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

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- 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

Are we taking children seriously ?

For this ?

Or for that ?

Children are high antibiotic consumers … but also need attention…

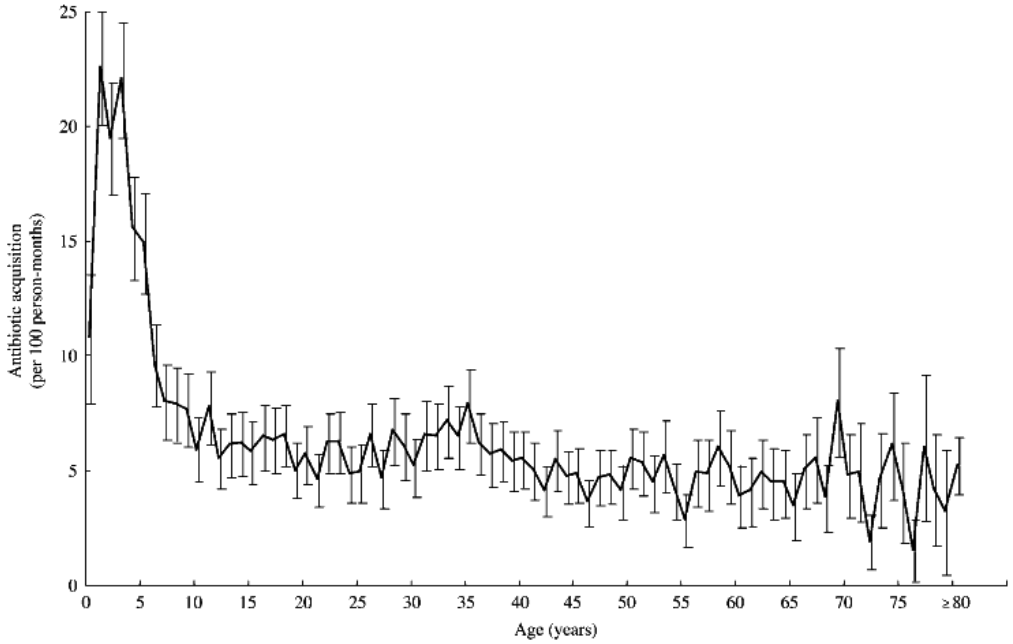

Figure 1. Frequency of antibiotic acquisition according to age (per 100 person-months, with 95% confidence intervals).

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

Children are high antibiotic consumers … but also need attention…

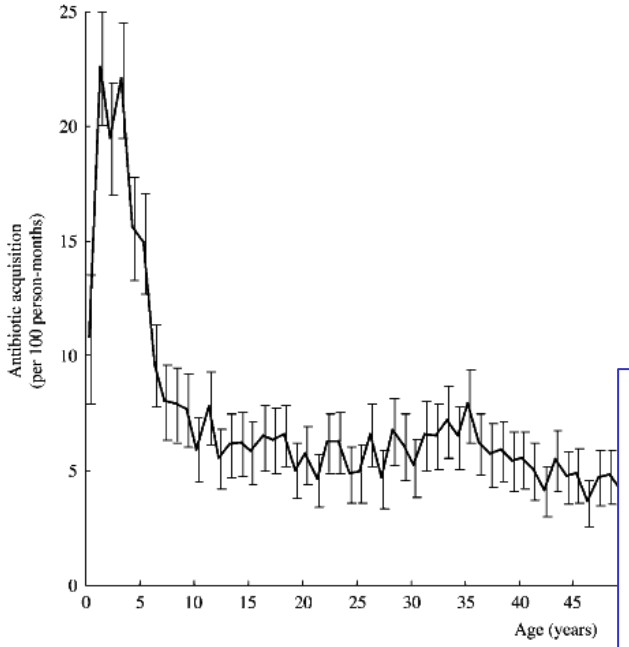

Figure 1. Frequency of antibiotic acquisition according to age (per 100 pe

Sommet *et al.* Journal of Antimicrobial Chemotherapy (

http://www.arpecproject.eu/

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

G Model
ANTAGE-4167; No. of Pages 8

ARTICLE IN PRESS

International Journal of Antimicrobial Agents xxx (2013) xxx–xxx

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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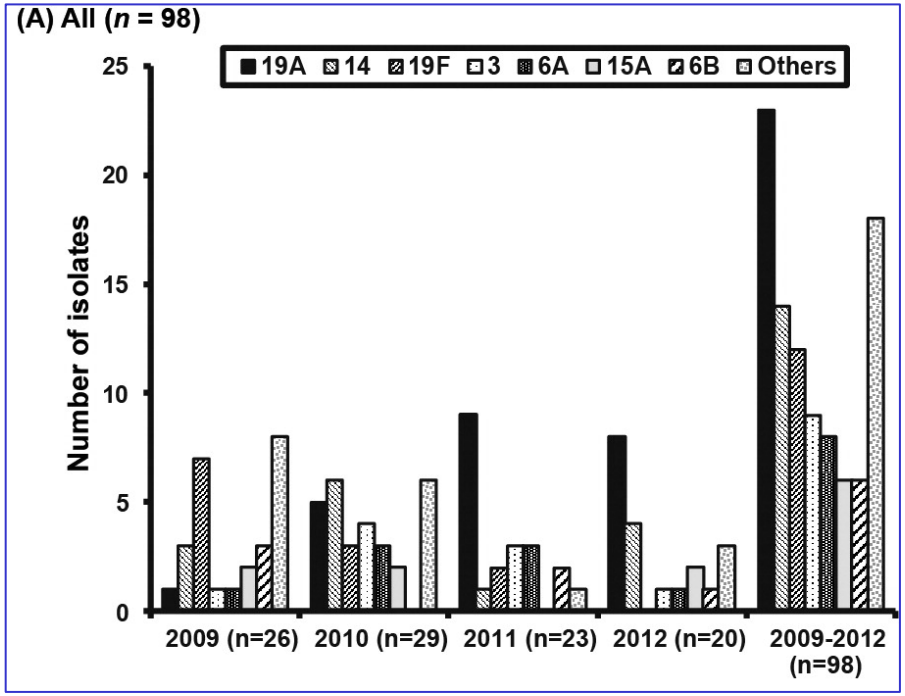
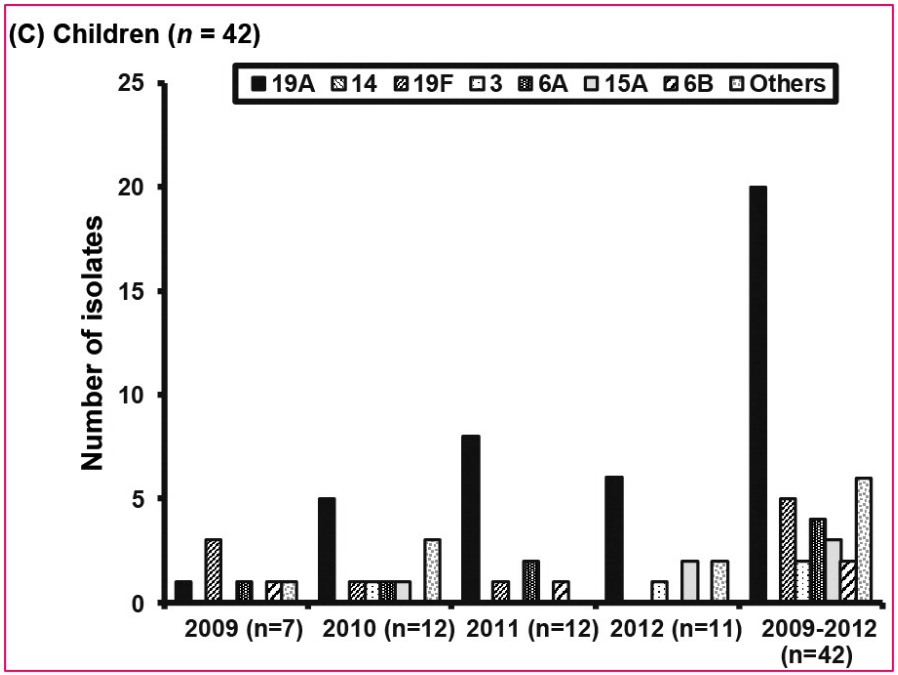
Capsular serotypes can be very different …





Lee et al. Int J Antimicrob Agents. 2013 Sep 6.
doi:10.1016/j.ijantimicag.2013.07.017

And so is resistance …

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

* CLSI breakpoints

Lee et al. Int J Antimicrob Agents. 2013 Sep 6.
doi:10.1016/j.ijantimicag.2013.07.017

But this was actually known since long …

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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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Received 17 January 2002; accepted 25 April 2002

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)						
		< 1 year	1–5 years	6–18 years	19–49 years	50–64 years	> 64 years	Overall
S. aureus	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)
Enterococcus spp.	Vancomycin	100 (167)	90 (62)	87 (47)	86 (724)	83 (645)	85 (980)	86 (2625)
S. pneumoniae	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)
E. coli	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)
Klebsiella 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)
P. aeruginosa	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)
Enterobacter 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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INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

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

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

Daryl Hoban [a,*], Fernando Baquero [b], Vaughan Reed [c], David Felmingham [d]

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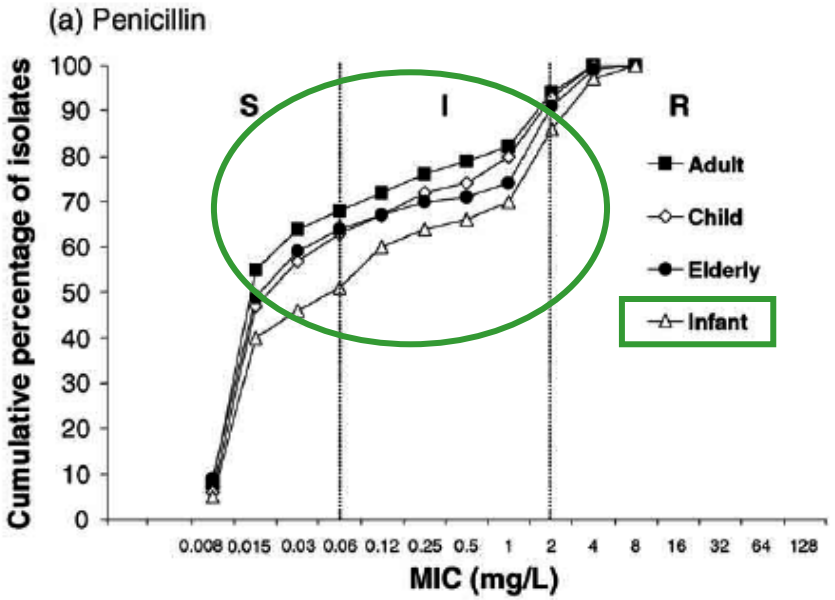
[d] *GR Micro Ltd, London, UK*

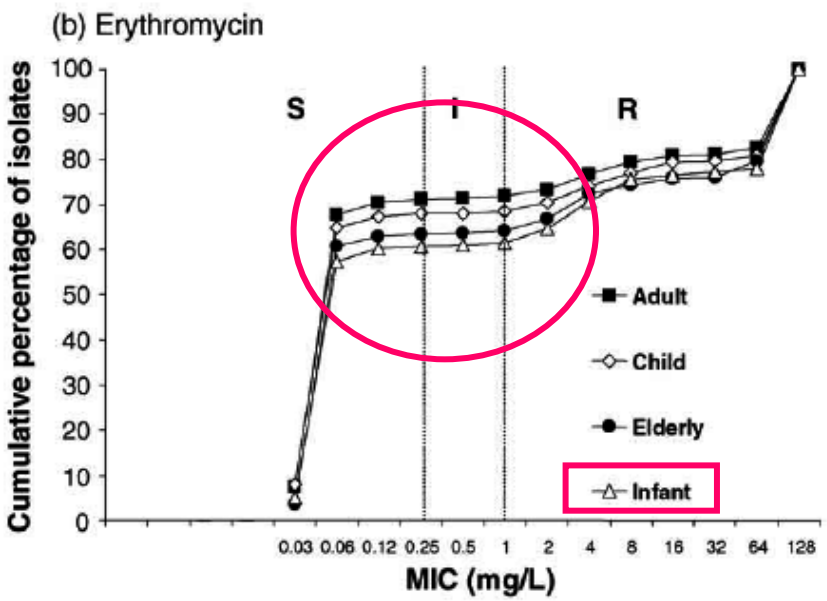
Received 15 December 2003; received in revised form 7 July 2004; accepted 7 July 2004
Corresponding Editor: Richard Oberhelman, New Orleans, USA

* 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 …





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) …

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

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

Servicio de Microbiología, Hospital Clínico Universitario de Santiago de Compostela, 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*.

			Niños (N=50)			Adultos (N=168)		
Antibiótico	Rango CMI (mg/l)	CMI_{90} (mg/l)	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) …

Journal of Chemotherapy Vol. 19 - n. 5 (519-527) - 2007

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

E. HAJDU [1] - M. MATUZ [2] - R. BENKO [2] - A. ORDAS [1] - E. NAGY [1]

[1] Institute of Clinical Microbiology, Faculty of Medicine,
[2] Department of Clinical Pharmacy, Faculty of Pharmacy, University of Szeged, Hungary.
Correspondence: Dr. Erzsebet Nagy, nagye@mlab.szote.u-szeged.hu

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

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

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

	Age group	No. of *S. pneumoniae* isolates Period I	Period II	Erythromycin-resistant No. of isolates (%) 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

And since then (some examples) …

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Available online at www.sciencedirect.com
ScienceDirect
Diagnostic Microbiology and Infectious Disease 65 (2009) 49–57

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE
www.elsevier.com/locate/diagmicrobio

Antimicrobial Susceptibility Studies

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 Ouest[1]

[a]*Faculté de Médecine, Paris-5-René Descartes, Service de Bactériologie, Hôpital Cochin-Saint Vincent de Paul, Paris, France*
[b]*Centre 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

DIAGNOSTIC MICROBIOLOGY AND INFECTIOUS DISEASE

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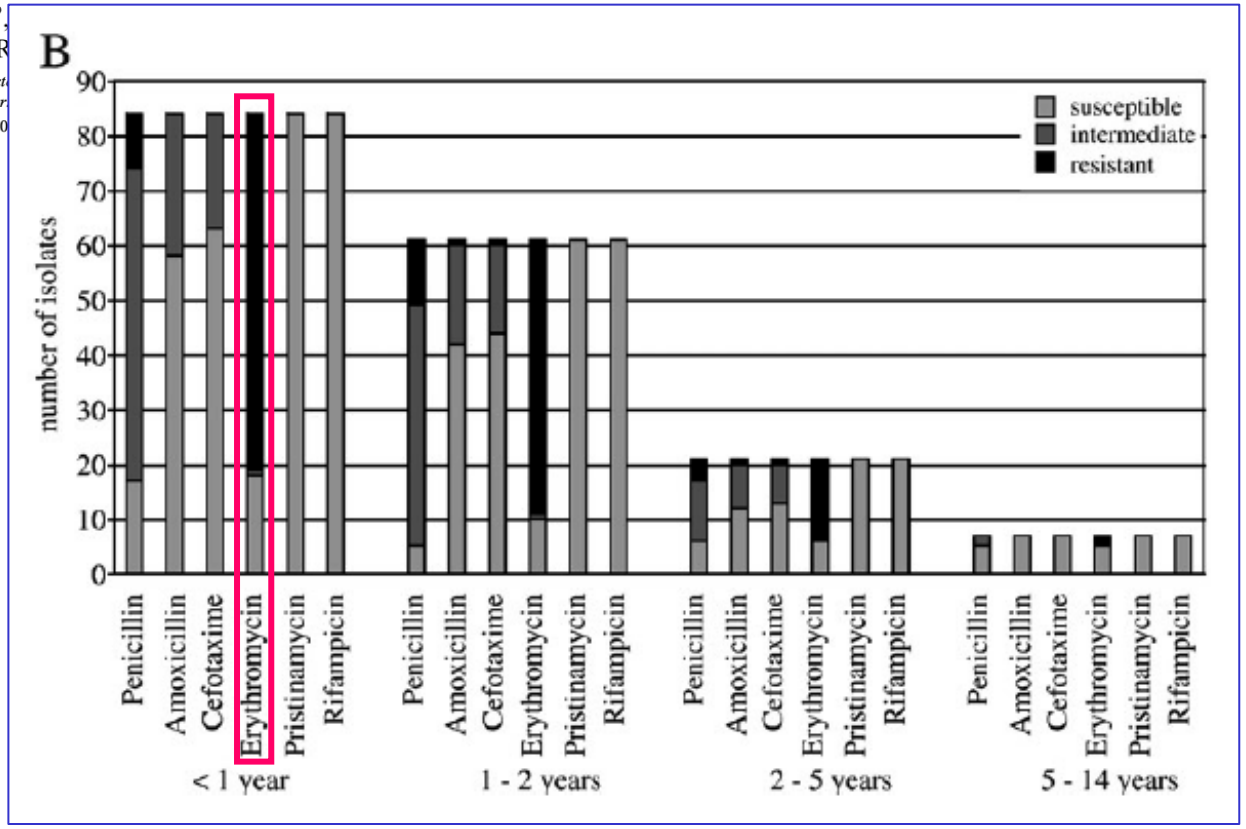
Received 13 February 200



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]	
		n	%	*n*	%
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 example …

Pathologie Biologie 58 (2010) 147–151

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Disponible en ligne sur ScienceDirect www.sciencedirect.com

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10th Survey of antimicrobial resistance in noninvasive clinical isolates of *Streptococcus pneumoniae* collected in Belgium during winter 2007–2008

Dixième surveillance de la résistance aux antibiotiques dans des souches non invasives de Streptococcus pneumoniae collectionnées en Belgique pendant l'hiver 2007 à 2008

R. Vanhoof [a,*], K. Camps [b], M. Carpentier [c], S. De Craeye [a], J. Frans [d], Y. Glupczynski [e], P. Goffinet [f], B. Gordts [g], D. Govaerts [h], L. Ide [i], P. Lefèvre [j], M. Lontie [k], R. Cartuyvels [l], F. Meunier [m], B. Mulongo [n], I. Philippart [o], I. Surmont [p], E. Van Bossuyt [a], J. Van Eldere [q], J. Verhaegen [q]

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[e] *Clinique universitaire de Mont-Godinne, 5530 Yvoir, Belgium*
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[j] *Hôpital Princesse-Paola, 6900 Marche-en-Famenne, Belgium*
[k] *Medisch Centrum Huisartsen, 3000 Leuven, Belgium*
[l] *Virga-Jessesiekenhuis, 3500 Hasselt, Belgium*
[m] *Hôpital de Jolimont, 7100 Haine St. Paul, Belgium*
[n] *Clinique Saint-Étienne, 1210 Bruxelles, Belgium*
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Vanhoof *et al.* Pathologie Biologie 2010; 147-151

And a last example …

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Vanhoof *et al.* Pathologie Biologie 2010; 147-15

In general, isolates showing resistance to an antibiotic (IR-isolates) were more present in children (36/78, 46.2%) than in adults (132/370; 35.7%) though the difference was not significant.

Resistance to erythromycin was significantly higher in children (42.3%; 33/78) than in adults (27.3%; 101/370) ($0.01 > P > 0.001$).

For tetracycline there was a significant difference between the age group 0–5 year (31.8%; 21/66) and 16–59 year (18.2%; 24/132) ($0.05 > P > 0.02$).

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

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Sanjeev K Swami[1] and Ritu Banerjee[2*]

[1]Division of Infectious Diseases, Nemours/Alfred I. duPo
Children, Wilmington, DE, USA. [2]Department of Pediatr
Medicine, Mayo Clinic, 200 First Street, SW, Rochester, M

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

***Not addressed in this lecture but do ask questions…**

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