

Prevalence of antibiotic resistance in CA-RTIs pathogens in adults and children: is it any different?



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<http://www.facm.ucl.ac.be>



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Jeddah, Saudi Arabia, 15 November 2013



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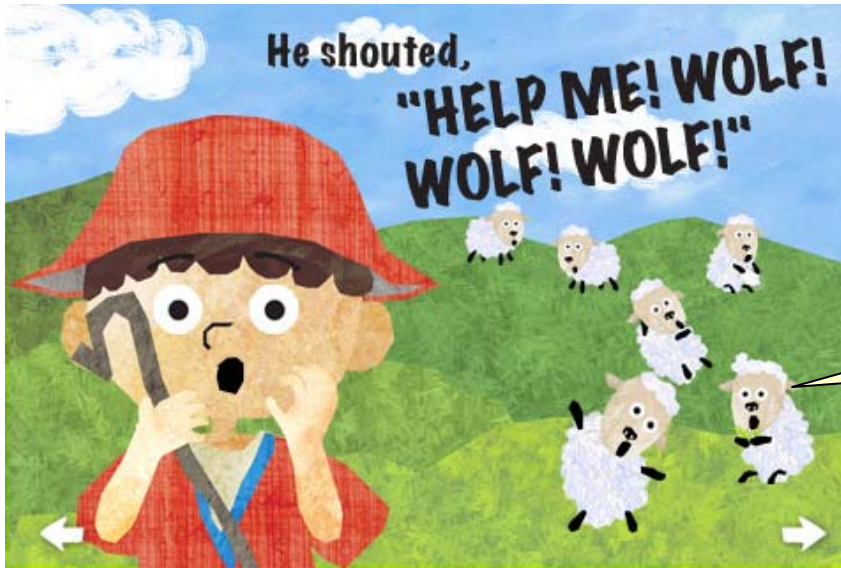
Disclosures

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- the Belgian *Fonds de la Recherche Scientifique* for basic research on pharmacology antibiotics and related topics
- *Université catholique de Louvain* for personal support
- Commercial Relationships:
 - AstraZeneca, GSK, Sanofi-Aventis, Bayer HealthCare, Cempra Pharmaceuticals, The Medicines Company, Northern Antibiotics...
- Other relationships in relation to this talk
 - Belgian Antibiotic Policy Coordination Committee,
 - Belgian Transparency and Reimbursement Committees
 - Participation to EMA expert meetings for novel antibiotics and as Industry supporting expert for assessment of toxicity of older ones

Slides are available at <http://www.facm.ucl.ac.be> → Lectures

Are we taking children seriously ?



For this ?

Or for that ?



Children are high antibiotic consumers ... but also need attention...

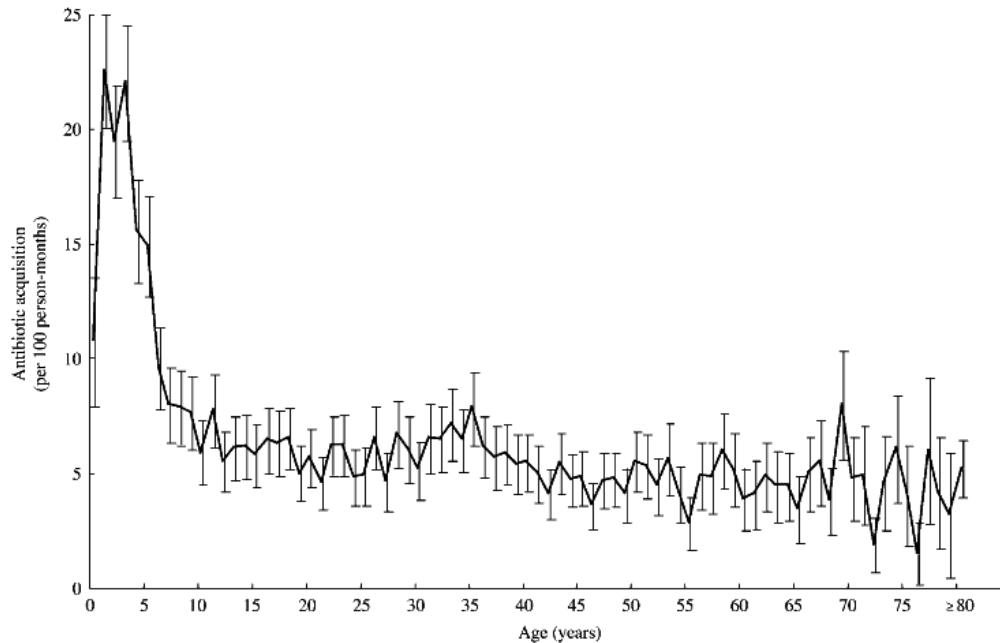


Figure 1. Frequency of antibiotic acquisition according to age (per 100 person-months, with 95% confidence intervals).

Sommet *et al.* Journal of Antimicrobial Chemotherapy (2004) 54, 524–528

Children are high antibiotic consumers ... but also need attention...

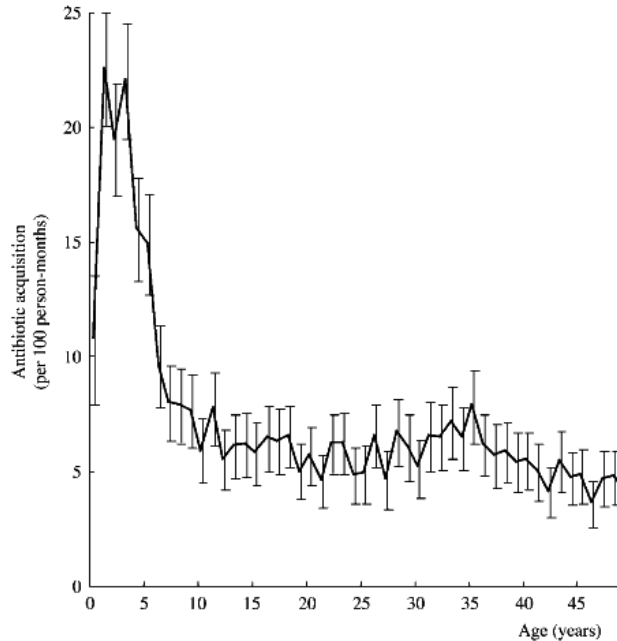


Figure 1. Frequency of antibiotic acquisition according to age (per 100 person-months)

Sommet *et al.* Journal of Antimicrobial Chemotherapy (2012)

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But what do we know specifically about resistance in children for respiratory pathogens ?

International Journal of Antimicrobial Agents 42 (2013) 395–402



Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: <http://www.elsevier.com/locate/ijantimicag>



Capsular serotypes and antimicrobial susceptibilities of *Streptococcus pneumoniae* causing invasive pneumococcal disease from 2009–2012 with an emphasis on serotype 19A in bacteraemic pneumonia and empyema and β -lactam resistance



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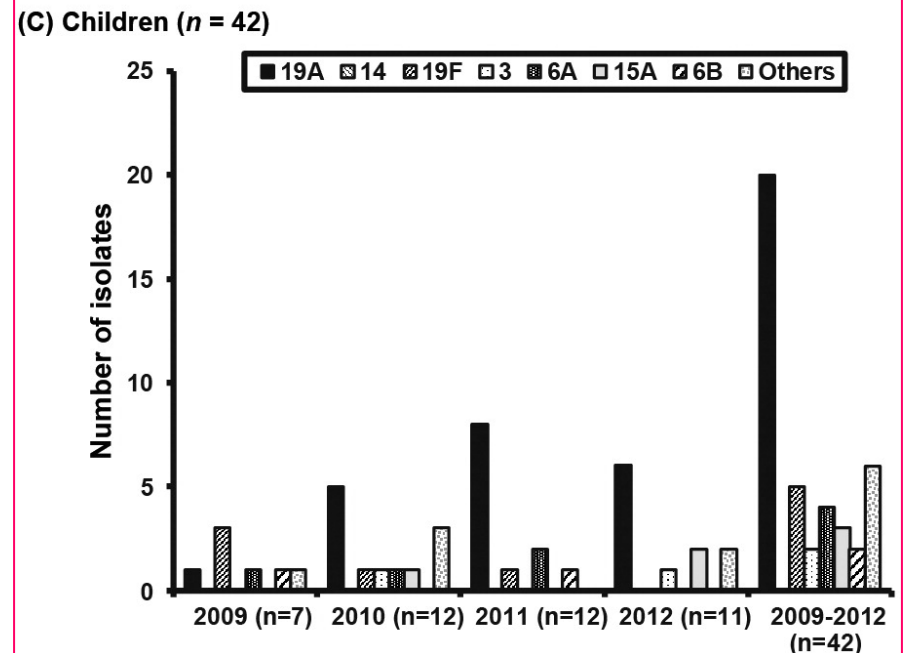
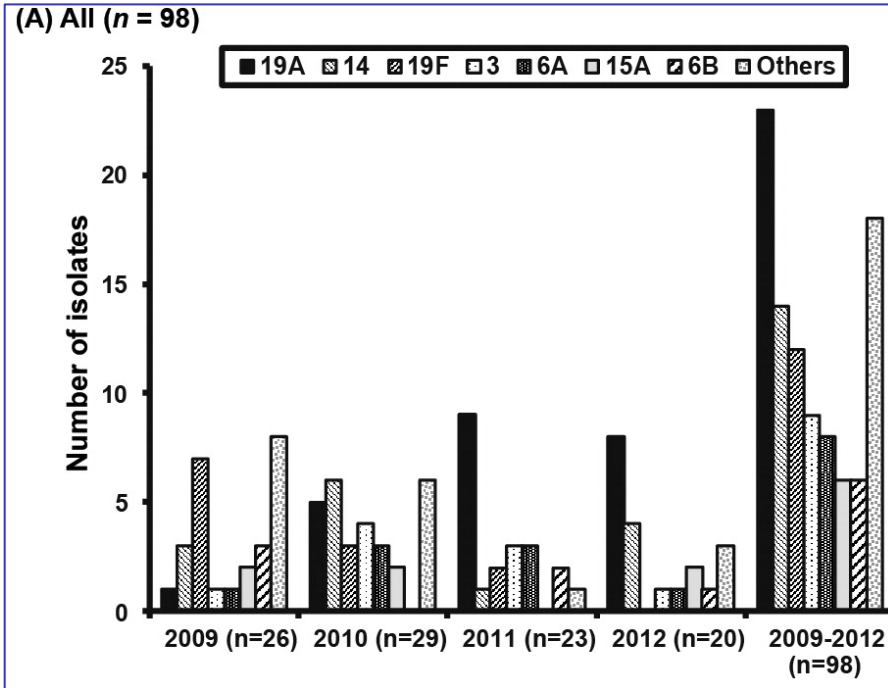
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Capsular serotypes can be very different ...



Lee et al. Int J Antimicrob Agents. 2013; 42:395-402

And so is resistance ...

Antibiotic	% susceptible *	
	Adults (n=98)	Children (n=42)
Penicillin (oral)	20.4	7.1
Ceftriaxone (non meningitis)	86.2	70.0
azithromycin	9.2	2.4

* CLSI breakpoints

But this was actually known since long ...



International Journal of Antimicrobial Agents 20 (2002) 412–418

Age-related trends in pathogen frequency and antimicrobial susceptibility of bloodstream isolates in North America SENTRY Antimicrobial Surveillance Program, 1997–2000

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^c *The Jones Group/JMI Laboratories, North Liberty, Iowa, and the Tufts University School of Medicine, Boston, MA, USA*

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Diekema et al. Int. J. Antimicrob. Agents 2002; 412–418

SENTRY * programme 1997-2000 ...

Table 2
Antimicrobial susceptibility of all bloodstream isolates by age group, SENTRY 1997–2000

Organism	Antimicrobial	% Susceptible (number tested)						Overall
		< 1 year	1–5 years	6–18 years	19–49 years	50–64 years	> 64 years	
<i>S. aureus</i>	Oxacillin	80 ^a (223)	85 ^b (89)	87 (229)	74 (2181)	73 (1580)	65 (2200)	72 (6502)
Coagulase-negative staphylococci	Oxacillin	19 ^a (400)	23 (99)	25 (122)	30 (947)	25 (661)	27 (1019)	26 (3248)
<i>Enterococcus</i> spp.	Vancomycin	100 (167)	90 (62)	87 (47)	86 (724)	83 (645)	85 (980)	86 (2625)
<i>S. pneumoniae</i>	Penicillin	62 ^a (66)	64 ^a (127)	73 (45)	77 (431)	78 (235)	75 (367)	74 (1271)
	Levofloxacin	100 (52)	100 (93)	100 (36)	100 (320)	99 (161)	99 (264)	> 99 (926)
<i>E. coli</i>	Ceftazidime	100 (193)	98 (41)	98 (100)	99 (1210)	99 (904)	99 (2013)	99 (4461)
	Cefepime	100 (193)	100 (41)	100 (100)	99 (1210)	99 (904)	99 (2012)	> 99 (4460)
	Ciprofloxacin	99 (192)	100 (41)	98 (100)	97 (1210)	96 (904)	97 (2012)	97 (4459)
<i>Klebsiella</i> spp.	Ceftazidime	98 (94)	95 (39)	89 (46)	96 (520)	96 (489)	97 (718)	96 (1906)
	Cefepime	100 (94)	97 (39)	96 (46)	99 (520)	99 (489)	99 (718)	99 (1906)
<i>P. aeruginosa</i>	Ceftazidime	83 (48)	90 (29)	85 (40)	81 (302)	88 (281)	87 (412)	85 (1112)
	Cefepime	94 (48)	97 (29)	83 (40)	84 (302)	90 (281)	89 (412)	88 (1112)
	Imipenem	96 (48)	83 (29)	93 (40)	89 (302)	90 (281)	94 (412)	90 (1112)
	Ciprofloxacin	100 (48)	97 (29)	95 (40)	81 (302)	87 (281)	86 (412)	86 (1112)
<i>Enterobacter</i> spp.	Ceftazidime	72 (90)	74 (31)	75 (40)	82 (305)	72 (208)	79 (243)	77 (917)
	Cefepime	100 (90)	97 (31)	98 (40)	99 (305)	100 (208)	99 (243)	> 99 (917)

^a $P < 0.01$ for MIC distribution compared to 19–49, 50–64 and > 64 years age groups for same organism.

^b $P = 0.005$ for MIC distribution compared to > 64 years age group for same organism.

* longitudinal surveillance program designed to track antimicrobial resistance trends nationally and internationally over a 5- to 10-year period and sponsored by Bristol-Myers Squibb

Diekema et al. Int. J. Antimicrob. Agents 2002; 412-418

PROTEKT * programme 1997-2000 ...

International Journal of Infectious Diseases (2005) 9, 262–273



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<http://intl.elsevierhealth.com/journals/ijid>

Demographic analysis of antimicrobial resistance among *Streptococcus pneumoniae*: worldwide results from PROTEKT 1999–2000[☆]

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Corresponding Editor: Richard Oberhelman, New Orleans, USA

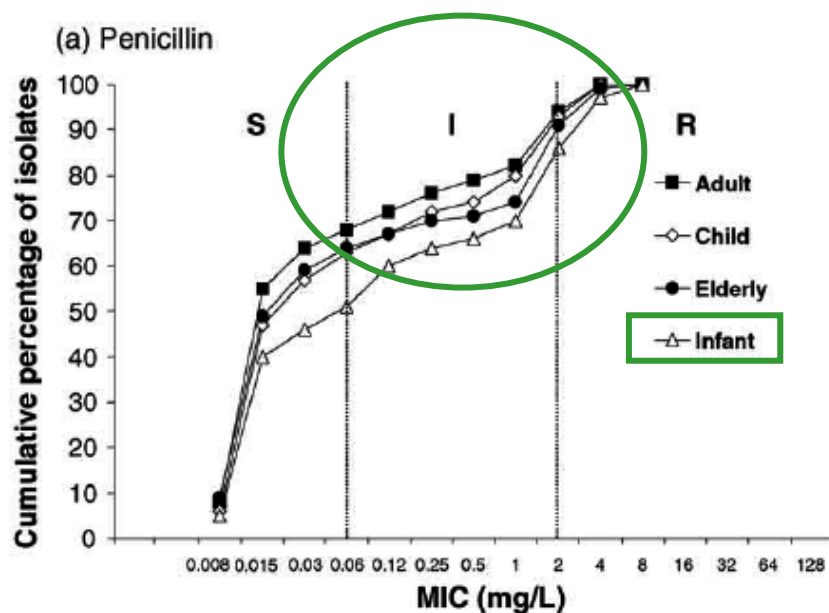
* Prospective Resistant Organism Tracking and Epidemiology for the Ketolide Telithromycin (sponsored by Aventis)

Hoban et al. Int. J. Infect. Dis. 2005; 262-273

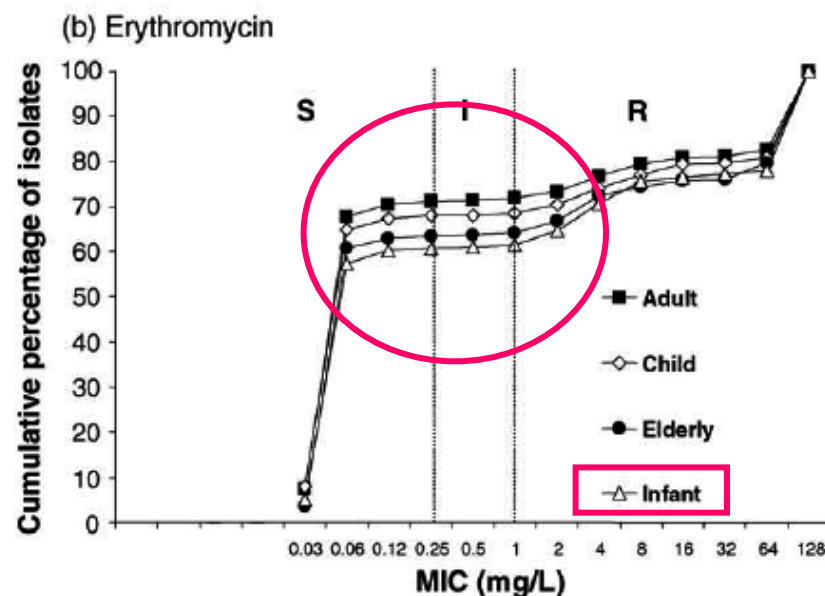
PROTEKT * programme 1997-2000 ...

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D. Hoban et al.



Intermediates are most affected
→ dosage adjustment !



Intermediate and full resistant affected
→ dosage readjustment will not work !

* Prospective Resistant Organism Tracking and Epidemiology for the Ketolide Telithromycin
(sponsored by Aventis)

Hoban et al. Int. J. Infect. Dis. 2005; 262-273

And since then (some examples) ...



International Journal of Antimicrobial Agents 23 (2004) 32–38

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Streptococcus pneumoniae in Saudi Arabia: antibiotic resistance and serotypes of recent clinical isolates

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Received 7 February 2003; accepted 8 May 2003

Memish et al. Int J Antimicrob Agents.
2004;23:32-8.

154 clinical *Streptococcus pneumoniae* isolates collected from or through three major hospitals serving the Western, Central, and Eastern regions of the Kingdom of Saudi Arabia.

And since then (some examples) ...



International Journal of Antimicrobial Agents 23 (2004) 32–38

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Streptococcus pneumoniae in Saudi Arabia: antibiotic resistance and serotypes of recent clinical isolates

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154 clinical *Streptococcus pneumoniae* isolates collected from or through three major hospitals serving the Western, Central, and Eastern regions of the Kingdom of Saudi Arabia.

Table 1
Susceptibility of *Streptococcus pneumoniae* isolates by age.

Demographics	Number of isolates	Resistance to penicillin	%
Age (year)			
<10	6	5	83.3
10–19	40	30	75.0
20–29	38	18	47.4
30–39	22	11	50.0
40–49	24	13	54.2
50–59	9	5	55.6
60+	15	9	60.0

And since then (some examples) ...

Rev Esp Quimioterap, Diciembre 2007; Vol. 20 (Nº 4): 421-428
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Original

Enfermedad invasiva por *Streptococcus pneumoniae*: serotipos y sensibilidad a los antimicrobianos en un Área Sanitaria de Galicia



F. Pardo Sánchez, M.L. Pérez del Molino Bernal, P.A. Romero Jung, L. Martínez Lamas y B. Regueiro García

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Travesía da Choupana s/n, 15706 Santiago de Compostela

Sanchez et al. Rev. Esp. Quimioter. 2007; 20:421-428

Tabla 2. Actividad *in vitro* de antibióticos frente a aislamientos de *S. pneumoniae*.

Antibiótico	Rango CMI (mg/l)	CMI ₉₀ (mg/l)	Niños (N=50)			Adultos (N=168)		
			S N (%)	I N (%)	R N (%)	S N (%)	I N (%)	R N (%)
Penicilina	0,015-2	1	40 (80)	9 (18)	1 (2)	140 (83,3)	26 (15,4)	2 (1,19)
Eritromicina	0,06->128	>128	31 (62)	1 (2)	18 (36)	134 (79,76)	–	34 (20,23)
Cloranfenicol	1-32	4	49 (98)	–	1 (2)	162 (96,42)	–	6 (3,57)
Tetraciclina	0,12-64	64	37 (74)	1 (2)	12 (24)	143 (85,1)	1 (0,59)	24 (14,28)



And since then (some examples) ...

An 8-Year Evaluation of Antibiotic Consumption and Antibiotic Resistance Among *Streptococcus pneumoniae* from In- and Out-Patients in Szeged, Hungary

E. HAJDU¹ - M. MATUZ² - R. BENKO² - A. ORDAS¹ - E. NAGY¹

¹ Institute of Clinical Microbiology, Faculty of Medicine,

² Department of Clinical Pharmacy, Faculty of Pharmacy, University of Szeged, Hungary.

Correspondence: Dr. Erzsebet Nagy, nagy@mlab.szote.u-szeged.hu



Hajdu et al. Hungary. J Chemother. 2007; 19:519-527

Prevalence of erythromycin-resistant *S. pneumoniae* isolates in two different periods.

	Age group	No. of <i>S. pneumoniae</i> isolates		Erythromycin-resistant No. of isolates (%)	
		Period I	Period II	Period I	Period II
In-patients	0-2	158	335	75 (47)	177 (53)
	3-14	193	297	98 (51)	126 (42)
	15-65	85	103	19 (22)	30 (29)
	>65	41	55	11 (27)	11 (20)
All	477	790	203 (43)	344(43)	0.770
Out-patients	0-2	115	373	62 (54)	170 (46)
	3-14	181	545	68 (38)	226 (41)
	15-65	84	92	17 (20)	28 (29)
	>65	4	9	2 (0)	3 (0)
All	384	1019	149/39	427 (42)	0.301

*FD: few data

Period I: 1998-2001
Period II: 2002-2005

And since then (some examples) ...



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Diagnostic Microbiology and Infectious Disease 65 (2009) 49–57

Antimicrobial Susceptibility Studies

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Emergence of *Streptococcus pneumoniae* of serotype 19A in France:
molecular capsular serotyping, antimicrobial susceptibilities,
and epidemiology

Laurent Dortet^a, Marie-Cécile Ploy^b, Claire Poyart^a, Josette Raymond^{a,*}

The members of the ORP Ile de France Ouest¹

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^bCentre Hospitalo-universitaire, Limoges, France

Received 13 February 2009; accepted 11 May 2009

Dortet et al. Diagn. Microbiol.
Infect. Dis. 2009; 65:49-57

And since then (some examples) ...



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Diagnostic Microbiology and Infectious Disease 65 (2009) 49–57

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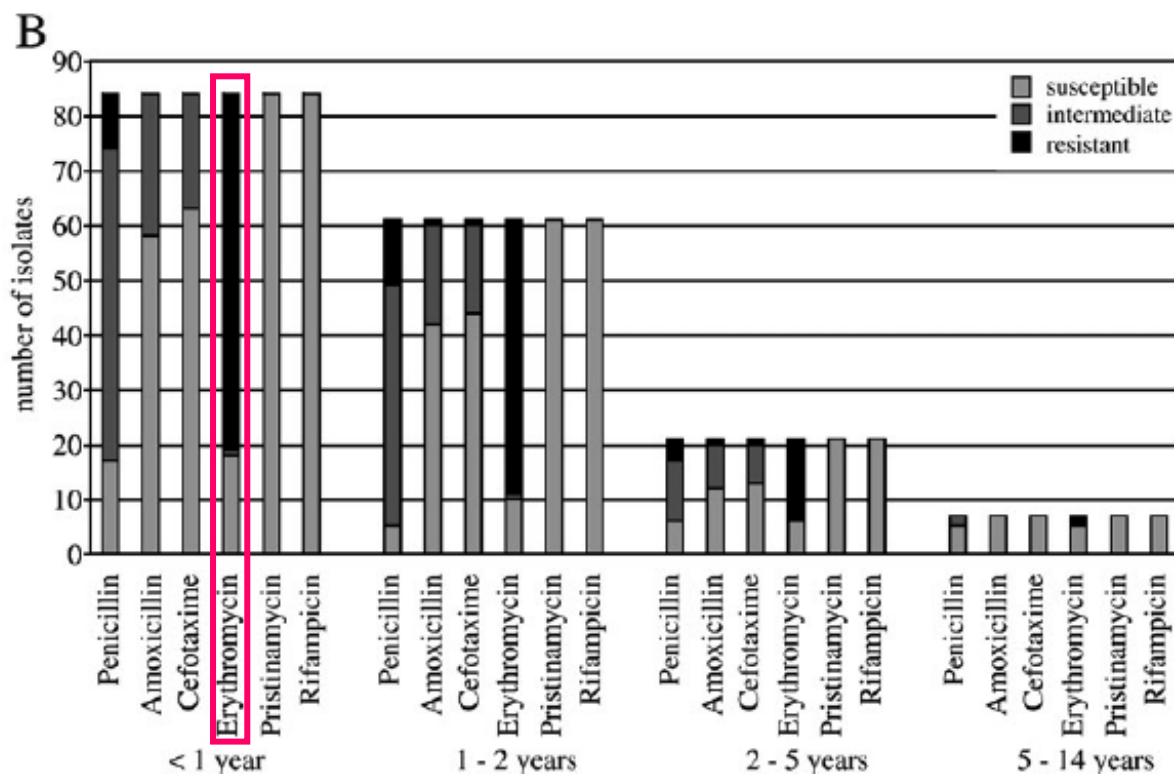
^aFaculté de Médecine, Paris-5-René Descartes, Service de Bact

^bCentre Hospitalo-univer

Received 13 February 200

Dortet et al. Diagn. Microbiol.
Infect. Dis. 2009; 65:49-57

Susceptibilities of *S. pneumoniae* isolated from acute otitis media in different children groups (younger than 1 year, 1–2 years old, 2–5 years, and 5–14 years).



Beware of the serotype !

Table 3

Serotype/serogroup-specific penicillin and erythromycin resistance

Serotype/ serogroup	No. of isolates	Penicillin- nonsusceptible isolates ^a		Erythromycin- resistant isolates ^a	
		<i>n</i>	%	<i>n</i>	%
1	28	0	0.0	0	0.0
3	37	0	0.0	0	0.0
4	9	0	0.0	0	0.0
5	6	2	33.3	2	33.3
6	25	11	44.0	9	36.0
7C	2	0	0.0	0	0.0
7F	21	0	0.0	0	0.0
8	10	1	10.0	1	10.0
9	24	11	45.8	12	50.0
10	2	0	0.0	0	0.0
11	8	0	0.0	0	0.0
14	21	17	81.0	15	71.4
15	19	11	57.9	9	47.4
17	1	0	0.0	0	0.0
18	8	1	12.5	1	12.5
19A	157	152	96.8	150	95.5
19F	18	17	94.4	15	83.3
20	2	0	0.0	0	0.0
22	4	0	0.0	0	0.0
23	24	8	33.3	6	25.0
24	6	2	33.3	1	16.7
29	1	1	100.0	0	0.0
31	1	1	100.0	0	0.0
33	5	1	20.0	4	80.0
35	2	1	50.0	0	0.0
NT	4	2	50.0	2	50.0
Other	12	4	33.3	2	16.7

n = number of nonsusceptible isolates within each serogroup/serotype;
% = percentage nonsusceptible isolates within each serogroup/serotype.

^a The coefficient of correlation between the number of penicillin-nonsusceptible isolates and that of erythromycin-resistant isolates was 0.9993.

Dortet et al. Diagn. Microbiol. Infect. Dis. 2009; 65:49-57

And a last (very recent) example ...



Contents lists available at SciVerse ScienceDirect

Vaccine

Vaccine 30S (2012) G32–G36

journal homepage: www.elsevier.com/locate/vaccine



Review

Antibiotic resistance and serotype distribution of invasive pneumococcal diseases before and after introduction of pneumococcal conjugate vaccine in the Kingdom of Saudi Arabia (KSA)

Atef M. Shibl^{a,c,*}, Ziad A. Memish^{b,c}, Khaled M. Al-Kattan^c

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^b Ministry of Health, Saudi Arabia

^c Alfaisal University College of Medicine, Riyadh, Saudi Arabia

Shibl et al. Vaccine. 2012; 30 Suppl 6:G32-6.

And a last example ...



Contents lists available at SciVerse ScienceDirect

Vaccine

Vaccine 30S (2012) G32-G36

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Review

Antibiotic resistance and serotype distribution of *S. pneumoniae* in children with pneumococcal diseases before and after introduction of pneumococcal conjugate vaccine in the Kingdom of Saudi Arabia (KSA)

Atef M. Shibl^{a,c,*}, Ziad A. Memish^{b,c}, Khaled M. Al-Kattan^c

^a King Saud University, Saudi Arabia

^b Ministry of Health, Saudi Arabia

^c Alfaisal University College of Medicine, Riyadh, Saudi Arabia

Shibl et al. Vaccine. 2012; 30 Suppl 6:G32-G36.

High- and intermediate-level penicillin resistance was defined as minimum inhibitory concentrations (MIC) ≥ 2 g/mL and 0.12–1 g/mL, respectively.

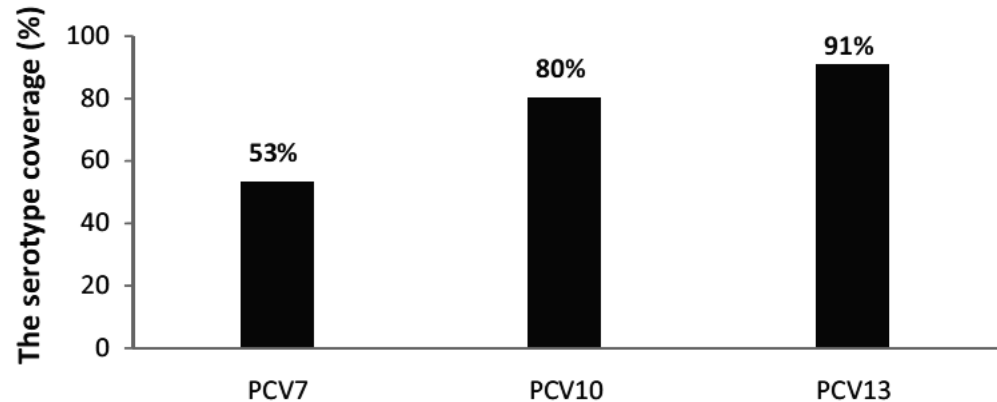


Fig. 3. Antibiotic resistance of *S. pneumoniae* isolates from children ≤ 5 years of age between 2005 and 2009. (Graph includes both intermediate and high-level resistance combined.)

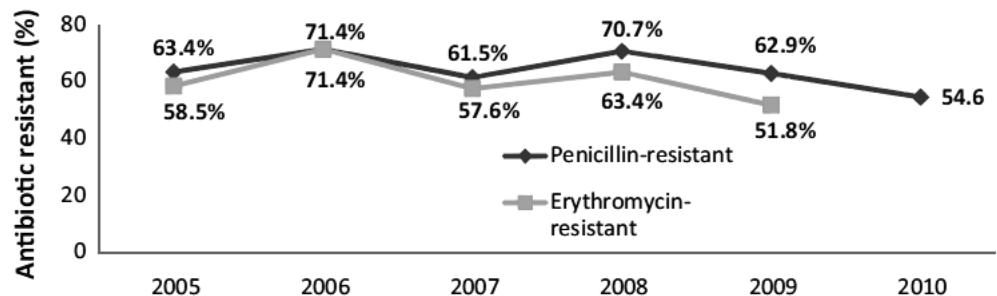


Fig. 4. Antibiotic resistance of *S. pneumoniae* isolates (2010) among children ≤ 5 years of age. (Graph includes by intermediate and high-level resistance combined.)

Towards an age-stratified antibiogram...

Swami and Banerjee *SpringerPlus* 2013, **2**:63
<http://www.springerplus.com/content/2/1/63>

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SHORT REPORT

Open Access

Comparison of hospital-wide and age and location - stratified antibiograms of *S. aureus*, *E. coli*, and *S. pneumoniae*: age- and location-stratified antibiograms

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Swami et al. Springerplus 2013; 2:63

Towards and age-stratified antibiogram

Swami and Banerjee *SpringerPlus* 2013, **2**:63
http://www.springerplus.com/content/2/1/63

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SHORT REPORT

Open Access

Comparison of hospital-wide and age and location - stratified antibiograms of *S. aureus*,

E. coli, and *S. pneumoniae*: location-stratified antibiogram

Sanjeev K Swami¹ and Ritu Banerjee^{2*}

¹Division of Infectious Diseases, Nemours/Alfred I. duPont Children, Wilmington, DE, USA. ²Department of Pediatric Medicine, Mayo Clinic, 200 First Street, SW, Rochester, MN

Swami et al. *Springerplus* 2013; **2**:63

Table 1 Susceptibility of *E. coli*, *S. aureus*, and *S. pneumoniae* isolates by patient age, Mayo Clinic Rochester, MN

	All patients	<18 y	18-64 y	≥65 y	p-value
<i>S. pneumoniae</i>	N = 499	N = 139	N = 203	N = 157	
Penicillin (IV)	98%	97%	98%	99%	0.61
Penicillin (oral)	58%	45%	60%	67%	0.001
Ceftriaxone (non-CNS)	98%	96%	98%	99%	0.101
Ceftriaxone (CNS)	87%	74%	92%	92%	<0.001
Tetracycline	73%	60%	81%	74%	<0.001
Erythromycin	52%	37%	60%	54%	<0.001
Levofloxacin	98%	100%	99%	96%	0.019
TMP-SMX	65%	51%	69%	75%	<0.001

Years (y); ampicillin-sulbactam (AMP-SLB), trimethoprim-sulfamethoxazole (TMP-SMX), intravenous (IV), central nervous system (CNS).

P-value compares differences across all age groups.

Conclusions (and food for thought)

- Differences in susceptibilities of *S. pneumoniae* are common, and often related to differences in serotypes ...
- Global antibiotic susceptibility reports that do not stratify patients according to age obscure these differences, decreasing their value for paediatricians ...
- The reasons for such differences are unclear and, beyond differences in serotypes, may reflect differences in previous exposure to antibiotics (hence the more marked difference for macrolides ?) ...
- Microbiologists should stratify according to age... and test more organisms (*H. influenzae*, *M. catarrhalis*, *Mycoplasma*, ...)
- Clinicians may need to modify their empiric treatments based on correct assessment of true susceptibilities in children...
- ~~Guidelines~~ Guidelines may need revision in this context *.

* Not addressed in this lecture but ask questions...

Please, help the child to grow... and to become adult...

