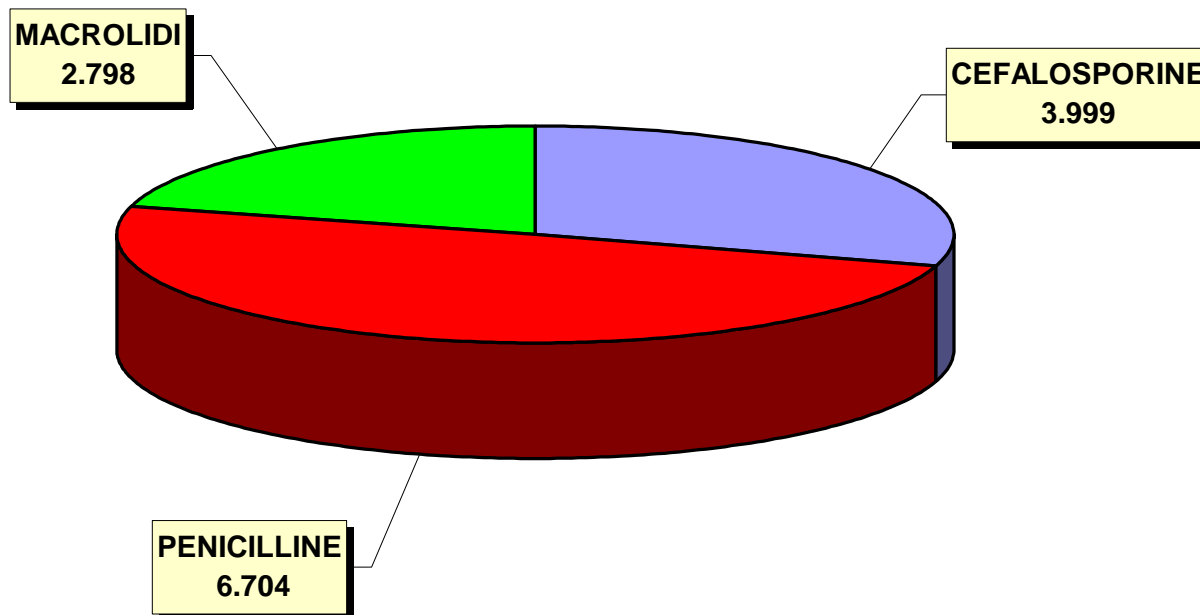
# **ANTIBIOTICI DA NON USARE PIÙ, ANTIBIOTICI DA USARE DI PIÙ**

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IRCCS Fondazione Ospedale Maggiore  
Policlinico, Mangiagalli e Regina Elena**

## Tot. Mercato sospensioni

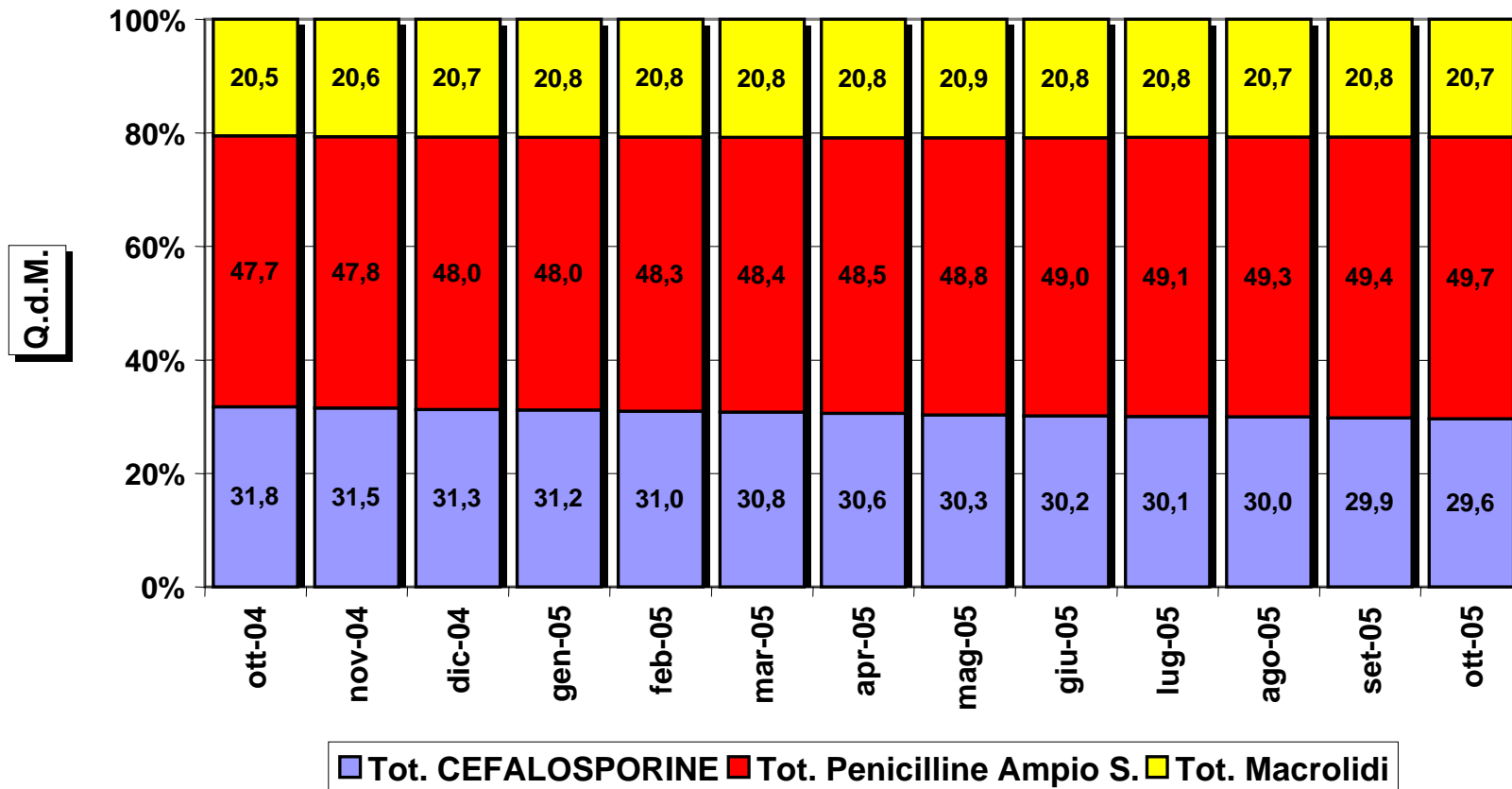
Vendite ad unità (+000) am 10/05



**Totale 13,5 milioni di unità**

Fonte dati: IMSHEALTH

## Trend Q.d.M. ad Unità



Fonte dati: IMSHEALTH

## PENICILLINE Sosp.

Risultati di vendita 2005

Molecola / Prodotto	Azienda	Gen-Ott '05	
		Unità (+000)	±%
<b>TOT. MERCATO Sosp.</b>		<b>10.926</b>	<b>3</b>
<b>PENICILLINE Sosp.</b>		<b>5.442</b>	<b>8</b>
<b>AMOXI + AC. CLAVULANICO</b>		<b>3.255</b>	<b>13</b>
AUGMENTIN Glaxo SK		2.448	14
CLAVULIN Fournier		791	9
NEO DUPLAMOX P & G		17	-19
<b>AMOXICILLINA</b>		<b>2.078</b>	<b>2</b>
ZIMOX Pfizer		1.180	-10
Amoxi Generico		898	24

Fonte dati: IMSHEALTH

## CEFALOSPORINE Sosp.

Risultati di vendita 2005

Molecola / Prodotto	Azienda	Gen-Ott '05	
		Unità (+000)	±%
<b>TOT. MERCATO Sosp.</b>		<b>10.926</b>	<b>3</b>
<b>CEFALOSPORINE Sosp.</b>		<b>3.230</b>	<b>-4</b>
<b>CEFACLOR</b>		<b>1.277</b>	<b>-5</b>
<b>PANACEF Valeas</b>		<b>1.008</b>	<b>-7</b>
Cefaclor Generico		269	2
<b>CEFIXIMA</b>		<b>827</b>	<b>1</b>
CEFIXORAL Menarini		581	4
SUPRAX Wyeth		123	-9
UNIXIME Firma		123	1
<b>CEFTIBUTEN</b>		<b>543</b>	<b>-3</b>
ISOCEF Recordati		299	4
CEDAX Schering		244	-10
<b>CEFPODOXIMA</b>		<b>311</b>	<b>5</b>
CEFODOX Scharper		157	17
OTREON Sankyo		79	3
ORELOX Altana		75	-12

Fonte dati: IMSHEALTH

## MACROLIDI Sosp.

Risultati di vendita 2005

Molecola / Prodotto	Azienda	Gen-Ott '05	
		Unità (+000)	±%
<b>TOT. MERCATO Sosp.</b>		<b>10.926</b>	<b>3</b>
<b>MACROLIDI Sosp.</b>		<b>2.254</b>	<b>3</b>
<b>AZITROMICINA</b>		<b>998</b>	<b>5</b>
ZITROMAX Pfizer		727	8
TROZOCINA Sigmatau		163	-13
RIBOTREX Pierre Fabre		108	22
<b>CLARITROMICINA</b>		<b>1.068</b>	<b>5</b>
KLACID Abbott		402	6
MACLADIN Menarini		365	8
VECLAM Malesci		301	0

Fonte dati: IMSHEALTH

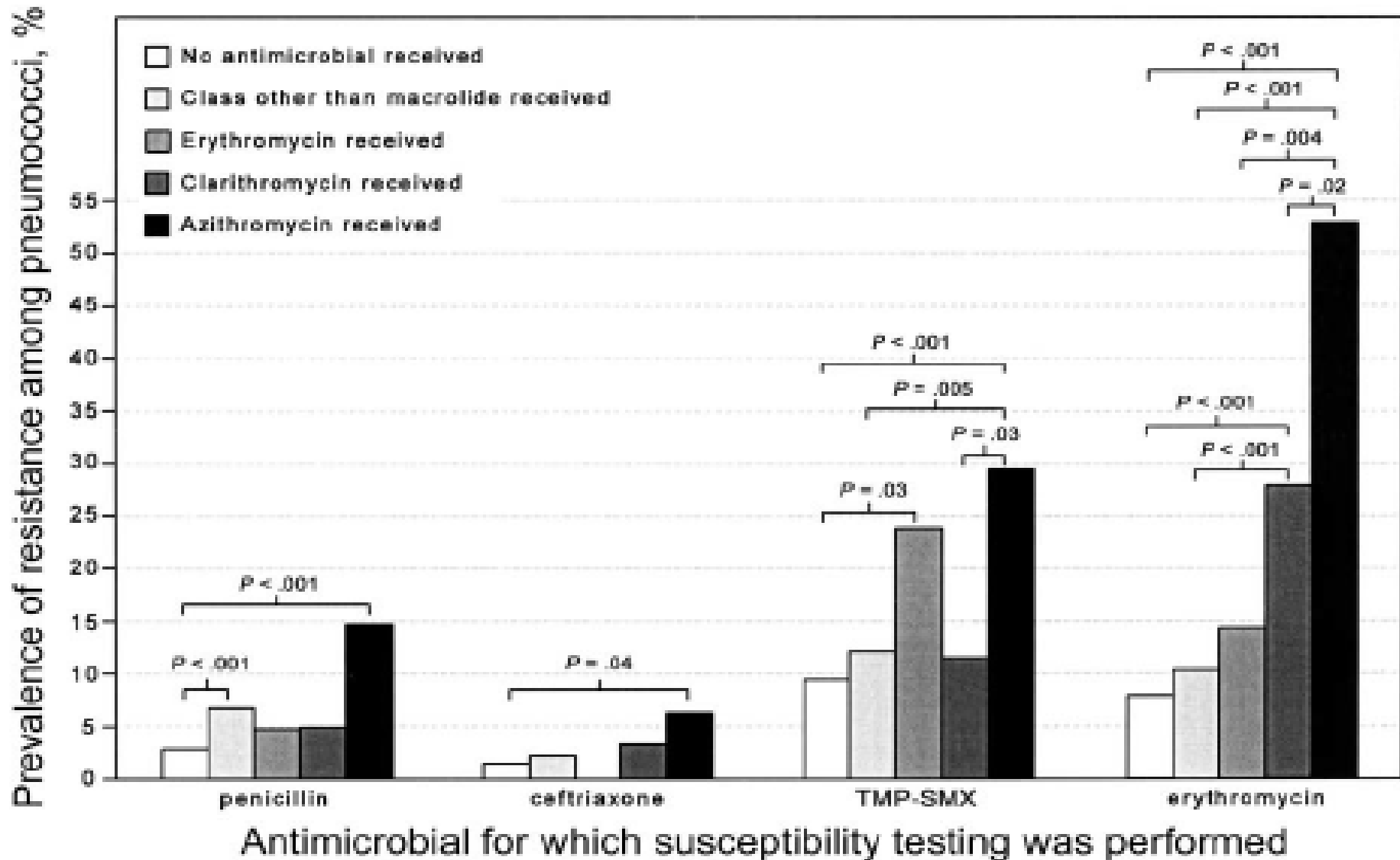
# FATTORI DI RISCHIO PER LA PRESENZA DI *STREPTOCOCCUS PNEUMONIAE* MULTI RESISTENTE

(da Vanderkooi OK et al, CID 2005)

Risk factor	Penicillin-resistant isolate		Ceftriaxone-resistant isolate <sup>a</sup>		TMP-SMX-resistant isolate		Erythromycin-resistant isolate	
	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Year of infection <sup>b</sup>	1.28 (1.14–1.42)	<.001	1.20 (1.04–1.38)	.01	NS	NS	1.11 (1.04–1.86)	.002
Chronic organ system disease	0.58 (0.35–0.94)	.03	...	NS	0.61 (0.45–0.82)	.001	...	NS
Drug use $\leq$ 3 months before infection								
Any penicillin	2.47 (1.36–4.71)	.006	...	NS	1.71 (1.06–2.77)	.03	1.77 (1.07–2.94)	.03
TMP-SMX	5.97 (2.71–13.2)	<.001	...	NS	4.73 (2.73–8.23)	<.001	2.07 (1.04–4.12)	.02
Azithromycin	2.78 (0.98–7.86)	.05	...	NS	3.49 (1.61–7.54)	.001	9.93 (4.85–20.3)	<.001
Clarithromycin	...	NS	...	NS	...	NS	3.93 (2.16–7.16)	<.001
Fluoroquinolone	...	NS	...	NS	...	NS	...	NS
Institution associated with acquisition								
Nursing home	...	NS	...	NS	...	NS	...	NS
Hospital	...	NS	...	NS	...	NS	...	NS

# RESISTENZA DELLO PNEUMOCOCCO AI MACROLIDI E TERAPIA PRECEDENTE

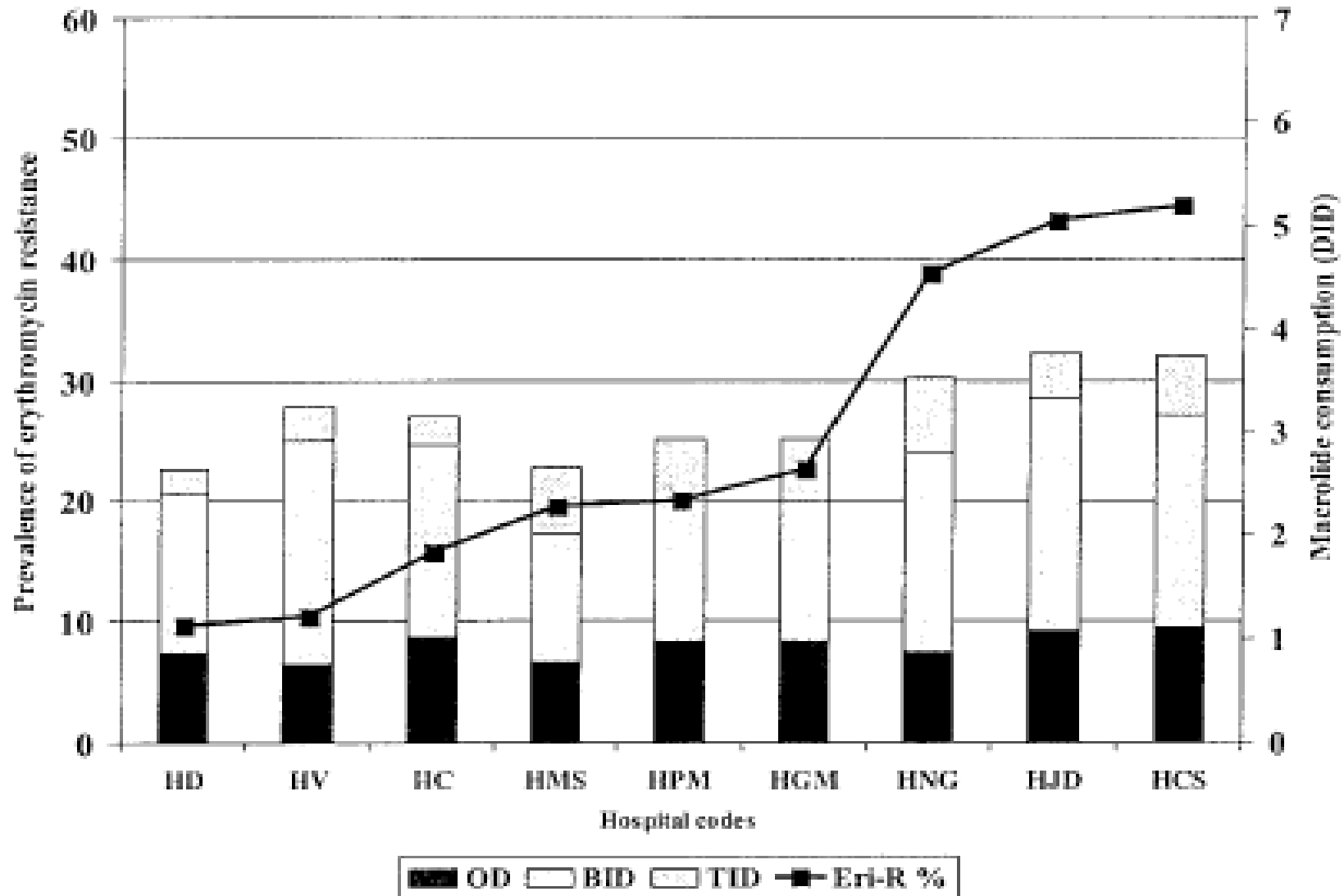
(da Vanderkooi OK et al. CID 2005)





# CORRELAZIONE TRA CONSUMO DI MACROLIDI E SVILUPPO DI RESISTENZA IN *S. PYOGENES*

(Da Garcia-Rey C. et al. J Clin Microbiol 2003)



# FARINGITE ACUTA: FARMACI UTILIZZATI

(Nov 04 - Ott 05)

- N° di Prescrizioni Totali (x1000): 1.197
- N° di Prescrizioni Amox-clav: 387 (32,3%)
- N° di Prescrizioni Amoxicillina: 151 (12,6%)

(Fonte dati: IMSHEALTH)

## LINEE GUIDA PER LA TERAPIA DELLA FARINGITE STREPTOCOCCICA (IDSA GUIDELINES 2002)

Route of administration, antimicrobial agent	Dosage	Duration <sup>a</sup>	Rating
<b>Oral</b>			
Penicillin V <sup>b</sup>	Children: 250 mg b.i.d. or t.i.d.	10 days	A-II
	Adolescents and adults: 250 mg t.i.d. or q.i.d.	10 days	A-II
	Adolescents and adults: 500 mg b.i.d.	10 days	C-III
<b>Intramuscular</b>			
Benzathine penicillin G	1.2 × 10 <sup>6</sup> U	1 dose	A-II <sup>c</sup>
	6.0 × 10 <sup>5</sup> U	1 dose <sup>d</sup>	A-II
Mixtures of benzathine and procaine penicillin G	Varies with formulation <sup>e</sup>	1 dose	B-II
<b>Oral, for patients allergic to penicillin</b>			
Erythromycin	Varies with formulation <sup>f</sup>	10 days	A-II
First-generation cephalosporins <sup>g</sup>	Varies with agent	10 days	A-II

<sup>a</sup> Although shorter courses of azithromycin and some cephalosporins have been reported to be effective for treating group A streptococcal upper respiratory tract infections, evidence is not sufficient to recommend these shorter courses for routine therapy at this time.

<sup>b</sup> Amoxicillin is often used in place of oral penicillin V for young children; efficacy appears to be equal. The choice is primarily related to acceptance of the taste of the suspension.

<sup>c</sup> See the discussion of benzathine penicillin G therapy in Management of Group A Streptococcal Pharyngitis.

<sup>d</sup> For patients who weigh <27 kg.

<sup>e</sup> Dose should be determined on basis of the benzathine component. For example, mixtures of 9 × 10<sup>5</sup> U of benzathine penicillin G and 3 × 10<sup>6</sup> U of procaine penicillin G contain less benzathine penicillin G than is recommended for treatment of adolescents or adults.

<sup>f</sup> Available as stearate, ethyl succinate, estolate, or base. Cholestatic hepatitis may rarely occur in patients, primarily adults, receiving erythromycin estolate; the incidence is greater among pregnant women, who should not receive this formulation.

<sup>g</sup> These agents should not be used to treat patients with immediate-type hypersensitivity to  $\beta$ -lactam antibiotics.

# AMPI-AMOXICILLINA VS PENICILLINA NELLA FARINGITE STREPTOCOCCICA: PRIMI DATI

Authors	Agent	Daily Dose	Schedule	Ampicillin/ Amoxicillin Percent Cure*	Penicillin Percent Cure*
Breese et al, <sup>1</sup> 1966	Ampicillin	10–20 mg/kg	t.i.d.	78	83
Ström, <sup>2</sup> 1968	Ampicillin	375–750 mg	t.i.d.	85	91
Stillerman et al, <sup>3</sup> 1972	Ampicillin	500 mg	t.i.d.	73	74
Stillerman et al, <sup>4</sup> 1974	Amoxicillin	375 mg	t.i.d.	87	80
Breese et al, <sup>5</sup> 1974	Amoxicillin	375 mg	t.i.d.	85	89
Breese et al, <sup>6</sup> 1977	Amoxicillin	15–20 mg/kg	t.i.d.	91	88

\*Percent cure defined as bacteriologic eradication at end of treatment.

t.i.d. = three times daily.

# AMOXICILLINA VS PENICILLINA NELLA TERAPIA DELLA FARINGITE STREPTOCOCCICA: DATI RECENTI

Antibiotic	Bacteriologic Outcome*		Clinical Outcome†	
	Number & Percent Cure	Number & Percent Failure	Number & Percent Cure	Number & Percent Failure
Penicillin n = 139	n=89* 64%*	n=50 36%	n=101† 73%†	n=38 27%
Amoxicillin n = 137	n=104 76%	n=33 24%	n=115 84%†	n=22 16%

\*tp = 0.04 comparing Penicillin V versus amoxicillin for bacteriologic and p = 0.03 for clinical cure differences.

**CLINICAL AND BACTERIOLOGIC EFFICACY OF AMOXYCILLIN B.D. (45 MG/KG/DAY) VERSUS AMOXYCILLIN T.D.S (40 MG/KG/DAY) IN CHILDREN WITH GROUP A BETA-HEMOLYTIC STREPTOCOCCAL TONSILLOPHARYNGITIS.**

**[Aguilar A](#), [Tinoco JC](#), [Macias M](#), [Huicho L](#), [Levy J](#), [Trujillo H](#), [Lopez P](#), [Pereira M](#), [Maqbool S](#), [Bhutta ZA](#), [Sacy RA](#), [Deacon S](#).**

Francisco De Icaza Bustamante Children's Hospital, Guayaquil, Ecuador

**This randomized, observer-blind, multicenter, parallel-group study compared the clinical and bacteriologic efficacy and safety of amoxicillin, 45 mg/kg/day b.d. and amoxicillin, 40 mg/kg/day t.d.s. after 7 days of treatment in 517 children with acute bacterial tonsillopharyngitis. At the end of treatment, a successful clinical response was recorded in more than 96% of patients in each of the treatment groups. A similar result was obtained at follow-up. Among those patients who were bacteriologically evaluable at the end of treatment, a successful bacteriologic response was achieved in more than 94% in each treatment group. Both treatments were well tolerated. Drug-related adverse events were recorded in just 12 patients (4.6%) in the b.d. group and six (2.4%) in the t.d.s. group. The study demonstrated that a twice-daily regimen of amoxicillin, 45 mg/kg/day, was as effective and as well tolerated as the standard three-times-daily regimen of amoxicillin, 40 mg/kg/day, in the treatment of acute bacterial tonsillopharyngitis in children.**

Da Herbert et al. *Pediatr Infect Dis J* 2006

**TABLE 2.** Bacteriologic and Clinical Outcomes in Evaluable Children Treated With Once- or Twice-Daily Amoxicillin for Group A Streptococcal Pharyngitis

Bacteriologic and Clinical Outcomes	No. (%) of Patients by Treatment Group		Percent Treatment Difference (90% confidence interval)
	Once Daily	Twice Daily	
Visit 2, all patients, n	294	296	
Bacteriologic failure	59 (20.1)	46 (15.5)	4.53 (−.6 to 9.7)
Bacteriologic persistence	32 (10.9)	25 (8.4)	2.44 (−1.6 to 6.4)
Clinical recurrence	27 (9.2)	21 (7.1)	2.09 (−1.6 to 5.8)
Visit 3, all patients, n	216	225	
Bacteriologic failure	6 (2.8)	16 (7.1)	−4.33 (−7.7 to −1.0)
Bacteriologic relapse	4 (1.9)	14 (6.2)	−4.37 (−7.4 to −1.3)
Clinical recurrence	2 (0.9)	2 (0.9)	0.04 (−1.4 to 1.5)

# OTITE MEDIA ACUTA: FARMACI UTILIZZATI

(Nov 04 - Ott 05)

- N° Prescrizioni Totali (x1000): 804
- N° Prescrizioni Cefalosporine orali: 388 (48,2%)
- N° Prescrizioni Amox-clav: 280 (34,8%)
- N° Prescrizioni Amoxicillina: 80 (9,9%)
- N° prscrizioni macrolidi: 56 (6,7%)



# TERAPIA DELL'OMA

(Guidelines AAC, Pediatrics 2004)

Temperature $\geq$ 39°C and/or Severe Otalgia	At Diagnosis for Patients Being Treated Initially With Antibacterial Agents	
	Recommended	Alternative for Penicillin Allergy
No	Amoxicillin, 80–90 mg/ kg per day	Non-type I: cefdinir, cefuroxime, cefprozime; type I: azithromycin, clarithromycin
Yes	Amoxicillin-clavulanate, 90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate	Ceftriaxone, 1 or 3 days

# TERAPIA DELL'OMA

(Guidelines AAC, Pediatrics 2004)

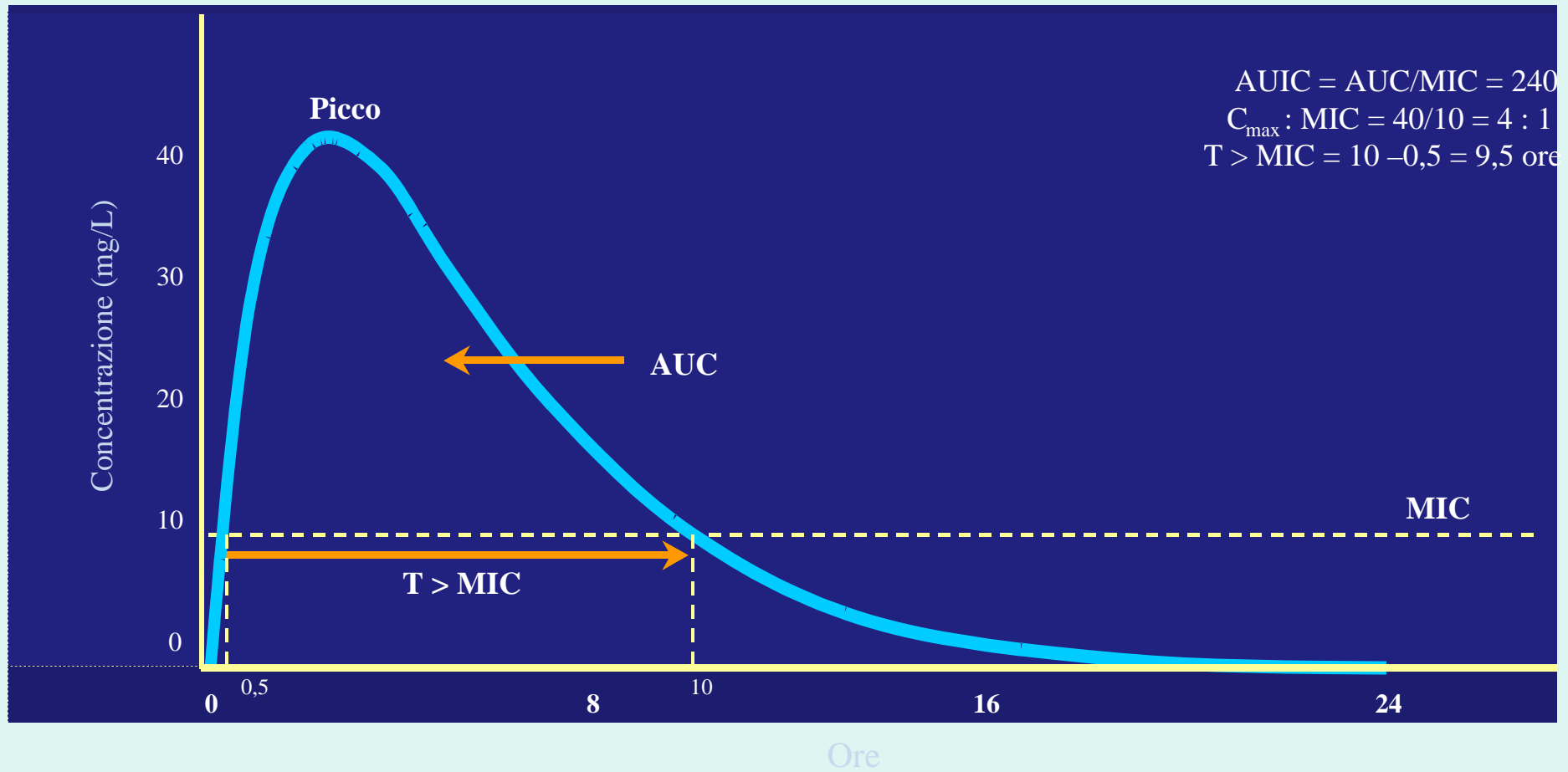
Temperature $\geq$ 39°C and/or Severe Otalgia	Clinically Defined Treatment Failure at 48–72 Hours After Initial Management With Observation Option	
	Recommended	Alternative for Penicillin Allergy
No	Amoxicillin, 80–90 mg/kg per day	Non-type I: cefdinir, cefuroxime, cefepodoxime; type I: azithromycin, clarithromycin
Yes	Amoxicillin, clavulanate, 90 mg/kg per day of amoxicillin, with 6.4 mg/kg per day of clavulanate	Ceftriaxone, 1 or 3 days

# TERAPIA DELL'OMA

(Guidelines AAC, Pediatrics 2004)

Temperature $\geq$ 39°C and/or Severe Otalgia	Clinically Defined Treatment Failure at 48–72 Hours After Initial Management With Antibacterial Agents	
	Recommended	Alternative for Penicillin Allergy
No	Amoxicillin-clavulanate, 90 mg/kg per day of amoxicillin component, with 64 mg/kg per day of clavulanate	Non-type I: ceftriaxone, 3 days; type I: clindamycin
Yes	Ceftriaxone, 3 days	Tympanocentesis, clindamycin

# PK-PD correlations



# Activity of antibiotics

TIME -  
DEPENDENT



Betalactams  
Glycopeptides  
Lincosamides  
Natural macrolides  
Oxazolidinones

CONCENTRATION -  
DEPENDENT



Aminoglycosides  
Fluoroquinolones  
Metronidazole  
Dalfopristin/quinopristin  
Clarithromycin  
Azithromycin

## PK-PD correlation

$T > MIC$   
(40-70%)

$AUC/MIC = 100-125$

$\sim 50$

$C_{max}/MIC = 8-12.5$

Gram+ and Gram- bacteria

*S. pneumoniae*

Gram+ and Gram- bacteria

Craig et al., ICAAC, 2000; N.L. Jumbe et al., ICAAC, 2000; P.G. Ambrose et al., ICAAC, 2000;  
S. Preston, JAMA, 1998; R.D. Moore, J. Infect. Dis., 1987



# CARATTERISTICHE DEI BAMBINI CON AOM

(da Arrieta A. Antimicrog Ag Chemother 2003)

Characteristic	Value for patient groups	
	Azithromycin (n = 151)	Amoxicillin- clavulanate (n = 145)
Gender ratio (male/female)	1.3	1.4
Mean age, mo ( $\pm$ SD)	24.6 $\pm$ 18.4	25.7 $\pm$ 19.7
No. (%) children $\leq$ 24 mo	98 (65)	93 (64)
Wt, kg ( $\pm$ SD)		
Male	12.8 $\pm$ 4	12.5 $\pm$ 4
Female	12.2 $\pm$ 4.2	13 $\pm$ 4.5
No. (%) of siblings with history of AOM	47 (31)	52 (36)
No. (%) attending day care	63 (42)	57 (39)
Prior medical history, no. (%)		
Persistent AOM	35 (23)	20 (14)
Recurrent AOM	101 (66)	99 (67)
Recurrent plus persistent AOM	16 (11)	27 (19)
Age < 6 mo at first AOM episode, no. (%)	59 (39)	68 (47)
Household smoke exposure, no. (%)	48 (32)	29 (20)
Pacifier use, no. (%)	46 (31)	29 (20)

# GUARIGIONE CLINICA DELL'AOM A SECONDA DEL TRATTAMENTO

(da Arrieta A. Antimicrog Ag Chemother 2003)

Baseline pathogen	Day 12 to 16			
	Azithromycin	Amoxicillin-clavulanate	P	95% CI of difference
All patients	63/80 (79)	67/83 (81)	0.846	-14.3, 10.4
<i>S. pneumoniae</i> <sup>b</sup>	22/26 (85)	31/39 (80)	0.749	-13.7, 23.9
<i>H. influenzae</i> <sup>c</sup>	24/36 (67)	25/31 (81)	0.271	-34.7, 6.8
<i>S. pneumoniae</i> and <i>H. influenzae</i> <sup>d</sup>	4/4 (100)	3/4 (75)	ND <sup>e</sup>	
<i>M. catarrhalis</i> alone	7/8 (88)	4/5 (80)	ND	
<i>S. pyogenes</i> alone	6/6 (100)	4/4 (100)	ND	



# GUARIGIONE CLINICA DELL'AOM A SECONDA DEL TRATTAMENTO

(da Arrieta A. Antimicrog Ag Chemother 2003)

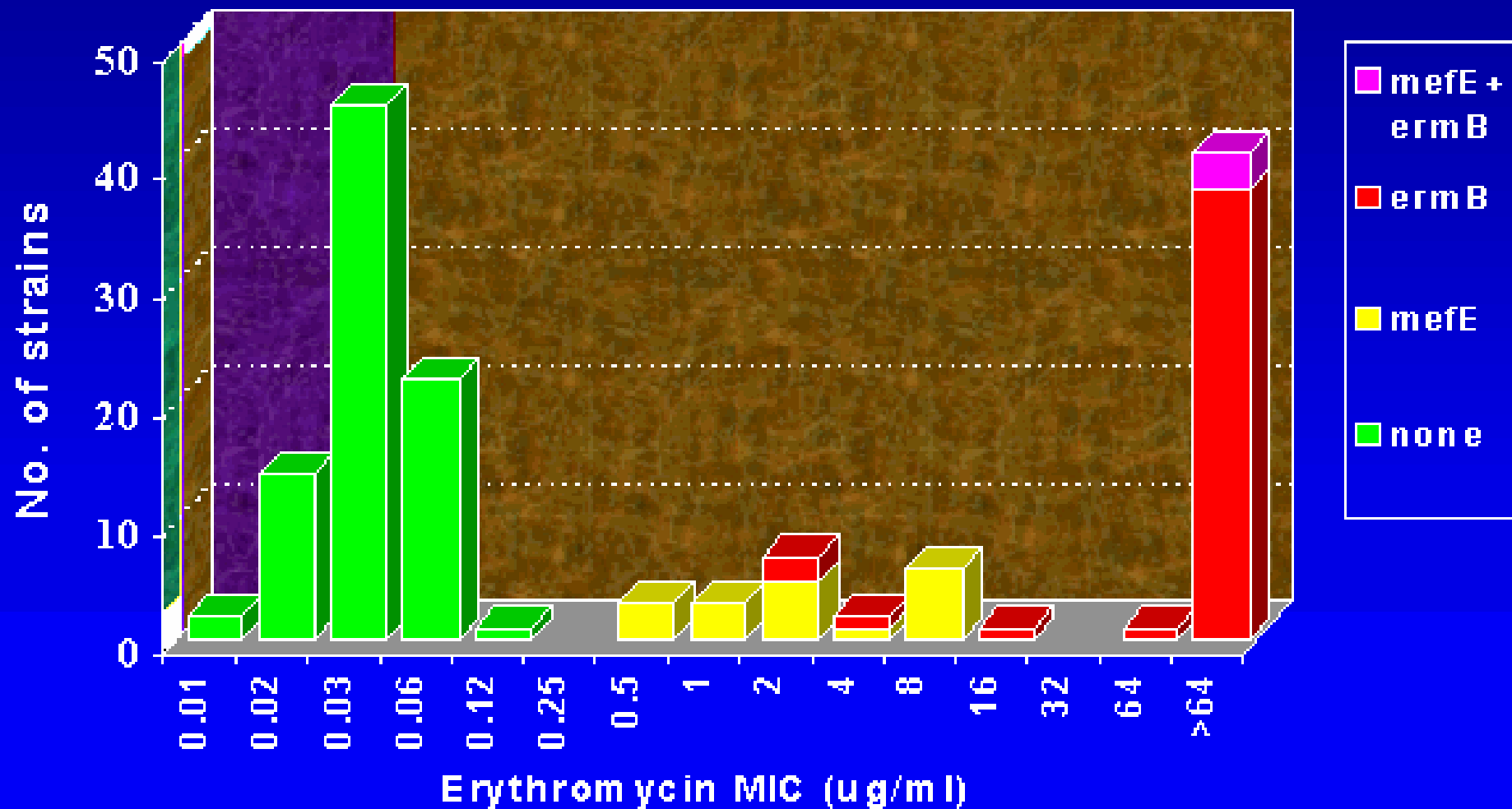
Baseline pathogen	Day 28 to 32			
	Azithromycin	Amoxicillin-clavulanate	P	95% CI of difference
All patients	49/78 (63)	47/82 (57)	0.521	-9.7, 20.7
<i>S. pneumoniae</i> <sup>b</sup>	17/26 (65)	26/39 (67)	1.000	-24.8, 22.2
<i>H. influenzae</i> <sup>c</sup>	17/36 (47)	16/31 (52)	0.808	-28.4, 19.6
<i>S. pneumoniae</i> and <i>H. influenzae</i> <sup>d</sup>	4/4 (100)	1/3 (33)	ND	
<i>M. catarrhalis</i> alone	7/8 (88)	2/5 (40)	ND	
<i>S. pyogenes</i> alone	4/4 (100)	2/4 (50)	ND	

# SENSIBILITÀ *IN VITRO* DI *S. PNEUMONIAE* RESPONSABILE DI OMA

(da Arrieta A. Antimicrog Ag Chemother 2003)

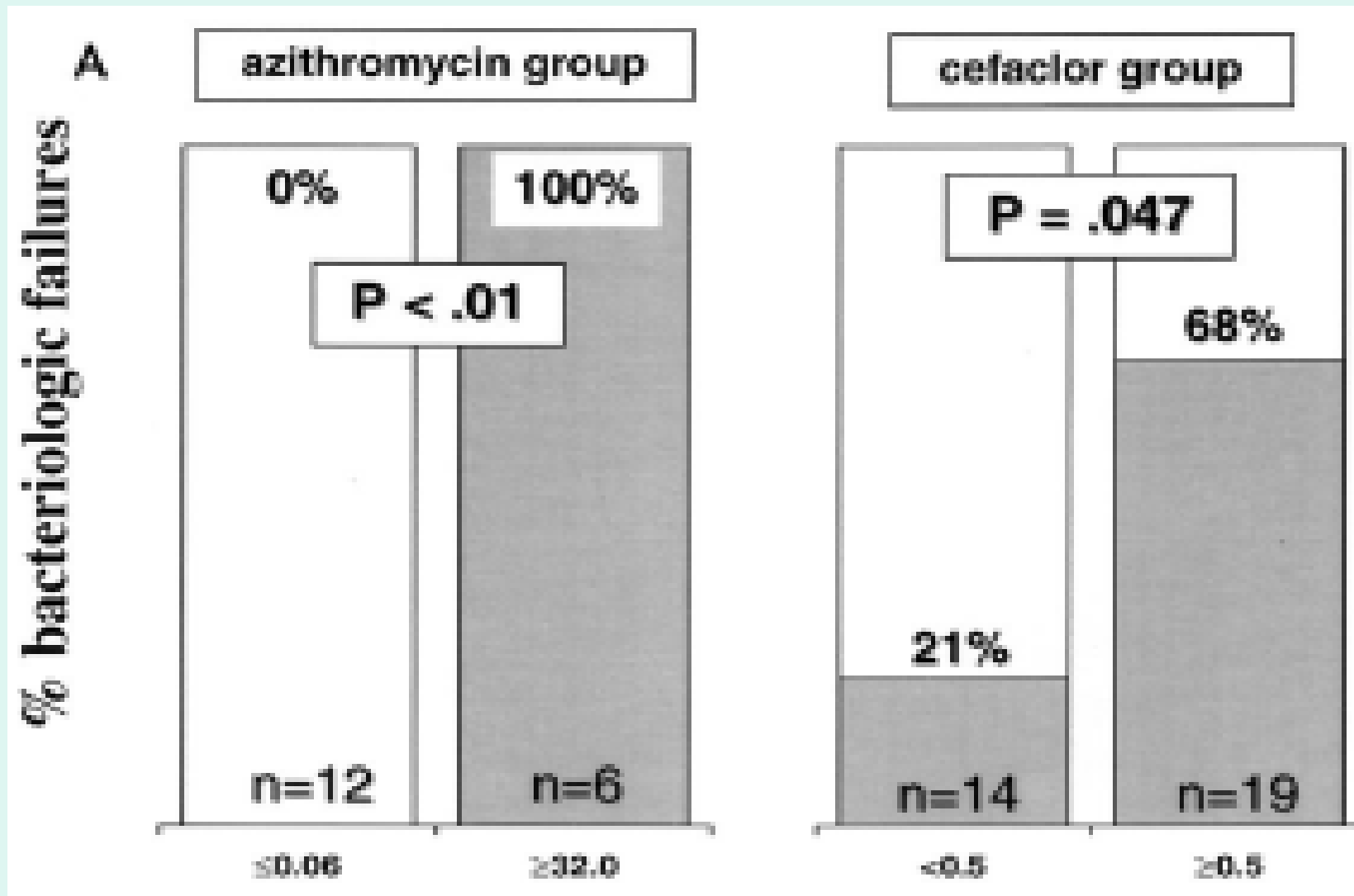
- Penicillina intermedio: 25%
- Penicillina resistente: 22%
- Azitromicina resistente: 27% (nell'80% dei casi resistenza da efflusso)

# Correlation between erythromycin MICs and resistance mechanisms

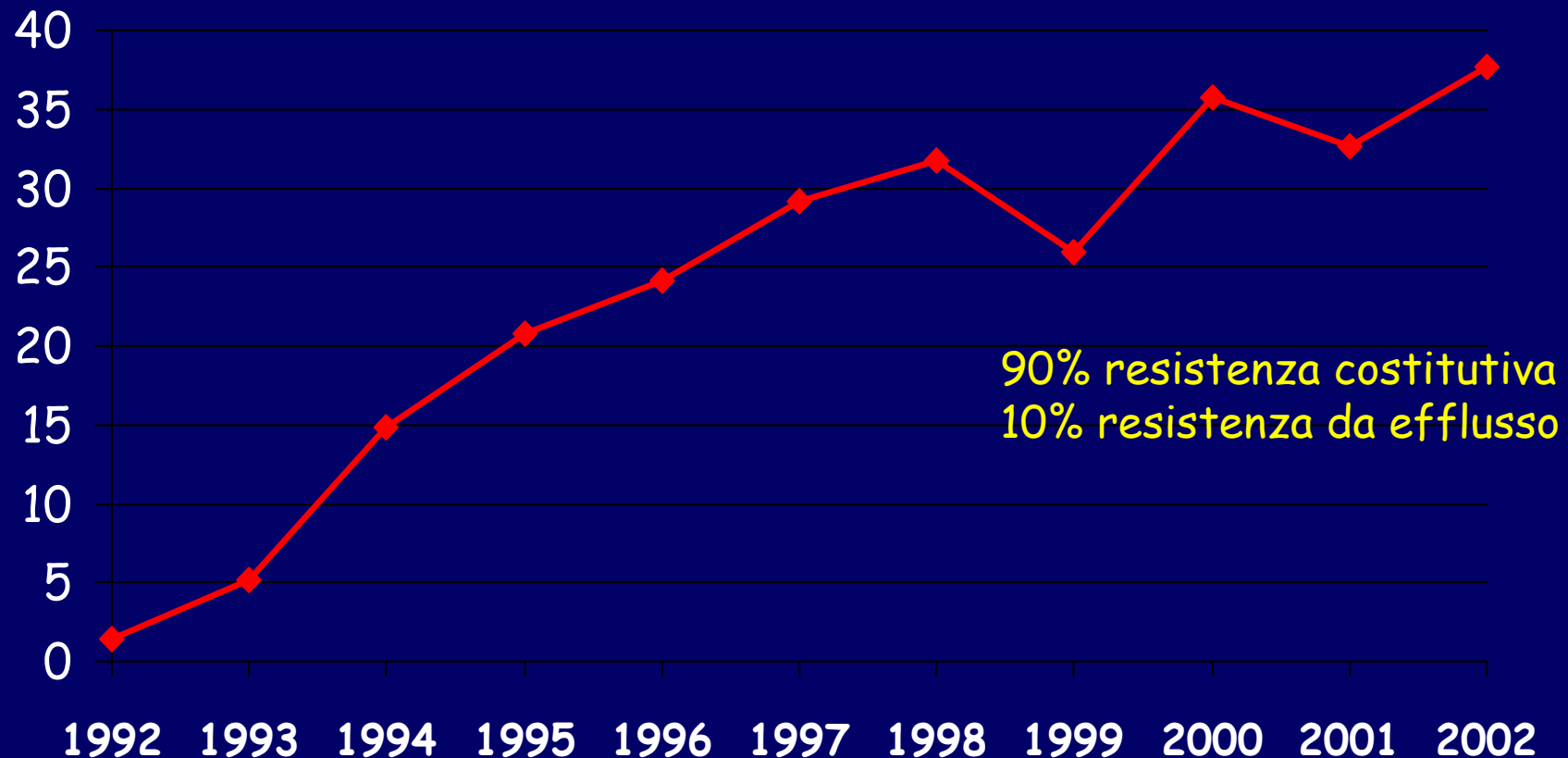


# CORRELAZIONE TRA MIC DI AZITROMICINA VERSO *S. PNEUMONIAE* E ESITO DELLA TERAPIA DELL'OMA

(da Dagan et al, Antimicrob Ag Chemother 2002)



# EVOLUZIONE DELLA RESISTENZA (%) DI *S.PNEUMONIAE* AI MACROLIDI IN ITALIA



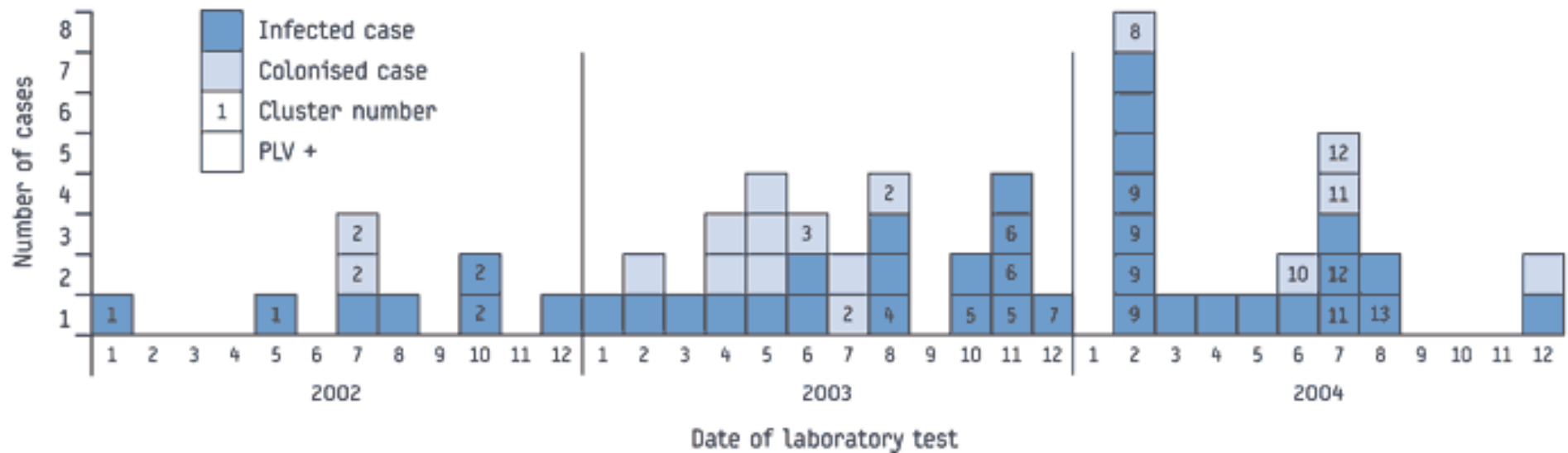
da Schito et al. JAC, 2003

# INDICAZIONI TRADIZIONALI ALL'USO DELLA CLINDAMICINA

- Sepsi ed endocarditi da anaerobi dove, tuttavia, il metronidazolo è da preferire perché più rapidamente battericida
- Ascessi polmonari e polmoniti *ab ingestis* dove, tuttavia, la penicillina ha dimostrato efficacia sovrapponibile
- Toxoplasmosi cerebrale in pazienti con AIDS nei pazienti che non tollerano i sulfamidici
- Vaginosi batterica
- Malaria clorochino-resistente e babiliosi

**FIGURE**

**Cases of community-acquired MRSA reported to the Geneva surveillance database, 2002-2004**



Da Aramburu C, et al. Eurosurveillance 2006

# INFEZIONI DA CA-MRSA

## FATTORI DI RISCHIO

- Giovane età (adolescenti!)
- Sesso maschile
- Basso livello socio-economico
- Scarsa igiene
- Vita di comunità

## QUADRI CLINICI

- Infezioni cutanee e dei tessuti molli di media o lieve gravità
- Polmoniti
- Sepsi



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**TRANSMISSION OF COMMUNITY-ASSOCIATED  
METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*  
FROM BREAST MILK IN THE NEONATAL  
INTENSIVE CARE UNIT**

*Dawn Terashita Gastelum, MD, MPH, David Dassey, MD, MPH,  
Laurene Mascola, MD, MPH, and Lori M. Yasuda, BA*

**Da Pediatr Infect Dis J 2005**

Table 1. Characteristics of staphylococcal cassette chromosome *mec* (SCC*mec*) types I–V [13,22,45–48]

SCC <i>mec</i>		<i>Staphylococcus aureus</i> carrying specified SCC <i>mec</i> type			
Type	Size (kb)	Presence of other antibiotic resistance genes	Origin of isolates	Mean doubling time (min)	Presence of PVL genes
I	34	No	Hospital	36	Infrequent
II	53	Yes	Hospital	32	Infrequent
III	67	Yes	Hospital	42	Infrequent
IV	21–24	No	Community	28	Frequent
V	28	No	Community	Unknown	Unknown

PVL, Panton–Valentine leukocidin.

Da Kluytmans-Vanlenbergh MFQ and Kluytmans JAJW. Clin Microbiol Infect 2006

TABLE 2. Antibiotic Susceptibility of 2003-2004 Community-Associated Methicillin-Resistant *Staphylococcus aureus* Isolates

Antibiotic	No. (%) Susceptible ( <i>N</i> = 23)	MIC <sub>90</sub> , μg/mL	MIC range, μg/mL
TMP-SMZ	23 (100)	0.06/1.19 <sup>a</sup>	0.03/0.59-0.5/9.5
Clindamycin <sup>b</sup>	21 (91)	0.13	0.06-64
Erythromycin	0	64	2-64
Gentamicin	23 (100)	0.13	0.06-25
Oxacillin	0	64	16-64
Rifampin	23 (100)	0.03	0.03-0.03
Tetracycline	21 (91)	0.5	0.13-32
Vancomycin	23 (100)	0.5	0.25-0.5
Linezolid	23 (100)	2	2-2
Daptomycin	23 (100)	0.25	0.12-0.25
Ciprofloxacin	19 (83)	16	0.12-64
Levofloxacin	20 (87)	4	0.06-32
Gatifloxacin	20 (87)	4	0.06-8
Gemifloxacin	20 (87)	1	0.03-16
Moxifloxacin	22 (96)	1	0.03-4

# INFEZIONI DA CA-MRSA: TERAPIA

Forme lievi:

- Clindamicina
- Tetracicline
- Co-trimossazolo

Forme gravi

- Vancomicina
- Teicoplanina