

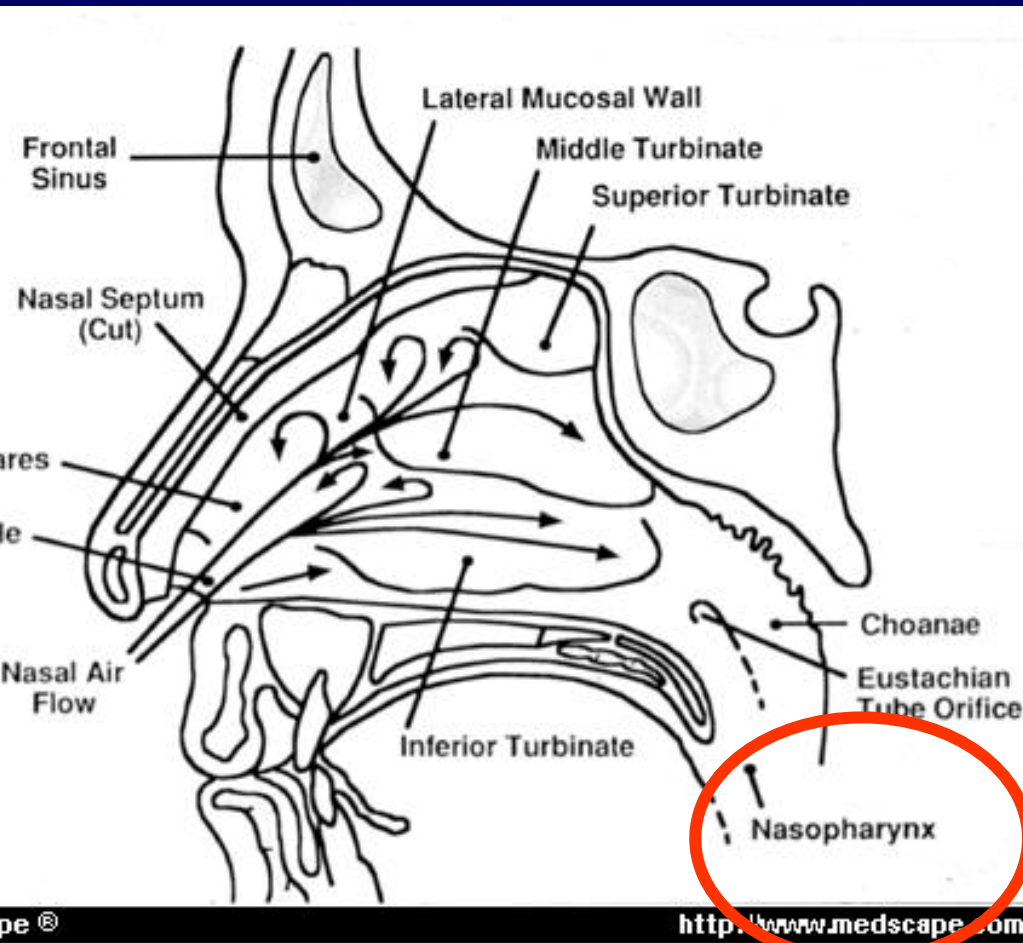
# Le otiti: dal carriage alla malattia

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SIPPS 31 maggio 2008



Il nasofaringe è un serbatoio di germi potenzialmente patogeni

- *S.pneumoniae*
- *H.influenzae*
- *M.catarrhalis*
- *S.pyogenes*
- *Staph aureus*

# sopharyngeal carriage of bacteria in children

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<b>STREP.PNEUMONIAE</b>	<b>20 - 40 %</b>
<b>H.INFLUENZAE</b>	<b>50 - 80 %</b>
<b>M.CATARRHALIS</b>	<b>5 - 30 %</b>
<b>STREP.PYOGENES</b>	<b>15 - 20 %</b>
<b>STAPH.AUREUS</b>	<b>20 - 40 %</b>

from Mandell 1995 and Obaro 1996

# La colonizzazione nasofaringea nel bambino sano



# Acquisition rates of pathogens during the first year of life in a cohort of 306 infants

68% of children colonized with one or more pathogens by 6 months

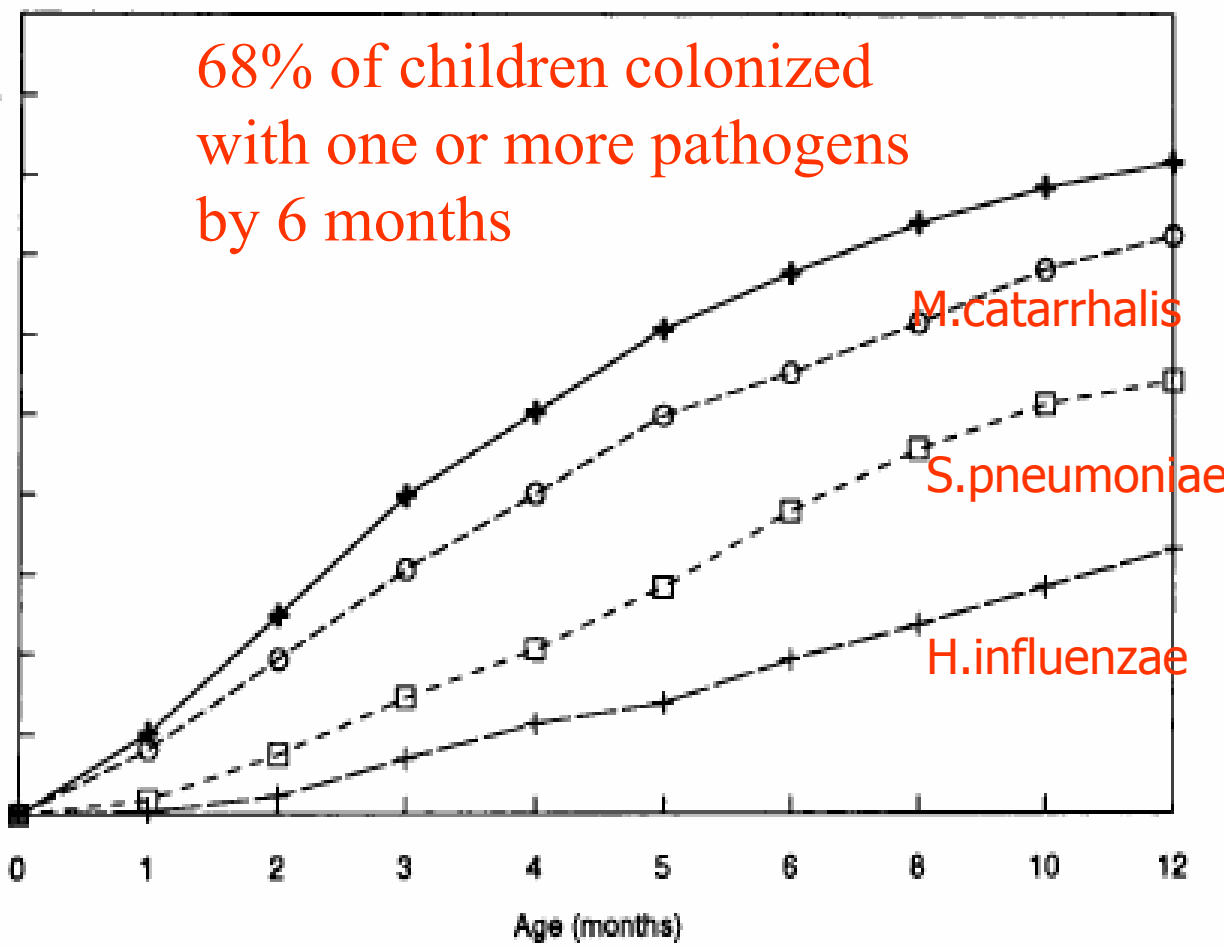
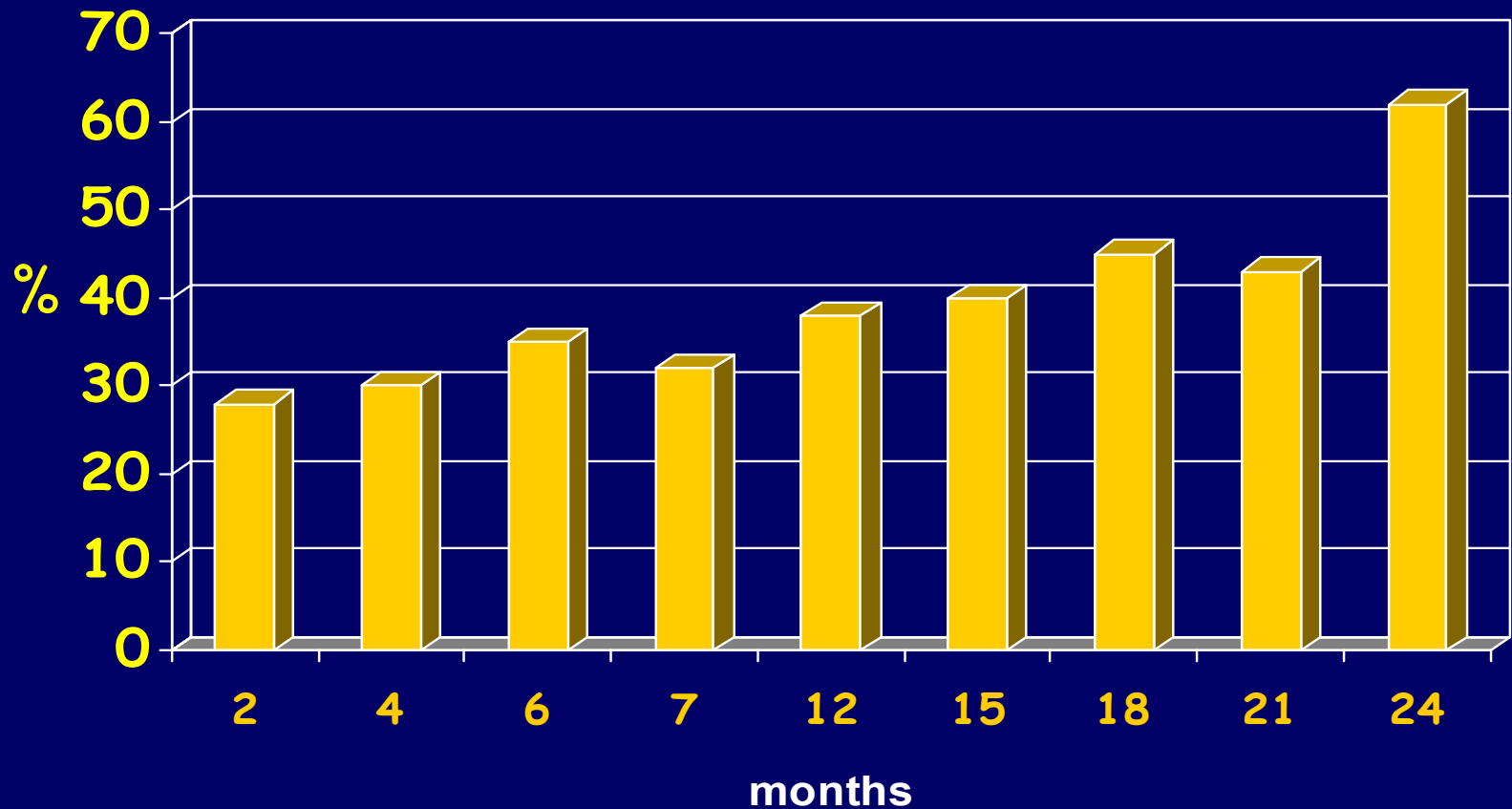


Figure 1. Cumulative acquisition rates of pathogens during first year of life. Top line: any pathogen; mean age,  $4.3 \pm 2.8$  months;  $\circ$ , *M. catarrhalis*; mean age,  $4.8 \pm 2.9$  months;  $\square$ , *S. pneumoniae*; mean age,  $5.7 \pm 2.9$  months;  $+$ , non-typeable *H. influenzae*; mean age,  $3.2$  months.

# nasopharyngeal carriage of *S.Pneumoniae* by age in healthy Israeli children



# Nasopharyngeal carriage of *S.Pneumoniae* by age in 678 healthy Swedish subjects monitored by weekly NP cultures

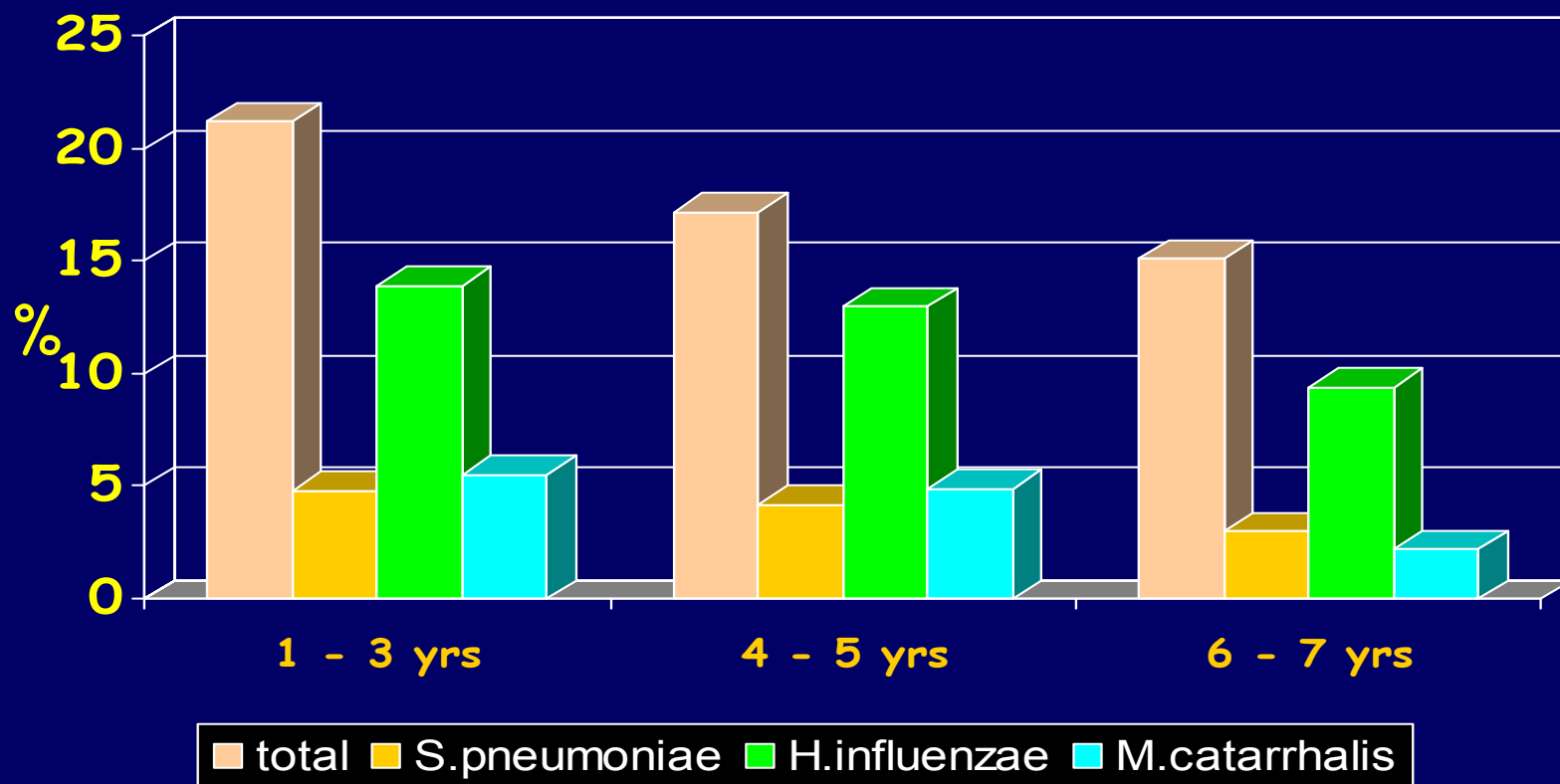
Median duration of carriage of any specific strain  
**19 days**

Longest for children < 1 year (median 30 days)

Shortest for adults (median 14 days)

Disappearance from NP within 12 weeks in 94% of the  
individuals

# Recovery of specific respiratory pathogens in the nasopharynx in 1723 Italian healthy children aged 1 to 7 years



# Risk factors for carriage of respiratory pathogens in the nasopharynx of 1723 Italian healthy children

Incipi et al, PIDJ 1999; 18: 517

Risk Factor	Carriage of One or More Pathogens		Carriage of <i>Streptococcus pneumoniae</i>		Carriage of <i>Haemophilus influenzae</i>		Carriage of <i>Moraxella catarrhalis</i>	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Living in a rural area	1.168	1.037–1.35*	1.04	0.50–2.02	1.033	0.89–1.20	1.186	1.03–1.36*
Presence of older sibling(s)	0.753	0.584–0.971‡	0.416	0.25–0.709§	0.461	0.343–0.621¶	0.773	0.46–1.31
Day-care attendance**	1.224	1.05–1.42	1.035	0.73–1.45	1.026	0.85–1.23	1.037	0.73–1.45
	1.265	1.07–1.45††	1.231	1.10–1.36‡‡	1.366	1.11–1.61§§	1.30	1.11–1.52¶¶

and breast-feeding were not significant variables.

# Influence of child care on nasopharyngeal carriage of *Streptococcus pneumoniae* and *Haemophilus influenzae*

de Boer et al, PIDJ 2003; 22:589

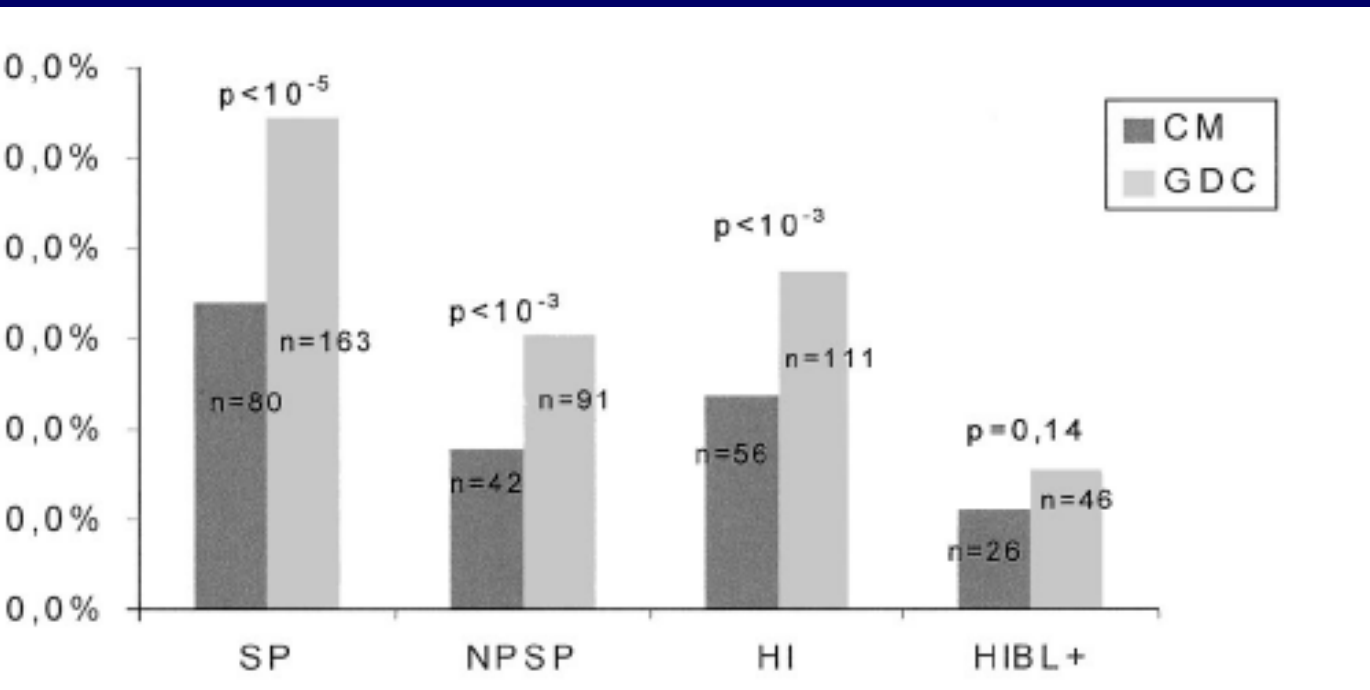


FIG. 1. Comparative prevalence rates for SP, NPSP, Hi and beta-lactamase-positive HI (*HIBL+*) according to type of day care.

CM = child minder for 1 to 2 children

GDC = group day care for 20 up to 100 children

# Seasonal variations in nasopharyngeal carriage of respiratory pathogens in healthy Italian children attending day-care centres or schools

GIULIA MARCHISIO, STEFANIA GIRONI, SUSANNA ESPOSITO, GIAN CARLO SCHITO\*, STEFANIA MANNELLI\*, NICOLA PRINCIPI and the ASCANIUS PROJECT COLLABORATIVE GROUP†

**Table 2.** Nasopharyngeal colonisation of respiratory pathogens in the autumn and spring

Carrier status	Number (%) of children (total = 1580)		p value
	Autumn	Spring	
Carriers of one or more pathogens	309 (19.5)	375 (23.7)	0.004
<i>S. pneumoniae</i>	60 (3.8)	75 (4.7)	0.23
<i>H. influenzae</i>	206 (13.0)	288 (18.2)	<0.0001
<i>M. catarrhalis</i>	71 (4.5)	82 (5.2)	0.40
Carriers of one pathogen	281 (17.8)	310 (19.6)	0.20
<i>S. pneumoniae</i>	47 (2.9)	39 (2.5)	0.44
<i>H. influenzae</i>	185 (11.7)	228 (14.4)	0.02
<i>M. catarrhalis</i>	49 (3.1)	43 (2.7)	0.59
Carriers of two pathogens	28 (1.8)	60 (3.8)	0.0008
<i>S. pneumoniae</i> + <i>H. influenzae</i>	6 (0.3)	26 (1.6)	0.0007
<i>S. pneumoniae</i> + <i>M. catarrhalis</i>	7 (0.4)	5 (0.3)	0.77
<i>H. influenzae</i> + <i>M. catarrhalis</i>	15 (0.9)	29 (1.8)	0.04
Carriers of three pathogens	0	5 (0.3)	0.06

# The Contribution of Smoking and Exposure to Tobacco Smoke to *Streptococcus pneumoniae* and *Haemophilus influenzae* Carriage in Children and Their Mothers

Greenberg et al, CID 2006; 42:897

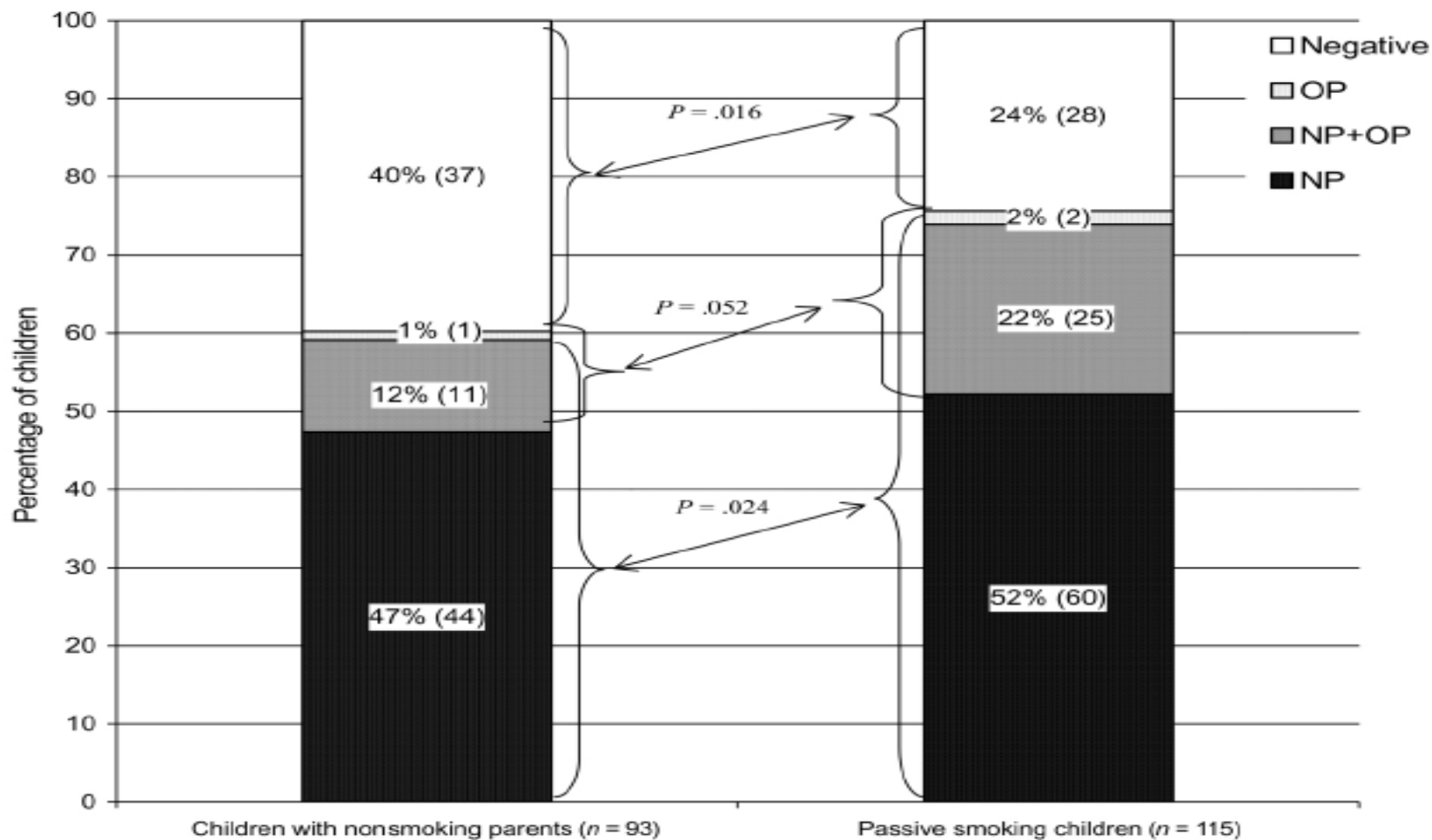
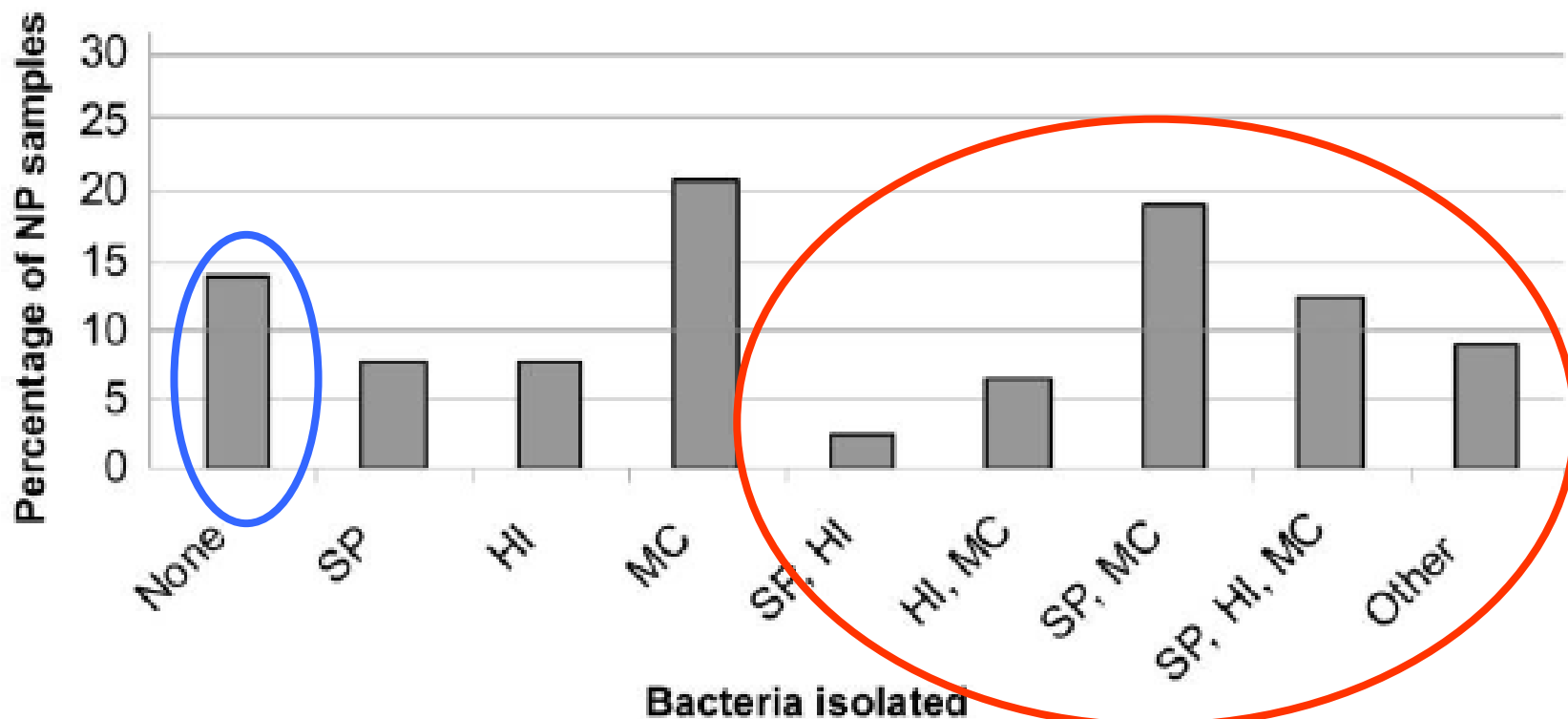


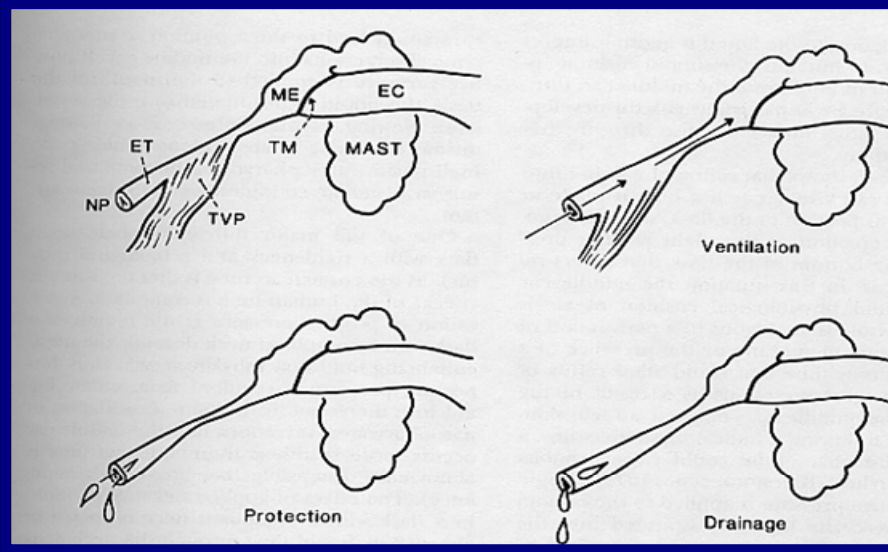
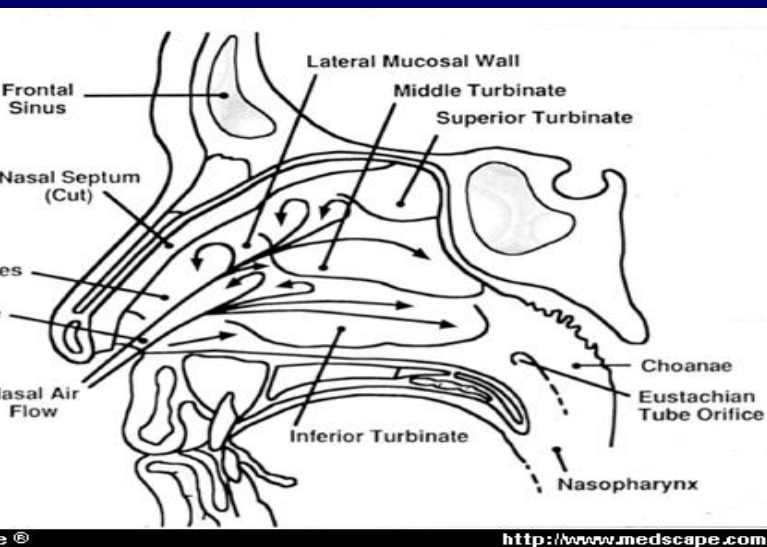
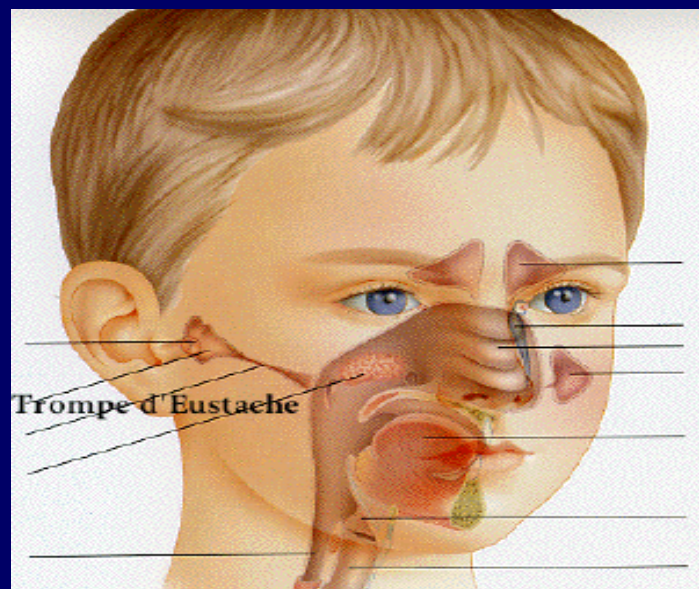
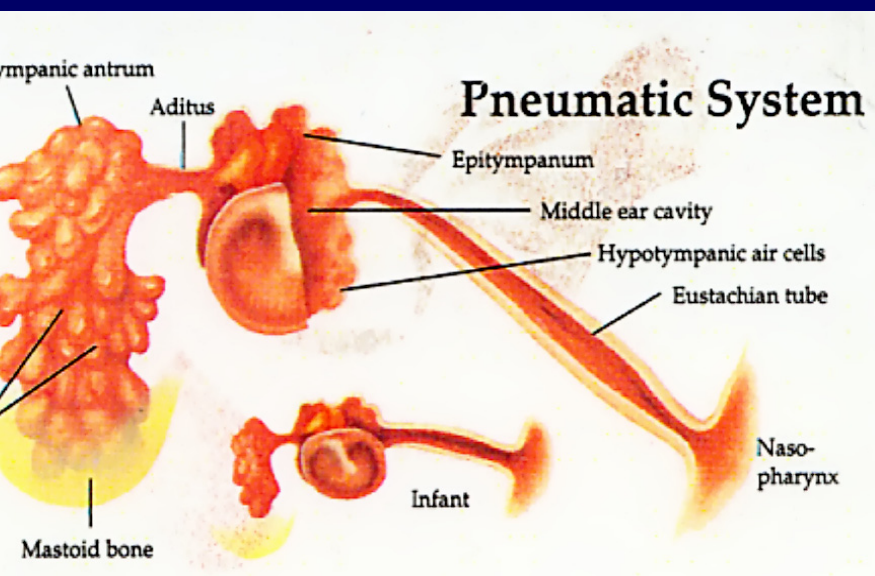
Figure 1. Nasopharyngeal (NP) and oropharyngeal (OP) carriage rates of *Streptococcus pneumoniae* in children with nonsmoking parents, compared

# Respiratory pathogens isolated in the nasopharynx at the time of upper respiratory infection



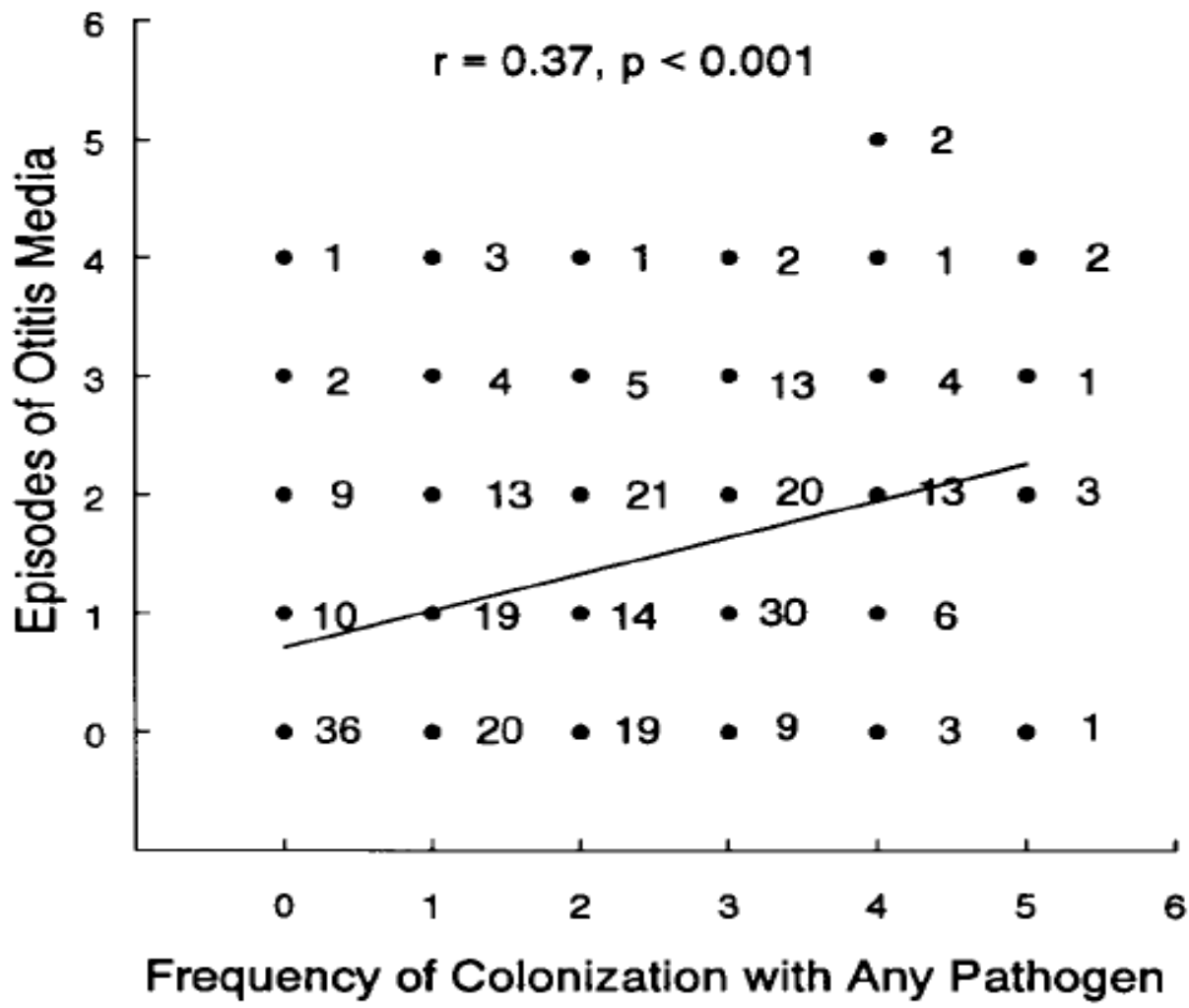
# Colonizzazione e rischio di otite media acuta





“rappresenta l'unica via di comunicazione della cassa timpanica con l'ambiente esterno” **Bartolomeo Eustachio (1563)**

# Relationship between frequency of colonization with any pathogen and number of episodes of otitis media

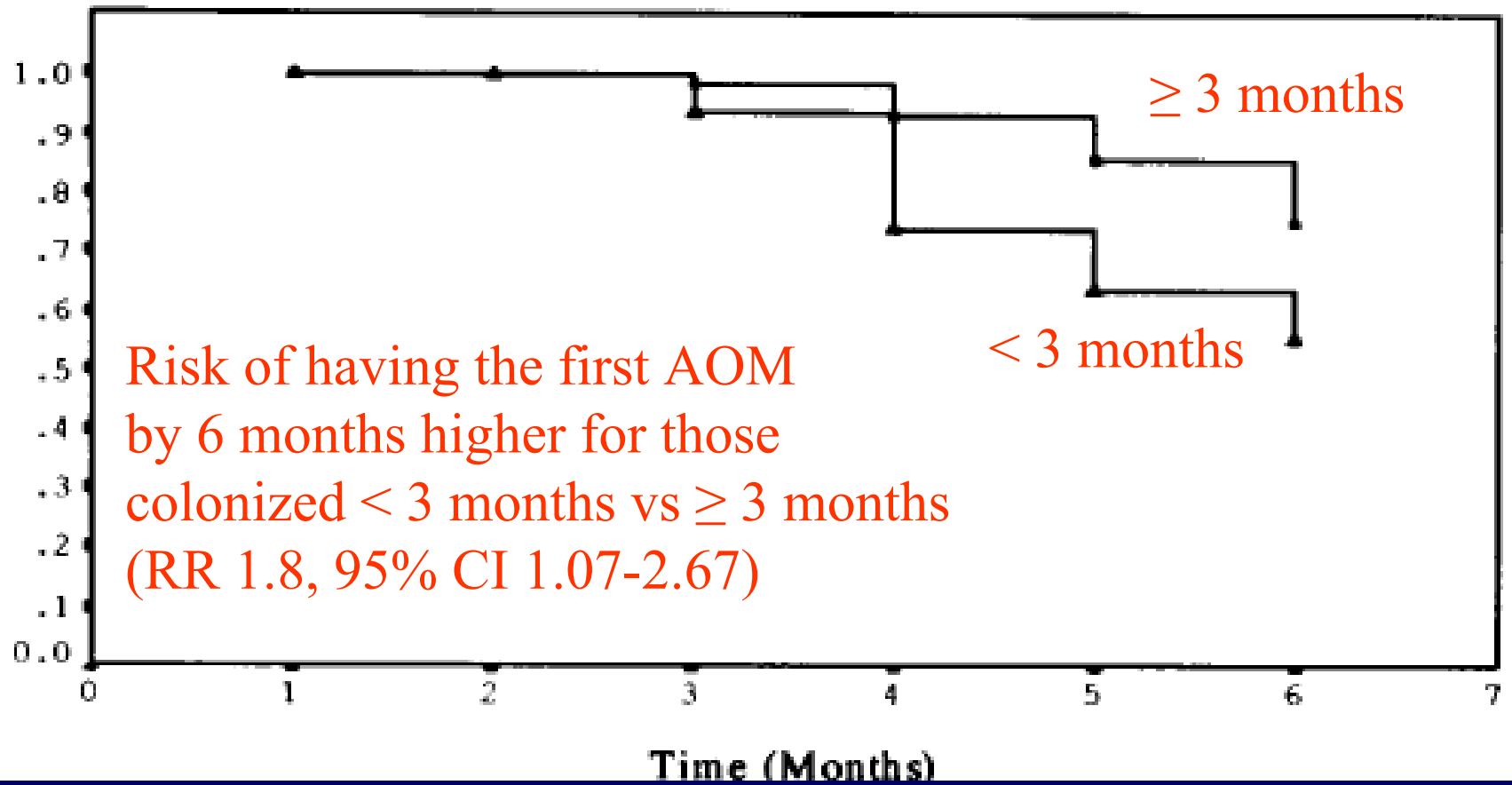


Il 75% dei bambini considerati portatori nel primo anno di vita sviluppano 3 o più episodi di otite media acuta

# CORRELATION BETWEEN FREQUENCY OF PATHOGEN COLONIZATION AND EPISODES OF OTITIS MEDIA (Faden et al, JID, 1997)

	OM	OME	OMA
pneumoniae	0.20 ( $<.001$ )	0.17 (.004)	0.22 ( $<.001$ )
influenzae	0.29 ( $<.001$ )	0.24 ( $<.001$ )	0.17 (.003)
catarrhalis	0.32 ( $<.001$ )	0.21 ( $<.001$ )	0.24 ( $<.001$ )
any pathogen	0.37 ( $<.001$ )	0.20 (.001)	0.31 ( $<.001$ )

# Risk at first colonization and first episode of AOM



# MODELLO ANIMALE

Chinchilla infettato da virus influenzale A  
e da *S.pneumoniae*

rispetto a

Chinchilla infettato da solo *S.pneumoniae*



AUMENTO RISCHIO DI OMA

3.2

# Risk of AOM complicating upper respiratory tract infection by pathogens colonized in the nasopharynx at the time of upper respiratory tract infection

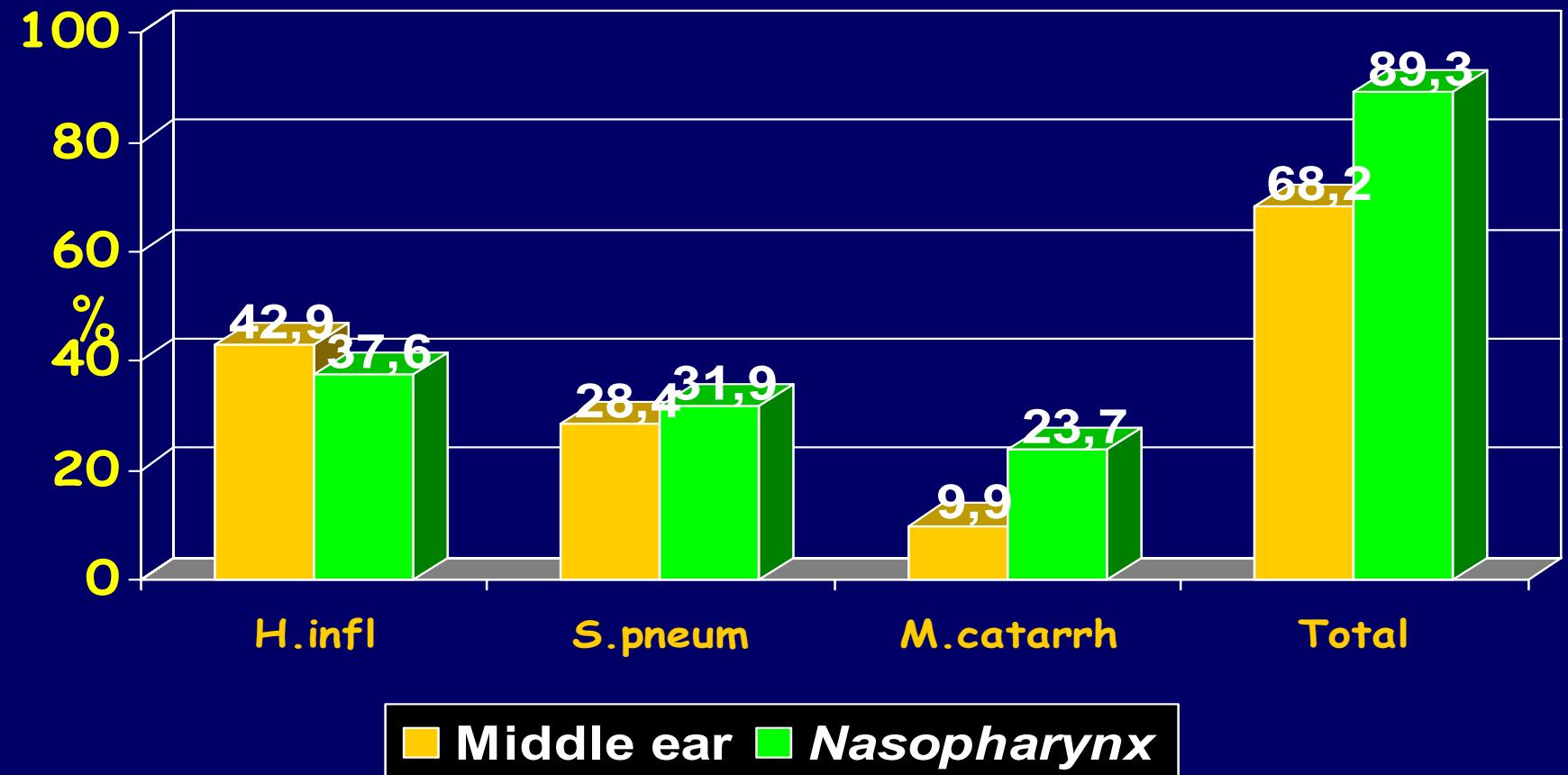
Nasopharyngeal bacterial colonization	No. of episodes	AOM incidence, %	OR (95% CI)	P
No bacteria	102	10	Ref	Ref
Sp only	55	29	3.7 (1.6–9.0)	<.05
Hi only	54	43	6.8 (2.9–15.9)	<.05
Mc only	148	32	4.4 (2.1–9.2)	<.05
Sp and Hi	18	50	9.2 (3.0–28.5)	<.05
Sp and Mc	136	41	6.4 (3.1–13.4)	<.05
Hi and Mc	45	51	9.6 (4.0–23.0)	<.05
Sp, Hi, and Mc	88	51	9.6 (4.4–20.9)	<.05

# Colonizzazione nasofaringea ed eziologia dell'otite media acuta

**Table 2. Bacterial isolates from middle-ear aspirates in infants and children with acute otitis media [10\*\*]**

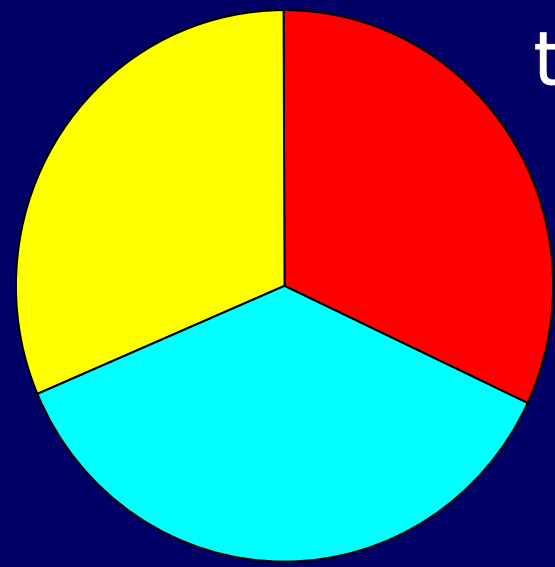
Bacterial pathogen	Percentage of children with pathogen			
	1952-1981		1985-1992	
	Mean	Range	Mean	Range
<i>Streptococcus pneumoniae</i>	33	26-53	38	27-52
<i>Haemophilus influenzae</i>	21	14-31	27	16-52
<i>Moraxella catarrhalis</i>	3	0-4	10	2-15
Streptococcus, group A	8	0.3-24	3	0-11
<i>Staphylococcus aureus</i>	2	0-3	2	0-16
Miscellaneous bacteria	1	0-2	8	0-24
None or nonpathogens	31	2-47	28	12-35

# CORRESPONDENCE BETWEEN NASOPHARYNGEAL AND MIDDLE EAR ISOLATES IN AOM (354 children – 22.1 months)



# Correspondence between nasopharyngeal and middle ear isolates in AOM

Partial agreement between the results at 2 sites



No agreement between the samples at 2 sites

Full correlation between the results at 2 sites

# Positive and negative predictive value of nasopharyngeal culture for the etiology of acute otitis media

Author, year	S.pneumoniae		H.Influenzae		M.catarrhalis	
	VPP	VPN	VPP	VPN	VPP	VPN
Wright, 1990	22	99	71	95	17	99
Edmondson, 1991	29	-	36	-	8	-
Chen, 1996	45	98	50	98	19	97

# The Value of Nasopharyngeal Culture in Predicting the Etiology of Acute Otitis Media in Children Less Than Two Years of Age

PIDJ 2006;25:10

K. Syrjänen, MD,\*† Elja E. Herva, MD,‡ P. Helena Mäkelä, MD,\* Heikki J. Puhakka, Kari J. Auranen, PhD,\*§ Aino K. Takala, MD,|| and Terhi M. Kilpi, MD\*

**TABLE 1.** *Streptococcus pneumoniae* (Pnc) and *Haemophilus influenzae* (Hi) Findings From 586 Middle Ear Fluid (MEF) Samples and Nasopharyngeal Aspirates (NPA) Obtained Concurrently From 200 Children During Acute Otitis Media

Bacterium Cultured From NPA	Homologous Bacterium Cultured From MEF		
	-	+	
Pnc			
-	269	1	270
+	157	159*	316
	426	160	586
Hi			
-	406	29	435
+	54	97	151
	460	126	586

# The Value of Nasopharyngeal Culture in Predicting the Etiology of Acute Otitis Media in Children Less Than Two Years of Age

PIDJ 2006;25:1032

K. Syrjänen, MD,\*† Elja E. Herva, MD,‡ P. Helena Mäkelä, MD,\* Heikki J. Puhakka, Kari J. Auranen, PhD,\*§ Aino K. Takala, MD,|| and Terhi M. Kilpi, MD\*

TABLE 2. Nasopharyngeal Culture of *Streptococcus pneumoniae* (Pnc) and *Haemophilus influenzae* (Hi) as a Predictor for Isolation of the Same Bacterium From a Middle Ear Fluid (MEF) Sample Obtained Concurrently During Acute Otitis Media (AOM)

Bacterium	Prevalence			Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
		MEF	NPA				
	N	Percent	Percent				
Pnc	586	27	54	99 (95–100)	63 (57–68)	50 (43–56)	>99 (97–100)
Hi	586	22	26	77 (69–83)	88 (85–91)	64 (56–71)	93 (90–95)

**POSITIVE PREDICTIVE VALUE OF QUANTITATIVE  
NP CULTURE FOR THE ETIOLOGY OF AOM  
(Schwartz et al, JAMA 1979)**

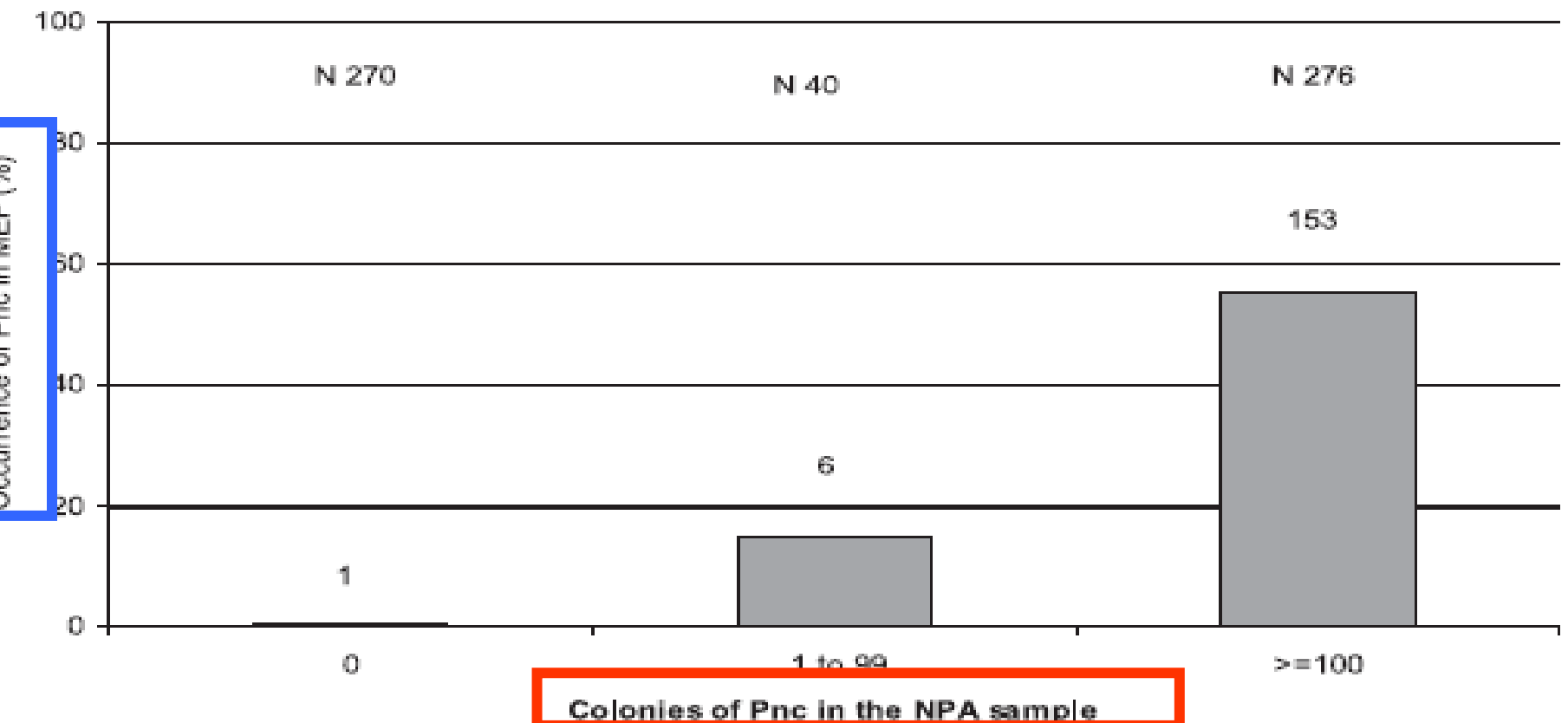
<b>S.PNEUMONIAE</b>	<b>59/73 (80%)</b>
<b>H.INFLUENZAE</b>	<b>30/38 (79%)</b>
<b>M.CATARRHALIS</b>	<b>7/15 (46%)</b>
<b>S.PYOGENES</b>	<b>6/6 (100%)</b>

**\*presence of a single pathogen greater than 25% up to 100% of total number of colonies**

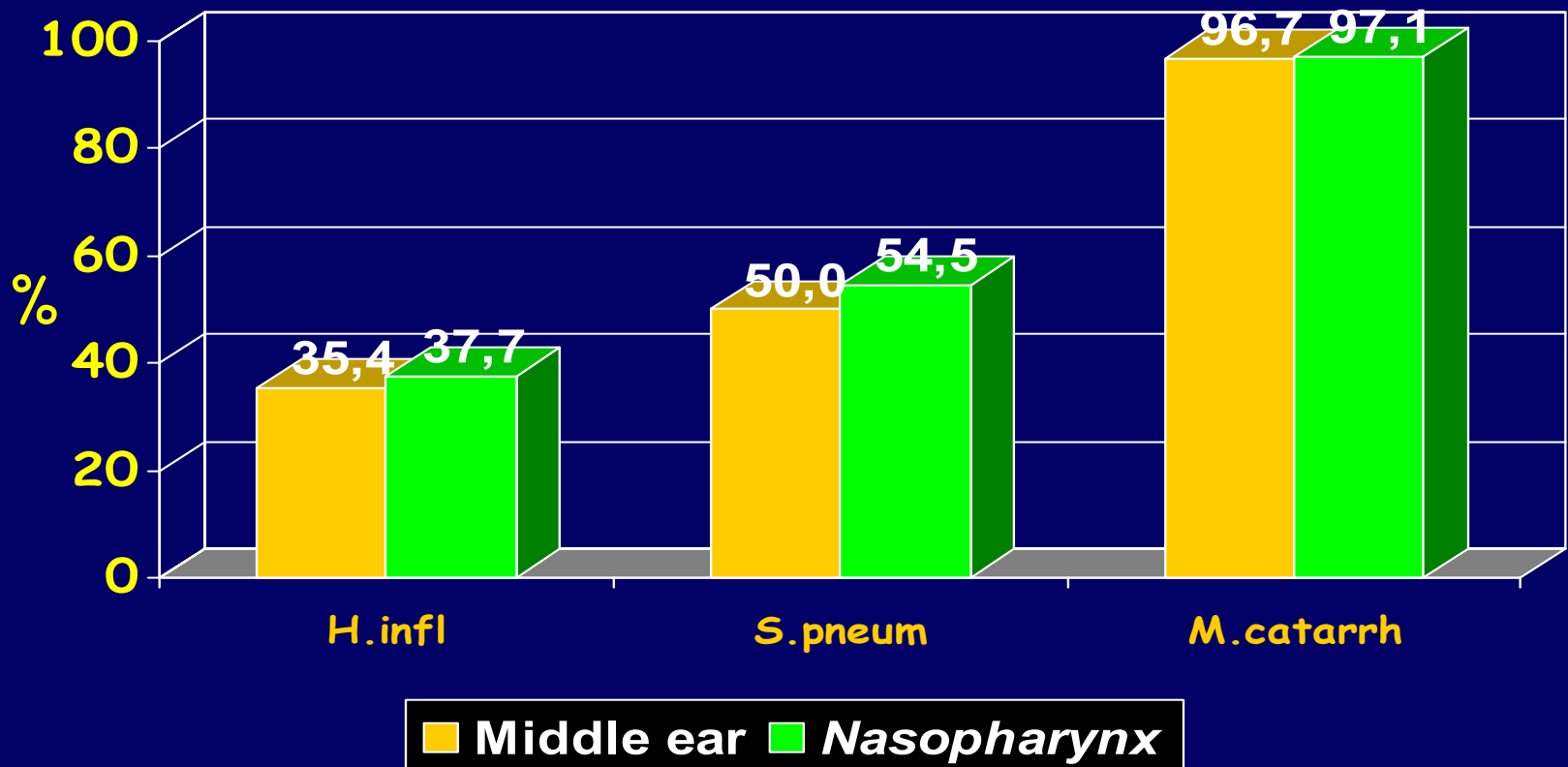
# The Value of Nasopharyngeal Culture in Predicting the Etiology of Acute Otitis Media in Children Less Than Two Years of Age

PIDJ 2006;25:1

*K. Syrjänen, MD,\*† Elja E. Herva, MD,‡ P. Helena Mäkelä, MD,\* Heikki J. Puhakka, Kari J. Auranen, PhD,\*§ Aino K. Takala, MD,|| and Terhi M. Kilpi, MD\**



# Correspondence of resistance \* between nasopharyngeal and middle ear isolates in AC



# predictive value of pneumococcal nasopharyngeal cultures for the assessment of penicillin-resistant acute otitis media in children

et al, PIDJ 2000; 19:298

**TABLE 4.** Sensitivity, specificity and positive and negative predictive values of nasopharyngeal cultures for recovering the same strain of *Streptococcus pneumoniae* from middle ear fluid: NT-AOM vs. NR-AOM

	All <i>S. pneumoniae</i>			Penicillin-nonsusceptible <i>S. pneumoniae</i>		
	NT-AOM	NR-AOM	<i>P</i>	NT-AOM	NR-AOM	<i>P</i>
Sensitivity	0.79	0.89	NS	0.79	0.88	NS
Specificity	0.41	0.58	0.001	0.79	0.69	NS
PPV	0.41	0.51	0.06	0.44	0.55	NS
NPV	0.78	0.91	0.009	0.95	0.93	NS

PPV, positive predictive value; NPV, negative predictive value; NS, not significant.

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negative nasopharyngeal culture for  
penicillin non susceptible *S.pneumoniae*  
**PRACTICALLY RULES OUT** its presence in the  
middle ear fluid of patients with AOM (and makes  
tympanocentesis not mandatory).

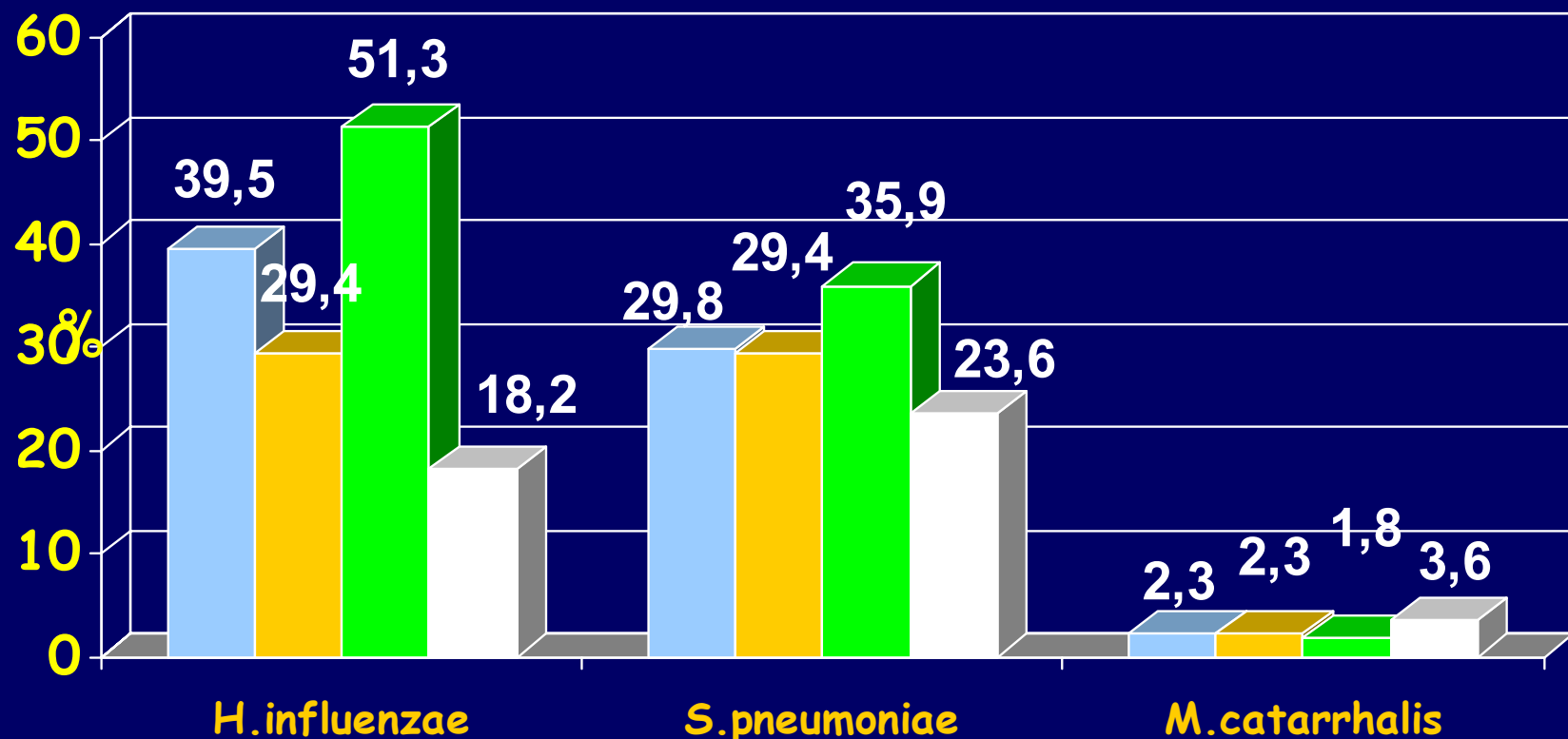
dan et al, PIDJ 2000; 19:298

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# Colonizzazione nasofaringea ed patologia otologica ricorrente e cronica

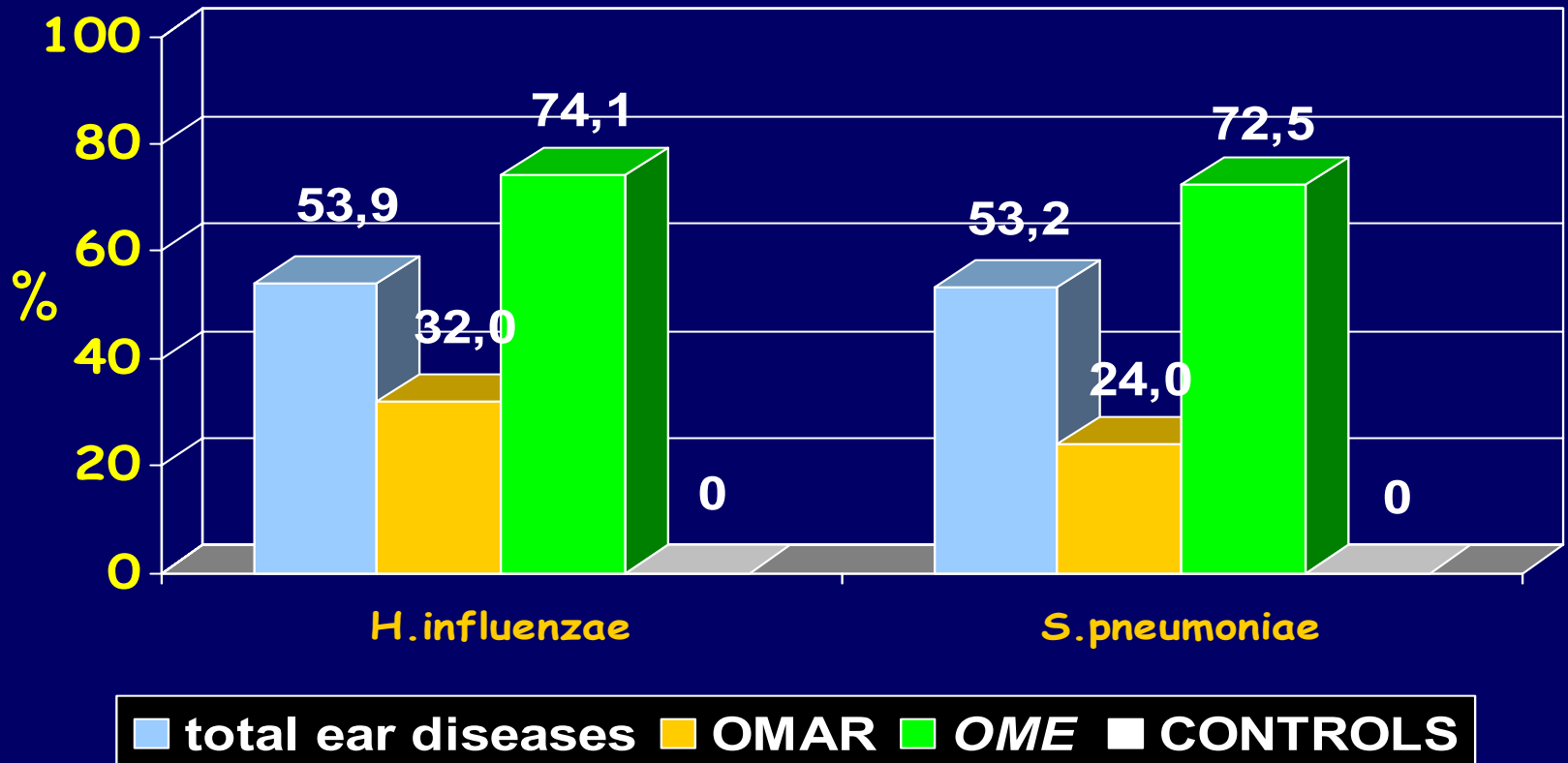


# Differences in nasopharyngeal bacterial flora in children with nonsevere recurrent acute otitis media and chronic otitis media with effusion: implications for management



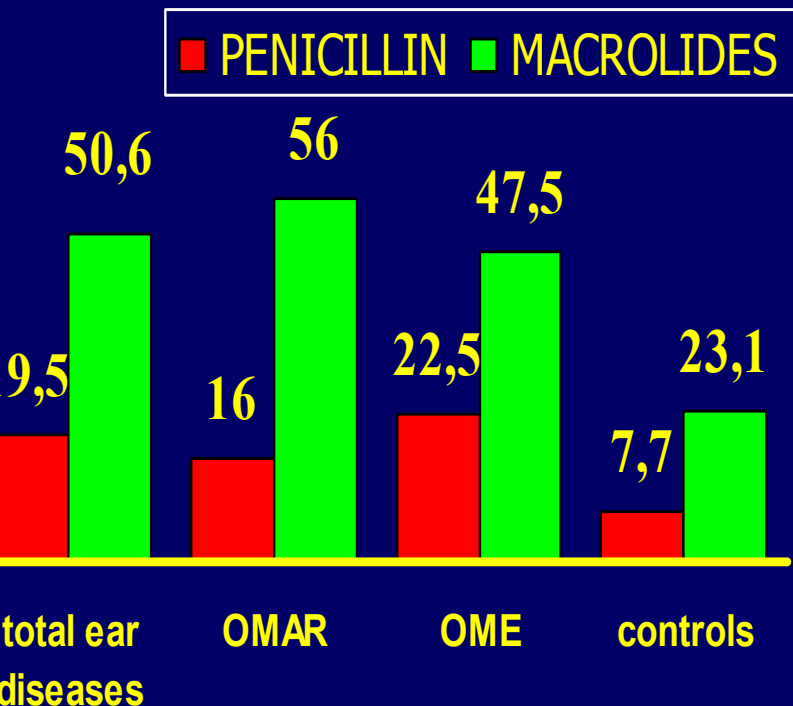
■ total ear diseases ■ OMAR ■ OME ■ CONTROLS

# HEAVY BACTERIAL LOAD OF RESPIRATORY PATHOGENS IN NASOPHARYNX IN EAR DISEASES VERSUS CONTROLS

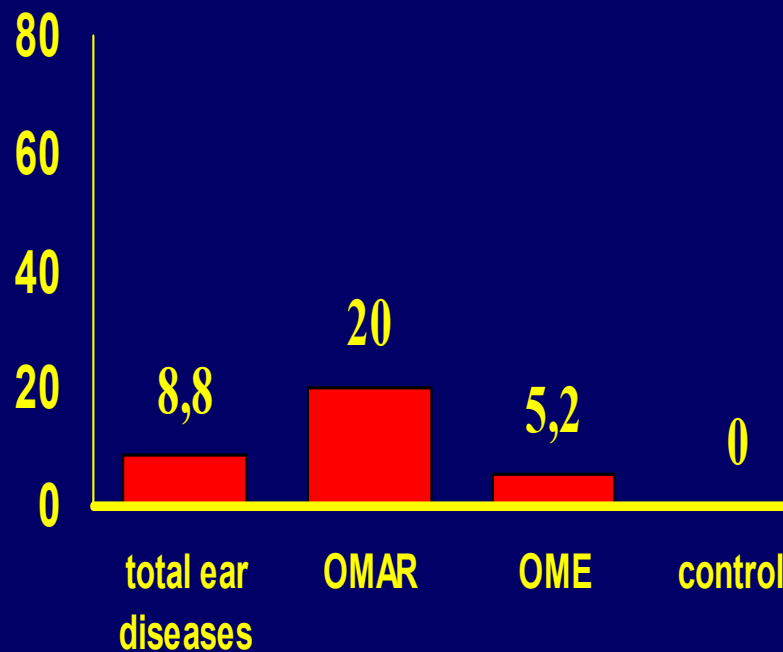


# Resistance of pathogens colonized in the nasopharynx children with ear disease

## S.pneumoniae



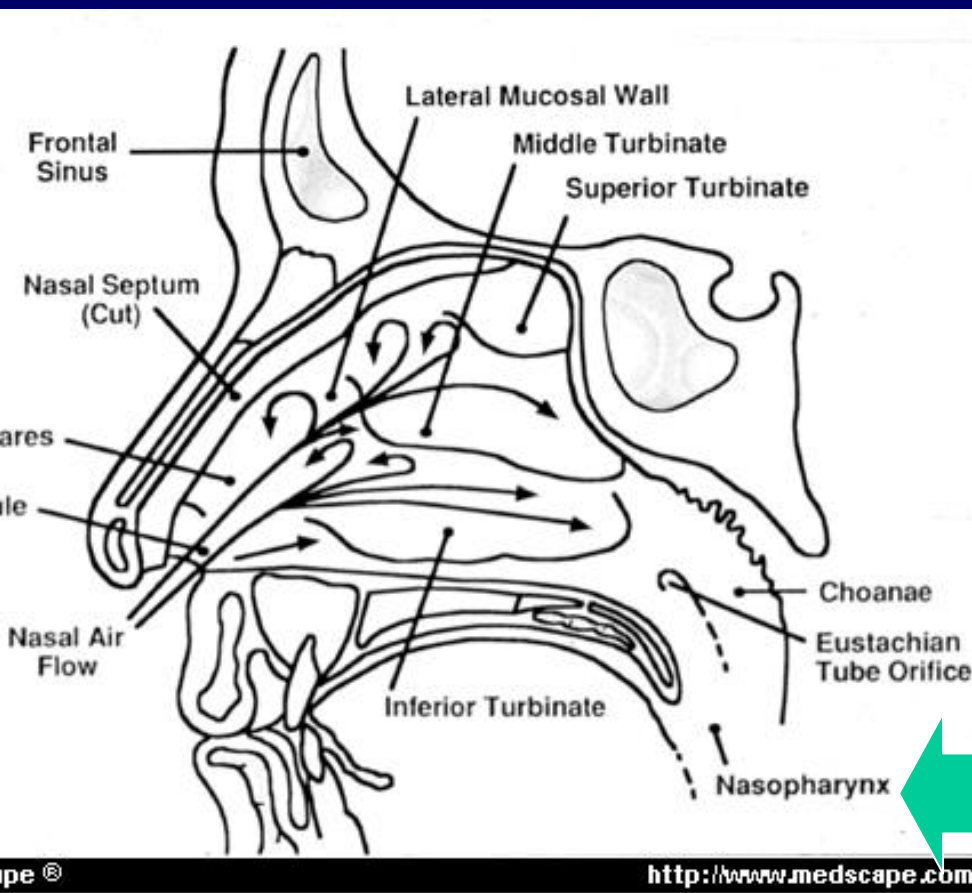
## H.influenzae



# PRE-TERM (12 weeks) OTOLOGIC EVOLUTION OF CHILDREN WITH OROPHARYNGEAL COLONIZATION

	Total	Carriers of respiratory pathogens	NON CARRIERS	p
<b>PRE-TERM (n=80)</b> Persistence at 2 weeks	52/80 (65%)	43/50 (86.0%)	9/30 (30.0%)	<0.00
<b>TERM (n=82)</b> Recurrence in 2 weeks	38/82 (46.3%)	23/37 (62.1%)	15/45 (33.3%)	0.01

# Come/dove fare il prelievo?



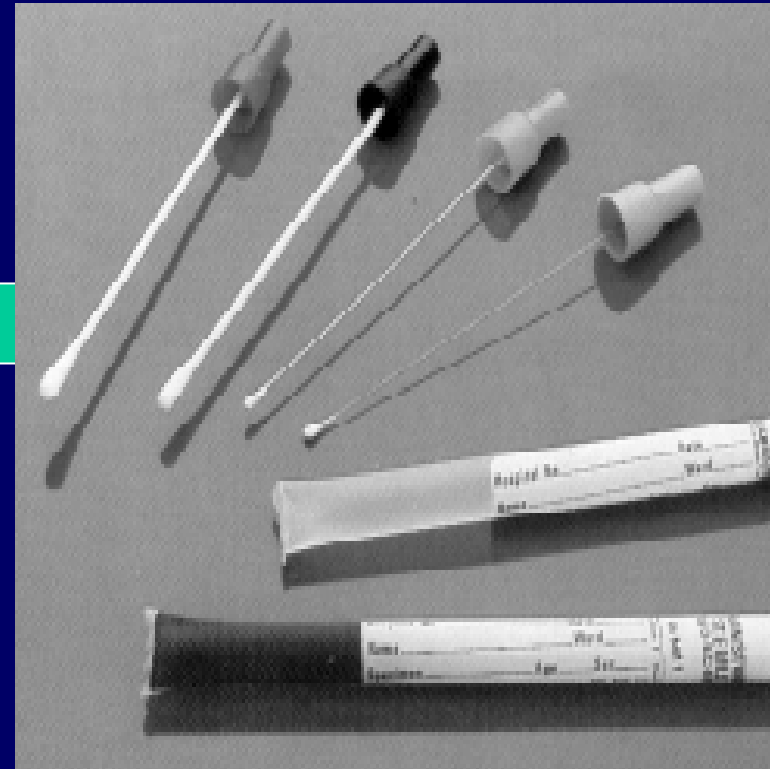
pe ©

<http://www.medscape.com>

**nasopharynx vs oropharynx** (Capeding et al, in Microbiol 1995)

**Staphylococcus aureus** is isolated significantly more often from the nasopharynx than from the oropharyngeal site.

**Influenzae** is found equally at both sites.



# Conclusioni di un prelievo nasofaringeo corretto:

## in un singolo bambino

(parzialmente) utile nell'individuare il singolo bambino a rischio (attenzione a elevata dinamicità dei patogeni trasportati)

(parzialmente) utile per predire la eziologia del singolo episodio di otite media acuta (quantitativo)

utile per conoscere la resistenza dei patogeni

## in una popolazione

Utile per monitorare le modificazioni di resistenza dei patogeni respiratori

molto utile per pianificare e monitorare le strategie vaccinali

Thank you for your  
attention!



“ Never look for the extraordinary  
but, on the contrary, concentrate  
on the more prevalent and  
common diseases, and try to cure  
them; these are the diseases you  
will most frequently encounter in  
your practice”

*Emile Ménière*  
*Deuxième Congrès Otologique*  
*Internationale*  
*Milan 1880*