

Topical antibiotics

Microbiological point of view

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- Topical antibiotics
- Efficacy
- Antibiotic resistance
 - Propionibacteria/acne
 - Tetracyclines
 - macrolides
 - Staphylococci/impetigo
 - Fusidic acid
 - Mupirocin
- Epilogue

Topical antibiotics in dermatology

- Bacitracin
- Chloramphénicol
- Clindamycin
- **Erythromycin**
- **Fusidic acid**
- Gentamicin
- Miconazol
- **Mupirocin**
- Neomycin
- Polymyxin B
- Sulfamides
- **Tétracyclines**

- **Benzoyl peroxyde**
- Azelaic acid

+ "bactéries (filtrat polyvalent) + huile de foie de morue 125 mg + sulfanilamide 200 mg/1 g"

Topical antibiotics in ophtalmology / ORL

- Bacitracine
- Chloramphénicol
- Fusidic acid
- Gentamicin
- Gramicidin*
- Quinolones: o-,nor-, cipro-, lome- floxacin*
- Neomycin
- Polymyxin B
- Rifamycin*
- Sulfamides
- Tétracyclines
- Trimethoprim*
- Tobramycin*
- Tyrothricine*

Topical antibiotics: efficacy

- **Impetigo: mupirocin & fusidic acid*: + ****
- **Acne: + ~ benzoyl peroxyde**
- Chronic suppurative otitis media*: + **
- Acute bacterial conjunctivitis*: +

* *(Cochrane review)*

** *better than antiseptics*

Topical antibiotics: resistance

- *Propionibacterium spp.*:

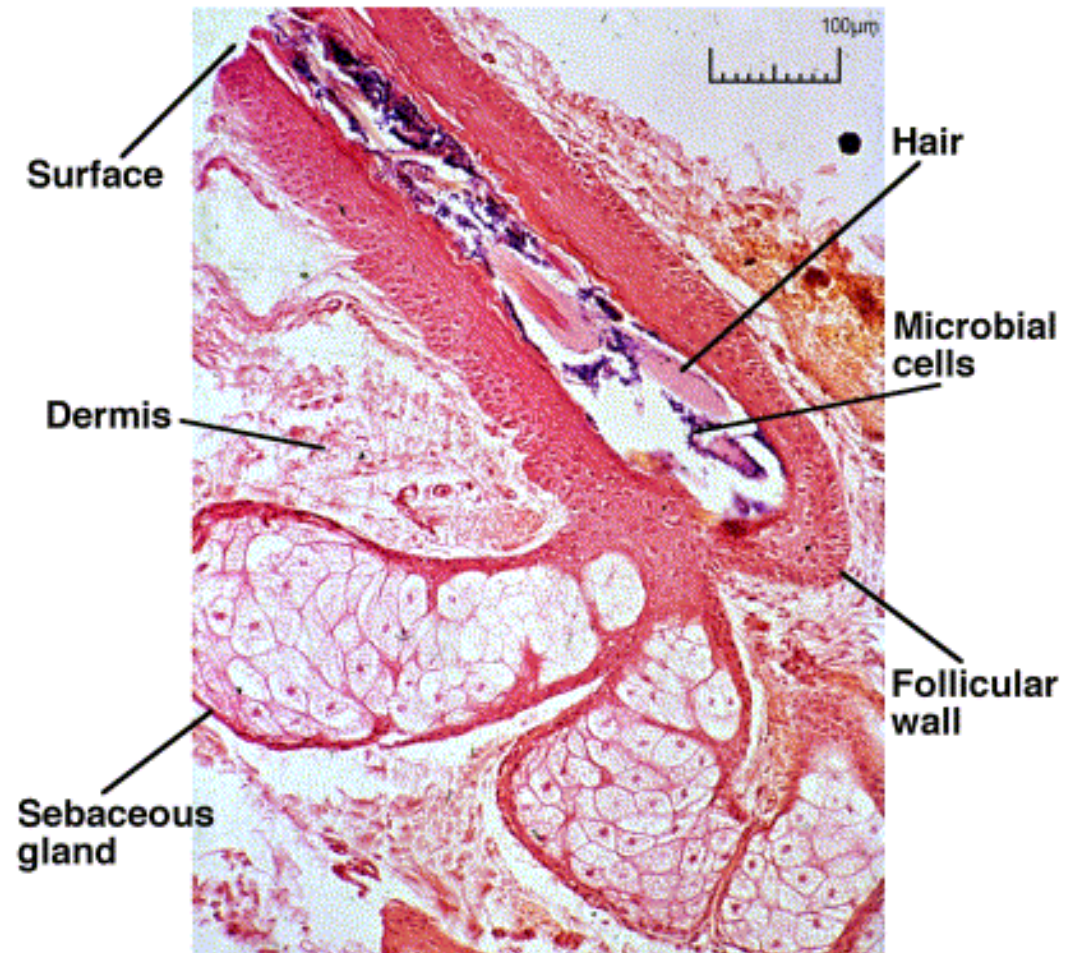
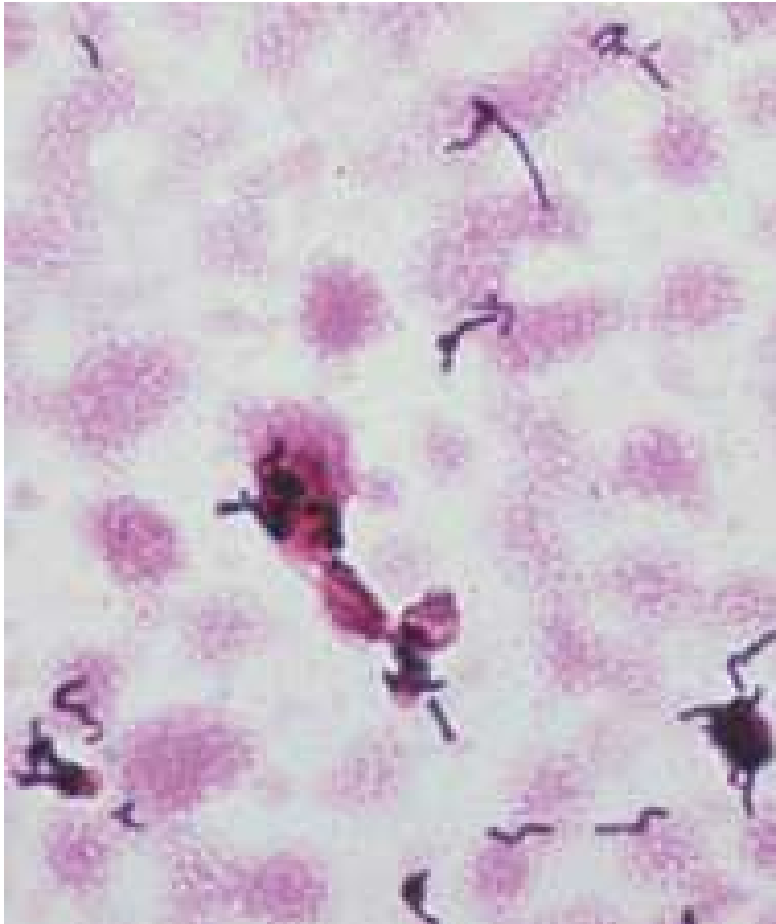
resistance to erythromycin:

- mutation in the genes encoding 23S ribosomal RNA (3 phenotypes)

resistance to tetracycline:

- Mutation of the gene encoding 16S ribosomal RNA

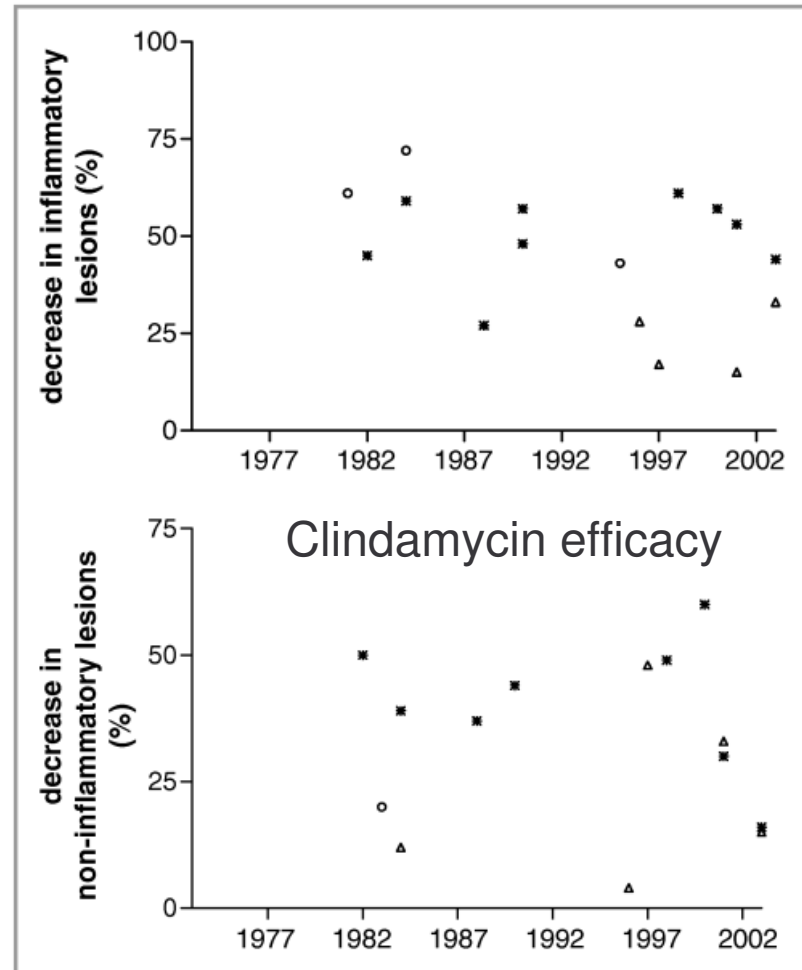
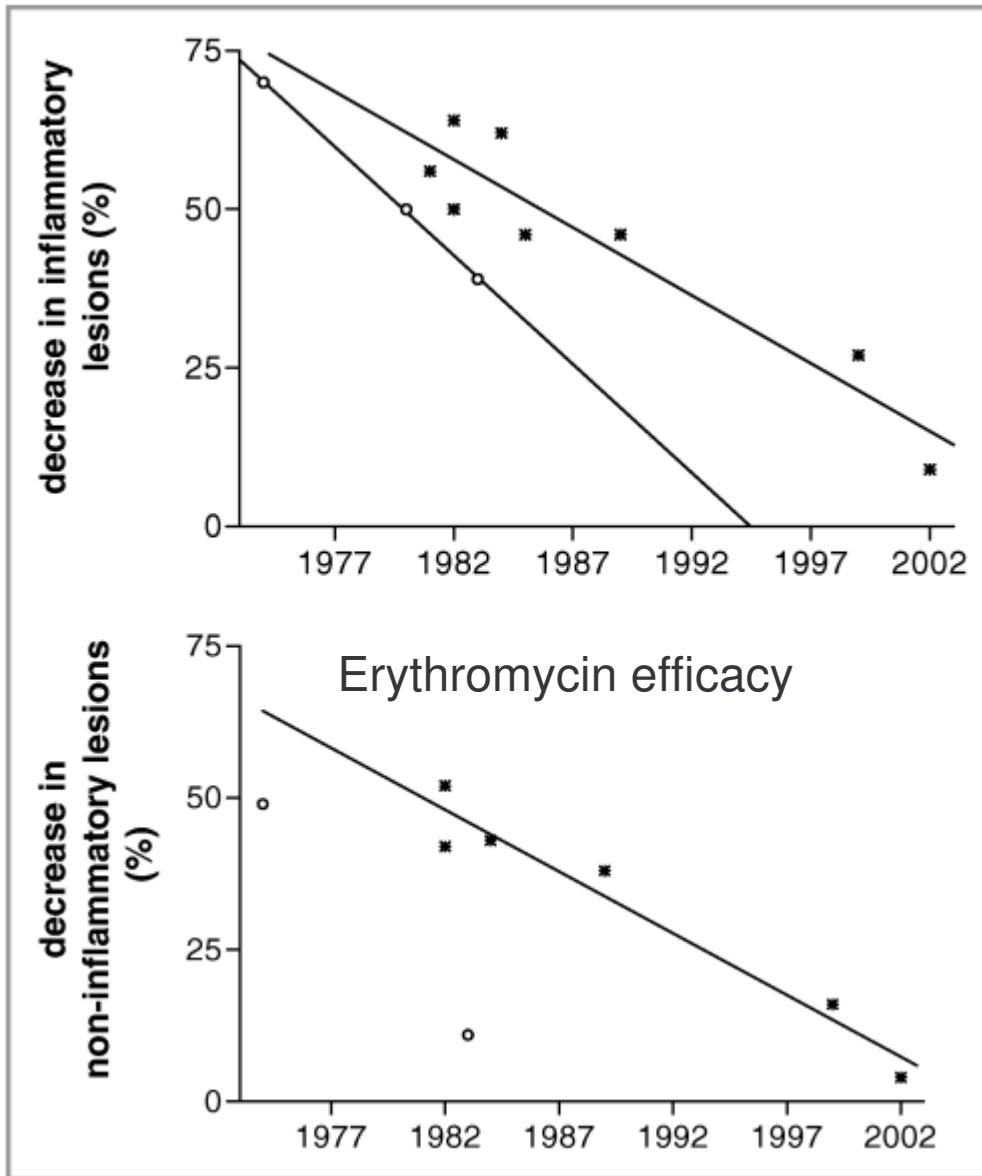
Propionibacteria



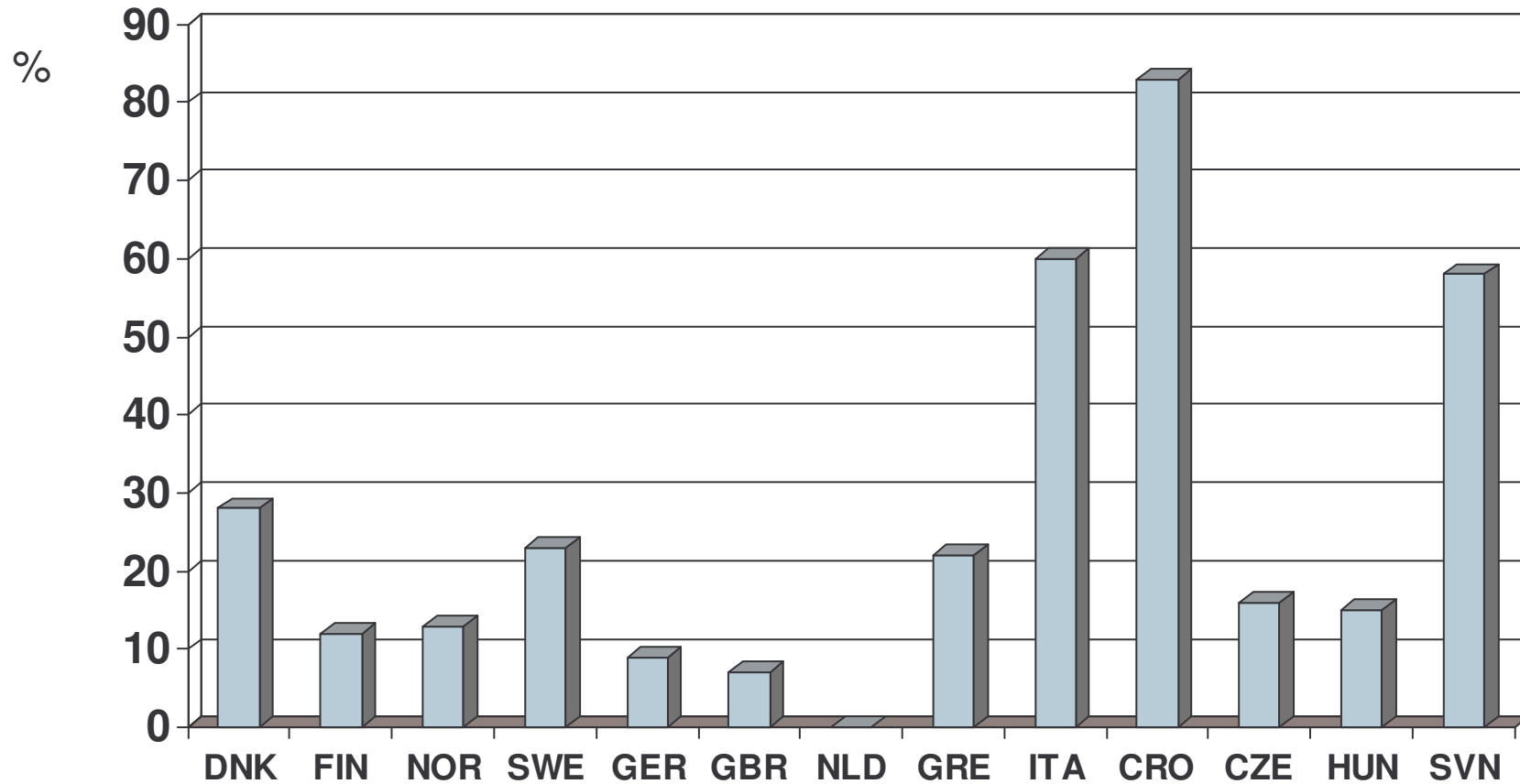
Distribution and differentiation of human commensal propionibacterium

		<i>P. acnes</i>	<i>P. avidum</i>	<i>P. granulosum</i>	<i>P. propionicum</i>
distribution	Skin	+++	+++	+++	-
	Eye	+	-	-	+++
	Mouth	++	-	+	+++
	Gut	+++	-	-	-
differentiation	Esculin	-	+	-	-
	Catalase	+	+	+	-
	Indole	+	-	-	-
	nitrate	+	-	-	+

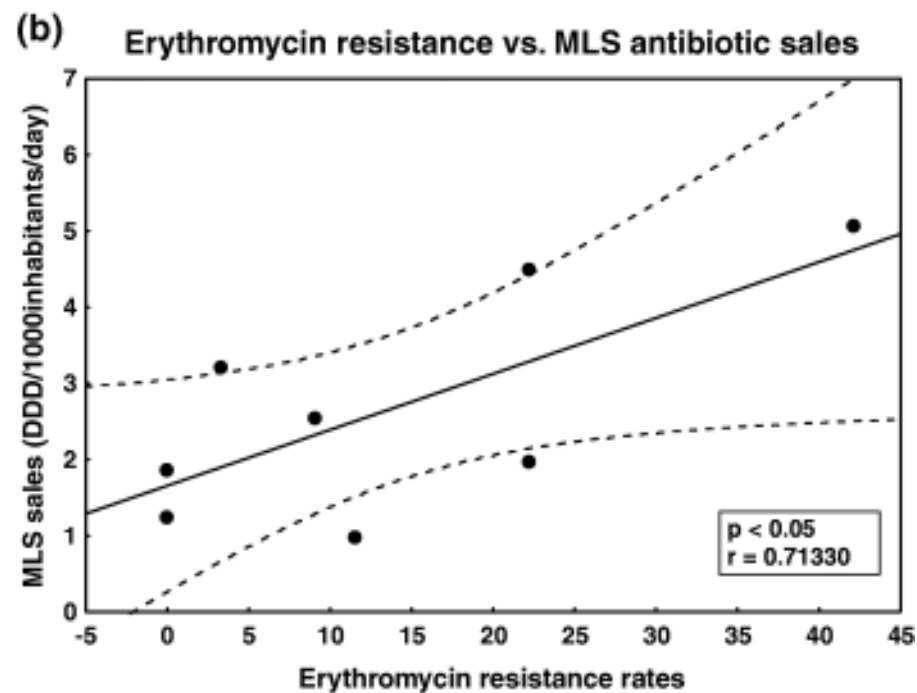
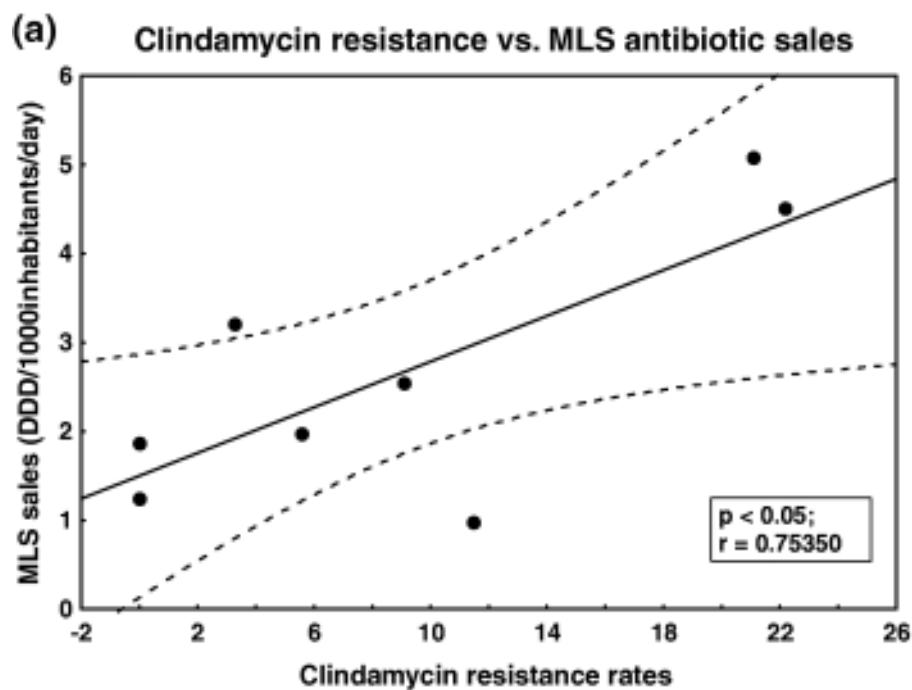
Treatment of acne with topical antibiotics: lessons from clinical studies



% resistant isolates of *P. acnes* from systemic origin from 13 European countries

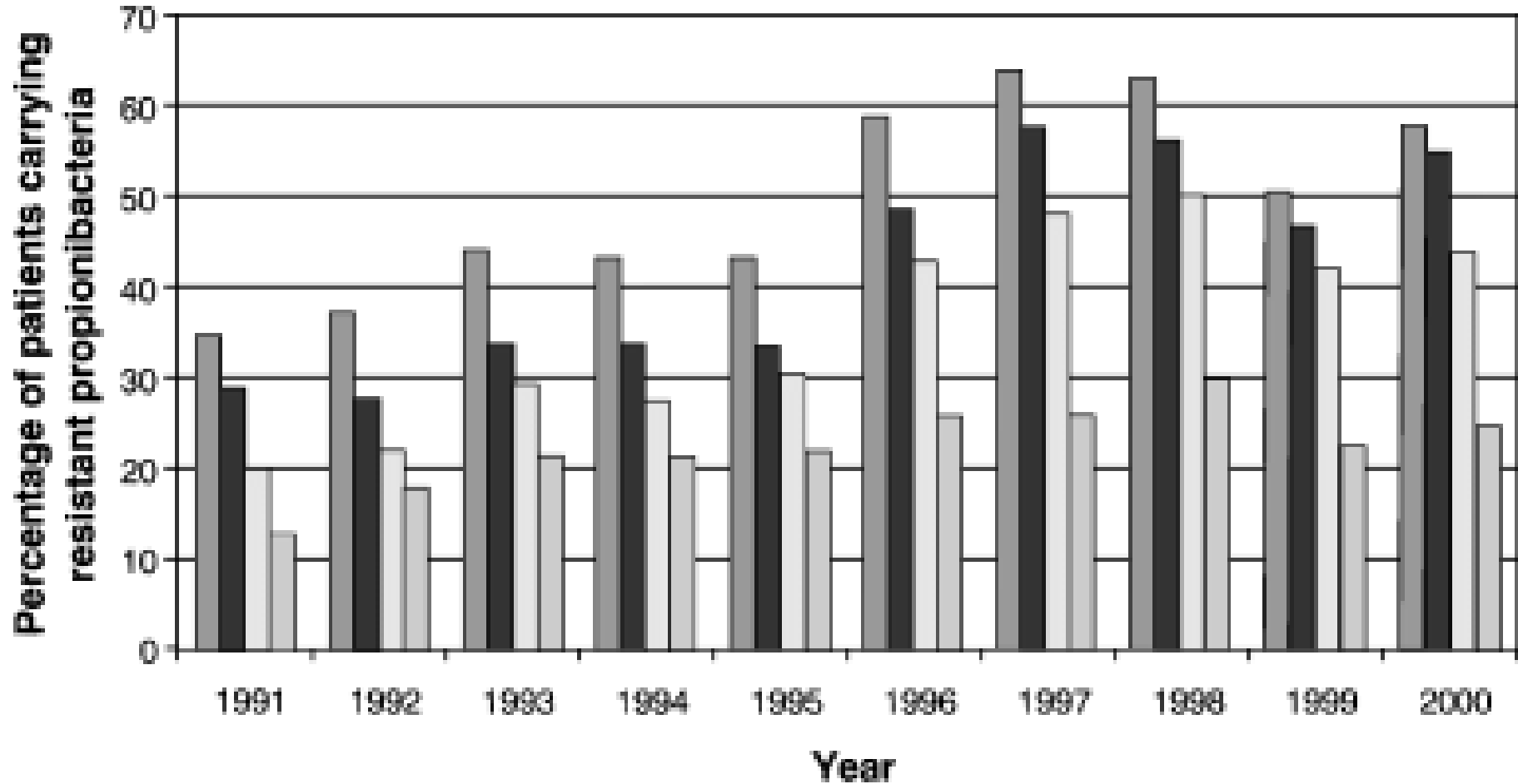


Correlation between reported sales of macrolides/lincosamides and resistance of *Propionibacterium acnes*



Prevalence of skin colonization by antibiotic-resistant propionibacteria among acne patients attending the out-patient clinic at Leeds General Infirmary, 1991–2000. ▨ Any antibiotic; ▩ erythromycin; ▪ clindamycin; ▫ tetracycline

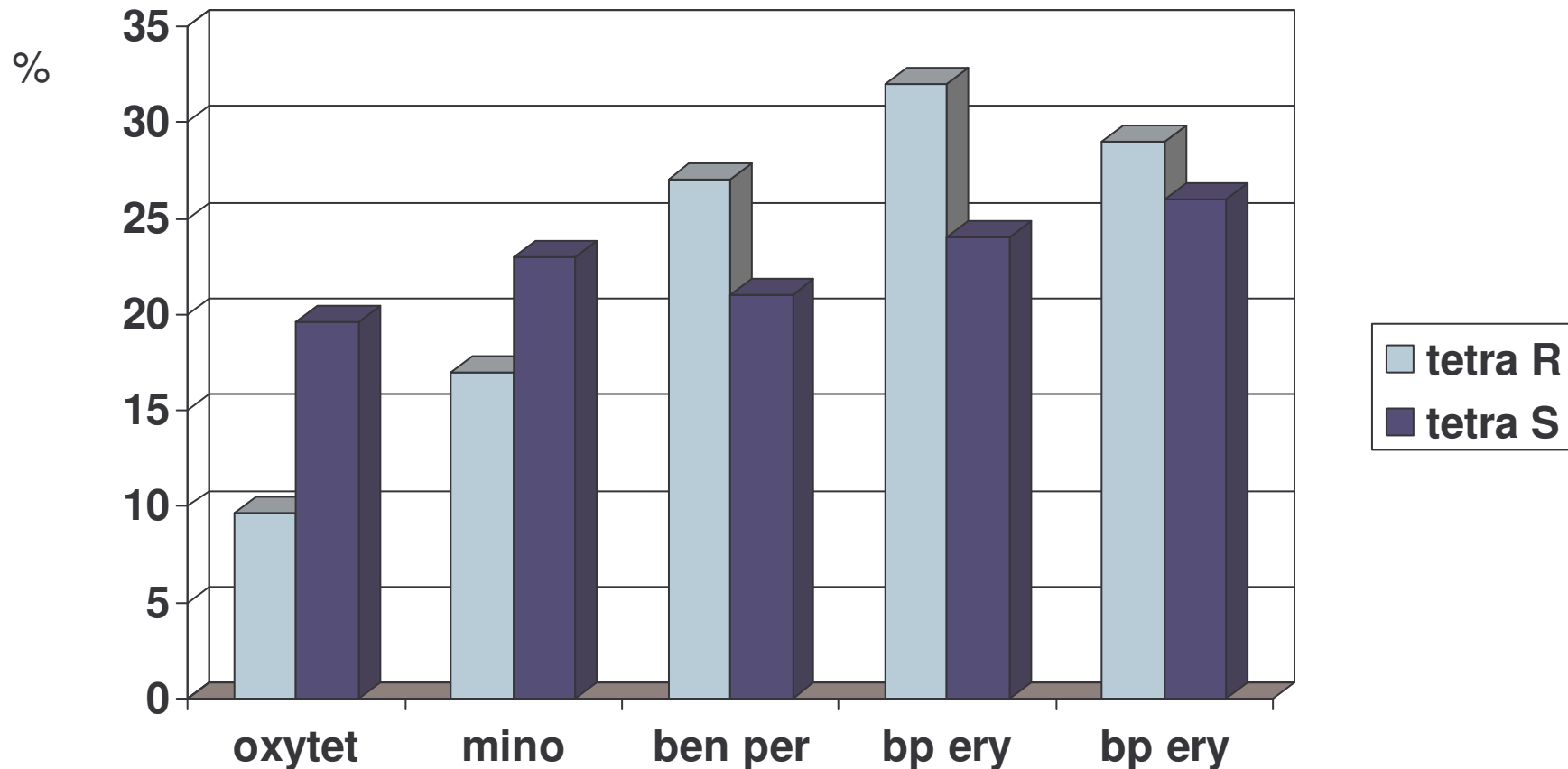
Br j Dermatol 2002 146 840-848



Skin colonization with antibiotic-resistant propionibacteria becomes more common

% reduction in lesions count according to skin colonization with tetracyclineR propionibacteria

Lancet 2004 364 2199-2195



Pre-existing tetracycline resistance reduces efficacy of tetracyclines

Propionibacterium resistance does not affect benzoyl peroxyde and erythromycin efficacy

Topical antibiotics: resistance

- *Staphylococcus aureus*, MSSA /MRSA
 - Fusidic acid
 - Chromosomal mutation ($1/10^6$ - 10^8)
 - Plasmid: ↓ permeability
 - Mupirocin
 - Low level: alteration of isoleucyl-tRNA synthetase (IRS)
 - High level: additional IRS (plasmidic)

National Surveillance of Methicillin-Resistant
Staphylococcus aureus in Belgian Hospitals:
 distribution of MRSA strains ($n = 455$) by
 susceptibility category

	% of strains per susceptibility category		
antibiotic	susceptible	intermediate	resistant
Fusidic acid	93,6	5,7	0,7
mupirocin	89,7	6,8	3,5

Impetigo: incidence and treatment in Dutch general practice

	1987		2001	
	No	%	No	%
episodes	357	100	1682	100
Oral AB	109	31	242	14
Topical AB	153	43	1078	64
Fus ac	64	18	855	51
Mup	-	0	210	12
Tet	54	15	3	0
Antiseptic	40	11	48	3

Increased incidence

Increased prescriptions of topical antibiotics

Retrospective case-control study on exposure to topical antibiotics and fusidic acid resistant MSSA isolates

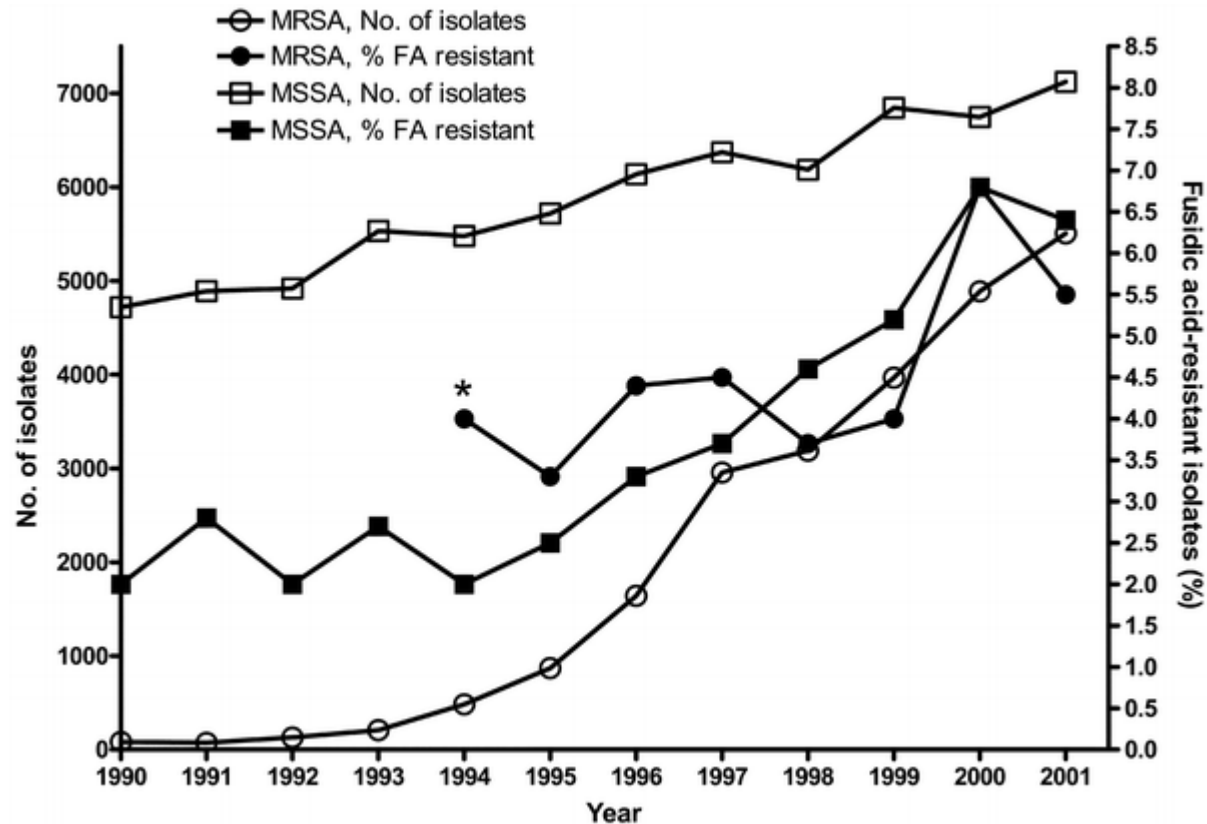
Int J Antimicrob Agents 2004 23 300-303

	Cases MSSA FA-R		Controls		
antibiotic	yes	no	yes	no	Odds ratio
any	21	28	18	41	1,71
Fusidic ac	17	32	9	47	2,77

Association between use of topical fusidic acid and resistance at individual level

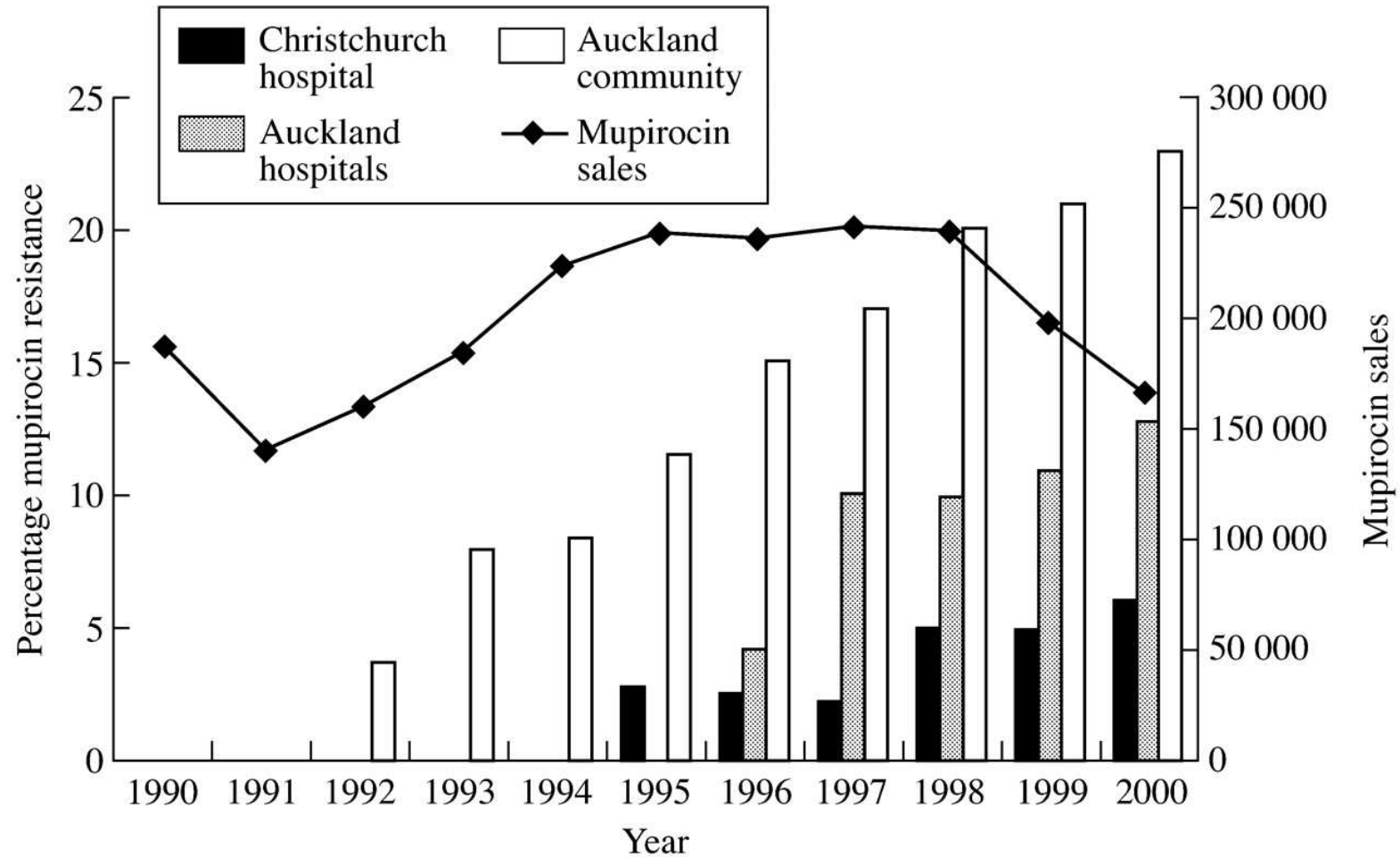
Observed increase in resistance is causally associated with increased use of topical fusidic acid

Number of methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) bloodstream isolates and percentage of those isolates that were fusidic acid (FA) resistant in the United Kingdom, 1990-2001.



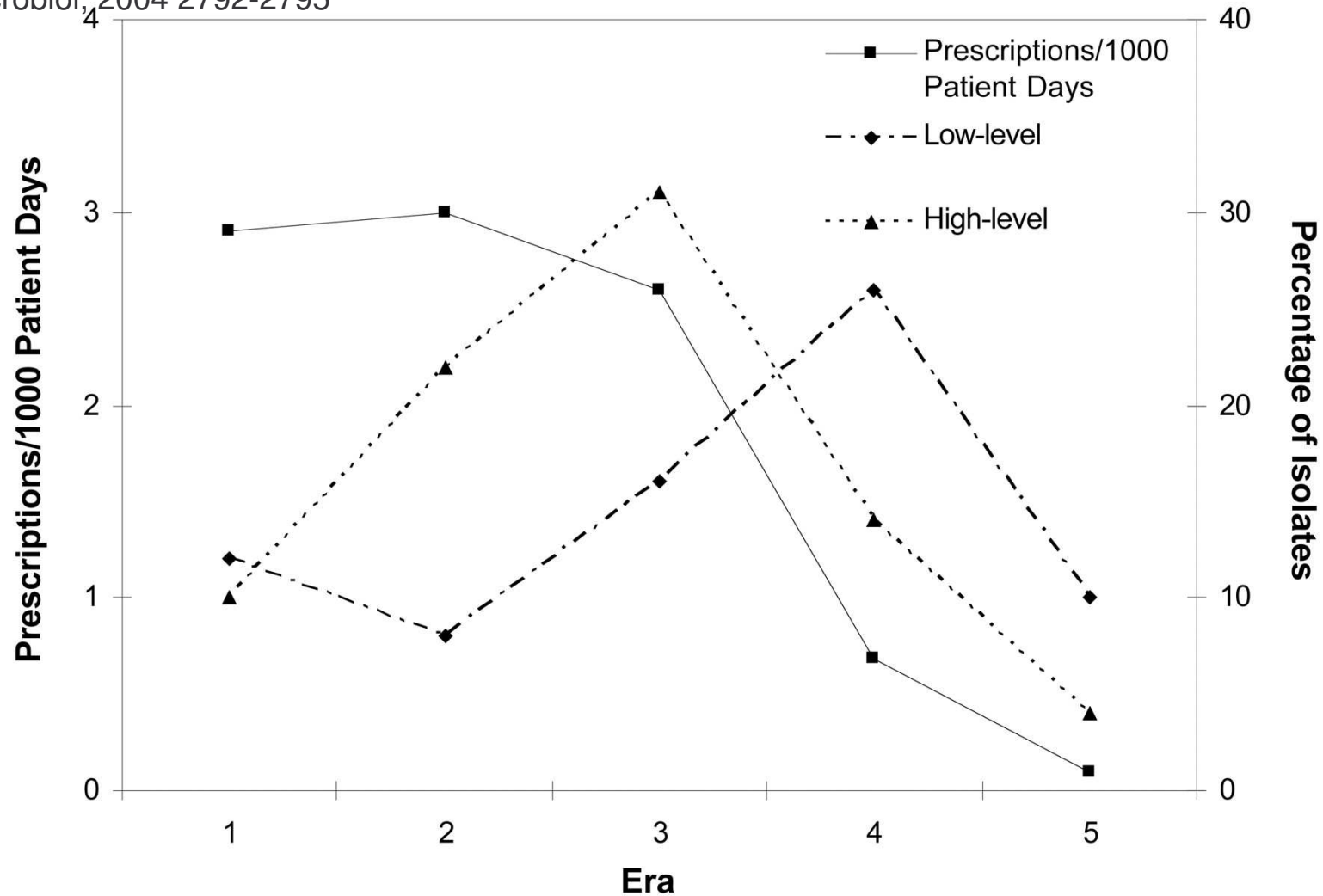
- Use of topical fusidic acid monotherapy for prolonged period should be reconsidered
- Common sense: antibiotics used topically should be the ones that **not** used systemically

Mupirocin resistance among *S. aureus* isolates in hospital and community laboratories and units of mupirocin sold



Number of mupirocin prescriptions per 1,000 patients/d and % of isolates showing mupirocin resistance per era

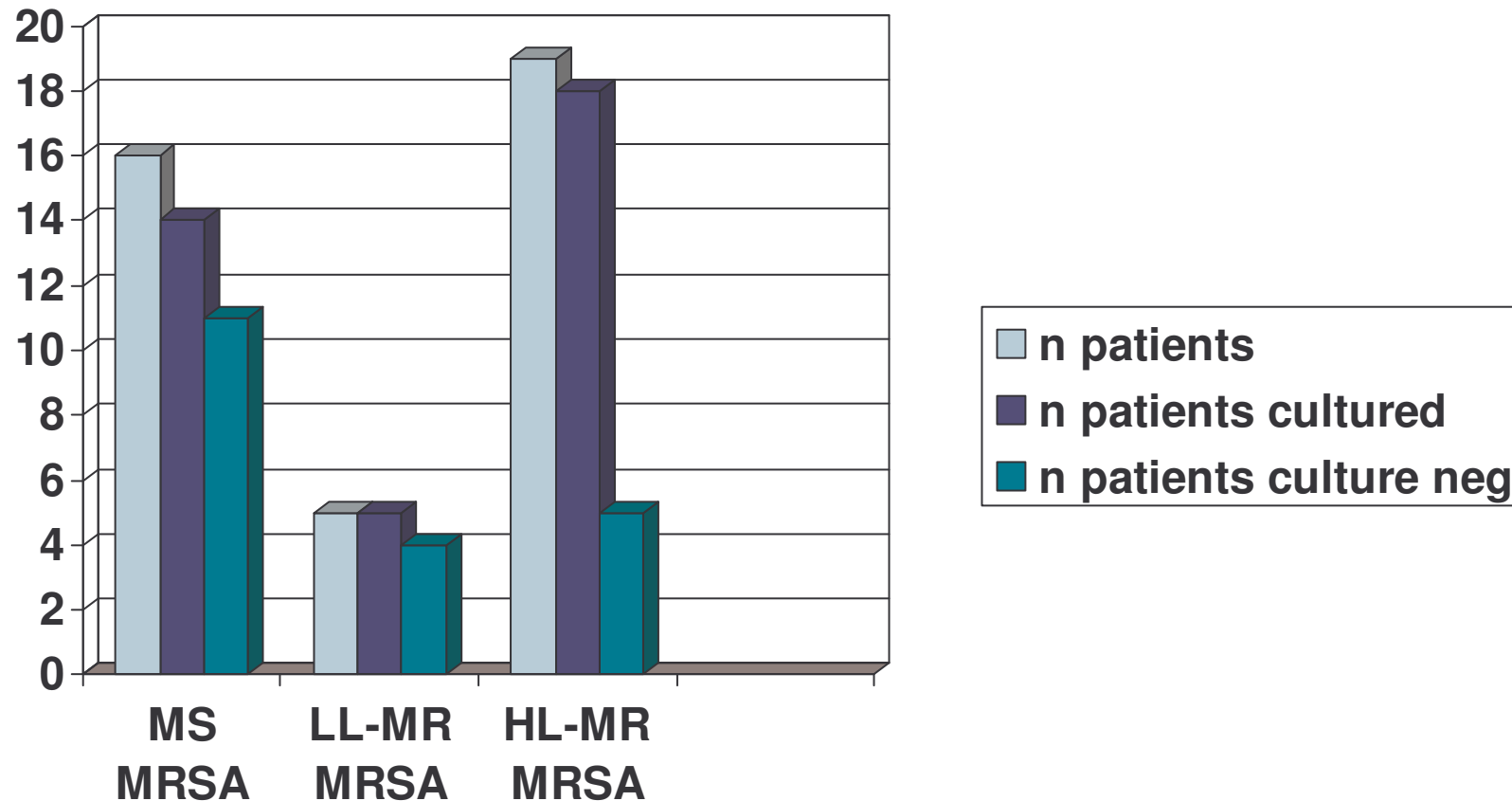
J Clin Microbiol, 2004 2792-2795



Era 1, introduction of mupirocin; era 2, unrestricted use; era 3, judicious use recommended; eras 4 and 5: early and later periods of administrative control.

Clearance of MRSA by post treatment day 3 according to mupirocin susceptibility

Infect Control Hosp Epidemiol 2003;24:342-346



Mupirocin was effective in eradicating MS MRSA, but strains of MR MRSA often persisted after treatment.

- Rise in mupirocin resistance among *S. aureus* is associated with high mupirocin consumption
- Mupirocin use has to be restricted to eradication of MRSA

Topical antibiotics in chronic skin wounds

- Published guidelines do not recommend the use of topical AB
- Chronic wounds patients represent a high risk group for the acquisition, the carriage and dissemination of antibiotic resistant organisms

Epilogue: what to consider before prescribing topical antibiotics?

Pro

- Proved efficacy
- High local concentration
- No systemic effects
- Low selective pressure
- Mupirocin and fusidic acid are the more effective (GPB)

Contra

- Comparable efficacy of benzoyl peroxide (acne)
- Highly variable local concentration
- Resistance selection
- Cells toxicity
- No reliable *in vitro* susceptibility tests
- Slow bacterial growth *in vivo*
- Sensitization
- Costs

recommendations

- Limit topical antibiotic use to strictly documented indications
- Limit duration of treatment to acute phase
- Restrain use of mupirocin
- Substitute antiseptic to antibiotic when feasible
- Substitute saline to antiseptic when feasible.....