Terapia antibiotica della polmonite di comunità di lieve e media gravità seguita sul territorio

Nicola Principi
Professore Emerito di Pediatria
Università di Milano

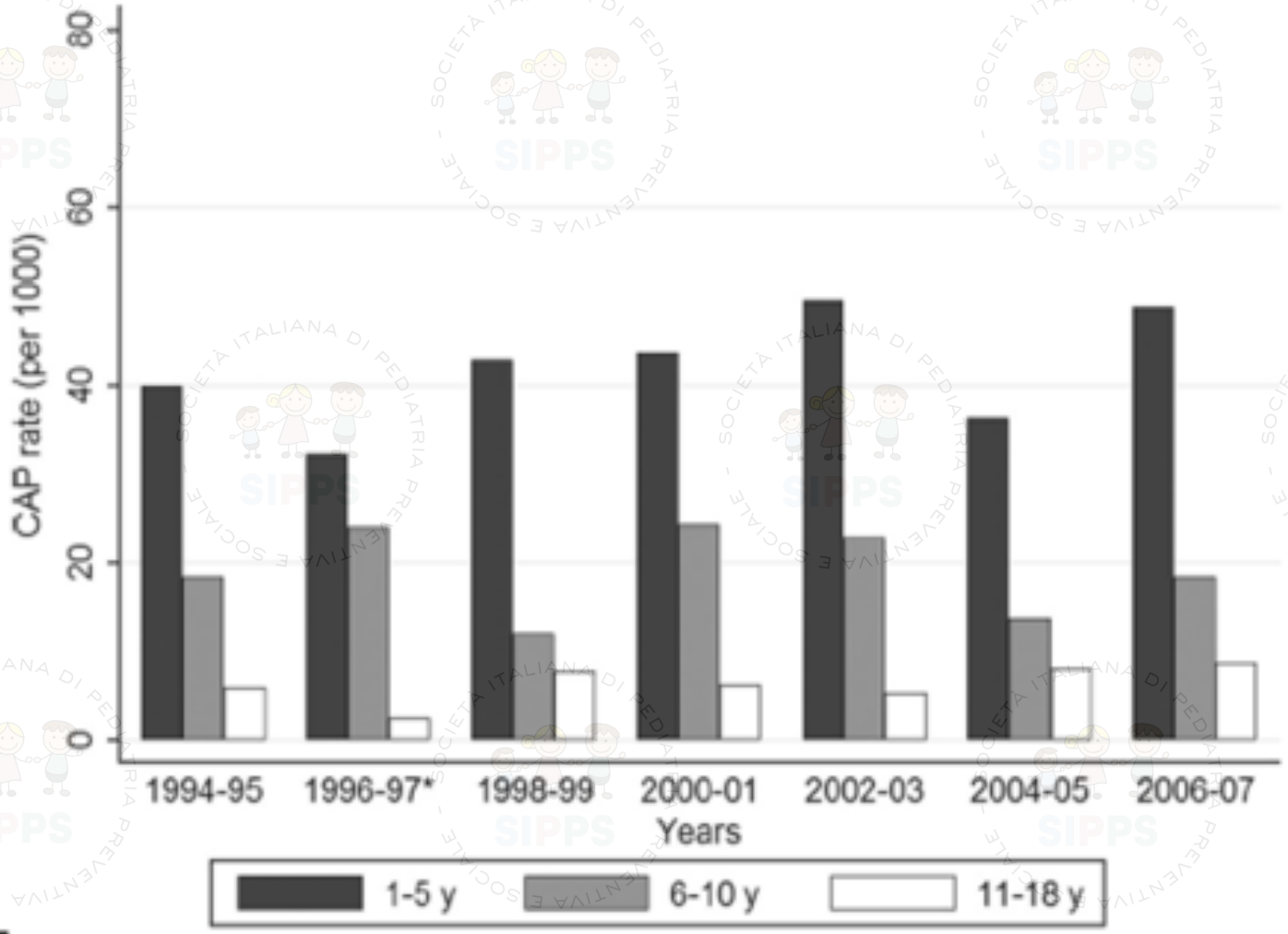
Criteria for Hospitalization of Children With CAP

Respiratory Distress

- Age-adjusted Tachypnea
- SpO2 <90–93% in room air (if FiO_2 >0.50, ICU or continuous cardiorespiratory monitoring are required to maintain saturation >92%)
- Cyanosis
- Retractions
- Grunting
- Nasal flaring

- Capillary refill time >2 min
- Dehydration
- Vomiting/not feeding
- Comorbidities (eg, congenital heart disease, chronic lung disease of prematurity, chronic respiratory conditions leading to infection such as cystic fibrosis, bronchiectasis, immunodeficiency)
- Etiological agent (eg, MRSA, bacterial/viral coinfections)
- Unreliable family environment

Esposito S, Cohen R, Domingo JD, Pecurariu OF, Greenberg D, Heininger U, Knuf M, Lutsar I, Principi N, Rodrigues F, Sharland M, Spoulou V, Syrogiannopoulos GA, Usonis V, Vergison A, Schaad UB. Pediatr Infect Dis J. 2012 Jun;31(6):e78-85.



Two-yearly community-acquired pneumonia rates by age group. *Estimate for the 11- to 18-year-old age group contains fewer than 30 unadjusted records.

From Kronman M et al., Pediatrics 2011

La Consensus sull'uso degli antibiotici nella polmonite seguita sul territorio non ha precedenti

E' stata ritenuta necessaria perché è la forma di polmonite per la quale è più alto il rischio di errore prescrittivo

Rispetto alla CAP grave che viene ospedalizzata, la CAP curata sul territorio è quella che pone il più elevato rischio di abuso e di cattivo uso degli antibiotici perché:

- Maggiore è il rischio di abuso e di cattivo uso perché:

- la diagnosi è meno certa (no radiografia, pochissimo uso dell'ecografia, scarsa utilità diagnostica dei segni e sintomi di malattia)
  la differenziazione delle forme batteriche dalle virali è estremamente difficile (poca efficacia dei test di laboratorio disponibili sul territorio)

- Più difficile, se non impossibile, l'identificazione del batterio responsabile della malattia

Performance of Symptoms In Diagnosing Pneumonia (I)

(from Shah SN, et al. JAMA 2017)

Finding, Source	Sample Size, No.	Sensitivity (95% CI), %	Specificity (95% CI), %	LR+ (95% CI)	LR− (95% CI)
Symptoms					
Chest pain[47,50,67]	3164	22 (5-62)	91 (56-99)	1.9 (1.1-3.4)	0.82 (0.66-1.0)
Poor feeding[47,48,50,52,63,69]	3784	58 (32-80)	60 (39-78)	1.4 (1.3-1.6)	0.71 (0.51-0.88)
Cough[45-47,50,53,55,57,61,63,67,68,70]	7446	88 (80-97)	25 (08-42)	1.2 (0.98-1.4) I^2 = 89%	0.47 (0.24-0.70) I^2 = 76%
Difficulty breathing[45,50,52,53,62,67b]	5723	37 (10-64)	69 (42-95)	1.2 (0.61-1.7)	0.92 (0.70-1.1)
Symptom duration >3 days (cough, fever, illness)[53,64]	2979	25 (18-32)	81 (72-87)	1.2 (1.1-1.4)	0.94 (0.90-0.98)
Vomiting or diarrhea[45,47,48,50,53,64]	11 377	27 (15-39)	76 (67-85)	0.96 (0.89-1.0)	0.96 (0.89-1.0)

Performance of Signs In Diagnosing Pneumonia (II)

(from Shah SN, et al. JAMA 2017)

Finding, Source	Sample Size, No.	Sensitivity (95% CI), %	Specificity (95% CI), %	LR+ (95% CI)	LR− (95% CI)
Fever					
Temperature, thresholds					
≥39°C,[47,59,64]	2281	40 (23-60)	68 (51-81)	1.3 (0.89-1.8)	0.90 (0.77-1.0)
>38°C or 38.5°C,[46,48,52,68]	1170	48 (23-73)	67 (45-90)	1.5 (0.88-2.0)	0.78 (0.57-0.99)
>37.5°C,[48,69]	366	80-92	47-54	1.7-1.8	0.17-0.37
Any fever during visit[57,63,67,70]	921	72 (53-86)	50 (37-63)	1.4 (1.2-1.7)	0.55 (0.35-0.79)
Fever, reported by parent[50,52,53,57,69]	5517	92 (73-98)	14 (4-38)	1.1 (1.0-1.2)	0.59 (0.39-0.87)
Respiratory rate					
Tachypnea, physician assessment[45,47,55,60,67,70]	3192	46 (27-64)	72 (60-83)	1.6 (1.2-2.0)	0.76 (0.59-0.93)
Respiratory rate >40 breaths/min[56,58,69]	859	79 (40-96)	51 (34-68)	1.5 (1.3-1.7) I^2 = 0%	0.41 (0.17-0.99) I^2 = 87%
Tachypnea, age defined[46,49,51,52,57,60,62,63]	4393	54 (23-82)	64 (35-86)	1.5 (0.49-4.4)	0.73 (0.25-1.7)
Oxygen saturation					
≤96%[58]	510	64 (49-78)	77 (73-81)	2.8 (2.1-3.6)	0.47 (0.32-0.67)
≤95%[45]	514	16 (11-22)	96 (93-97)	3.5 (2.0-6.4)	0.88 (0.82-0.94)
≤92%[46]	394	26 (21-32)	88 (82-93)	2.2 (1.3-3.8)	0.84 (0.76-0.92)
<90%[64]	588	37 (31-43)	75 (70-79)	1.5 (1.1-1.9)	0.84 (0.76-0.94)

Performance of Signs In Diagnosing Pneumonia (III)

(from Shah SN, et al. JAMA 2017)

Finding, Source	Sample Size, No.	Sensitivity (95% CI), %	Specificity (95% CI), %	LR+ (95% CI)	LR− (95% CI)
Auscultatory findings					
Discontinuous sounds[45-52,55,57,58,60-64,67,69,70c]	10 599	39 (29-48)	71 (62-81)	1.4 (0.96-1.7)	0.86 (0.74-0.98)
Rales[45,47,49,51,55,60,62,70]	4136	43 (32-54)	64 (47-81)	1.2 (0.53-1.8)	0.90 (0.14-2.5)
Wheeze (not rhonchi)[45-47,53,58,60,63,67,70]	5888	16 (10-21)	83 (75-91)	0.93 (0.64-1.2)	1.0 (0.95-1.1)
Continuous sounds (wheezes or rhonchi)[45-47,50,53,58,60,63,67,70]	8842	16 (7-24)	83 (76-90)	0.91 (0.54-1.3)	1.0 (0.94-1.1)
Diminished breath sounds[46,47,51,57,58,60,62,63]	4434	25 (13-36)	72 (48-95)	0.88 (0.04-1.7)	1.0 (0.67-1.4)
Work of breathing					
Grunting[47,48,55,57,58,63]	1836	13 (5-32)	95 (83-99)	2.7 (1.5-5.1) I^2 = 62%	0.92 (0.80-0.97) I^2 = 67%
Nasal flaring[45,47,49,52,55,58,61,64,68,69]	3541	36 (17-54)	84 (71-97)	2.2 (1.3-3.1) I^2 = 85%	0.77 (0.64-0.90) I^2 = 77%
Retractions or indrawing[47-50,52,57,58,60,61,63,68,69]	8080	38 (20-56)	80 (70-90)	1.9 (1.2-2.5) I^2 = 81%	0.78 (0.61-0.94) I^2 = 89%

Episodes of Rx-confirmed CAP with viruses in children aged 0-12 months

(Esposito S et al., Influenza Other Respir Viruses. 2013)

	2007-08		2008-09		2009-10		Total episodes	
VIRUS	No. (%) *	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^
RSV	14 (33.3)	3 (21.4)	26 (44.8)	13 (50.0)	22 (22.2)	10 (45.4)	62 (36.8)	26 (41.9)
Rhinovirus	17 (40.4)	11 (64.7)	15 (25.8)	10 (66.6)	15 (15.1)	7 (87.5)	47 (28.1)	28 (59.5)
Bocavirus	7 (16.6)	6 (85.7)	2 (3,4)	2 (100)	5 (5,0)	5 (100)	14 (10.1)	13 (92.8)
Influenza	2 (4.7)	1 (50.0)	5 (8.6)	1 (20.0)	3 (3.0)	2 (66.6)	10 (7.2)	4 (40.0)
Metapneu.	10 (23.8)	3 (30.0)	5(8.6)	1 (20.0)	2 (2.0)	1 (50.0)	17 (12.2)	5 (29.4)
Coronavirus	2 (4.7)	2 (100)	0 (0.0)	0	5 (5.0)	5 (100)	7 (5.0)	7 (100)
Parainfluenza (1-4)	0 (0)	0	1 (1.7)	0 (0.0)	1 (1.0)	1 (100)	2 (1.4)	1 (50.0)
Adenovirus	0 (0)	0	0 (0.0)	0 (0.0)	1 (1.0)	1 (100)	1 (0.7)	1 (100)
Episodes with viruses	38/42 (90.4)	12/38 (31.5)	43/58 (74.1)	16/43 (37.2)	37/39 (94.8)	15/37 (40.5)	118/139 (84.9)	43/118 (36.4)

- % among the total number of CAP investigated;
- ^ % of the total number of infections in which the virus was identified

Episodes of Rx-confirmed CAP with viruses in children aged 13-36 months

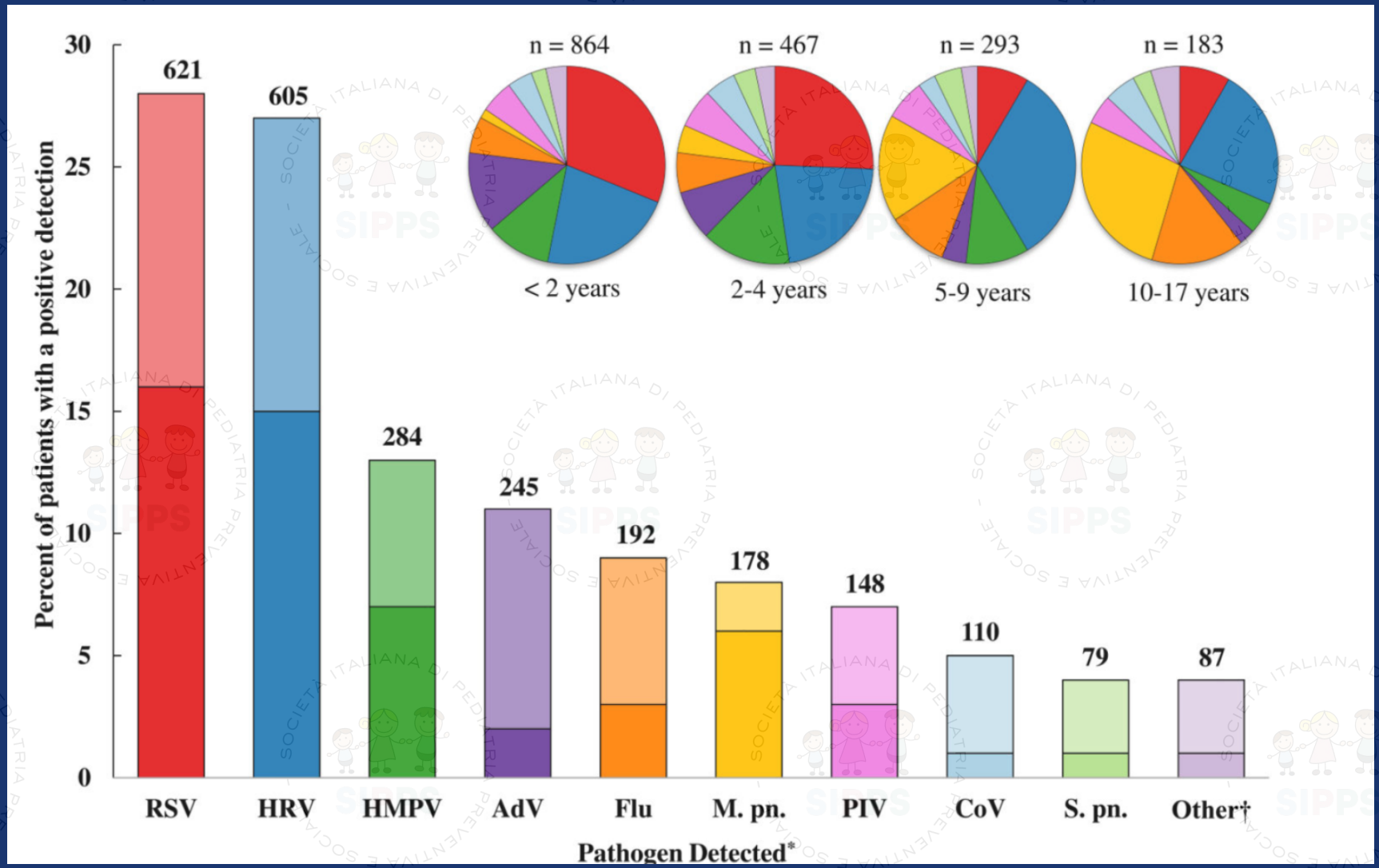
(Esposito S et al., Influenza Other Respir Viruses. 2013)

	2007-08		2008-09		2009-10		Total episodes	
VIRUS	No. (%) *	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^
RSV	35 (41.1)	16	58 (38.6)	21	30 (30.3)	10	123 (36.8)	47
Rhinovirus	26 (30.5)	15	44 (29.3)	21	24 (24.2)	7	94 (28.1)	43
Bocavirus	12 (14.1)	9	15 (10.0)	11	12 (12.1)	6	39 (11.6)	26
Influenza	4 (4.7)	1	16 (10.6)	6	10 (10.1)	1	39 (11.6)	8
Metapneumo .	12 (14.1)	5	13(8.6)	4	6 (6.1)	0	31 (9.2)	9
Coronavirus	3 (3.5)	2	7 (5.8)	3	5 (5.0)	4	15 (4.5)	9
Parainfluenz a (1-4)	0 (0)	0	4 (2.6)	2	6 (6.1)	2	10 (3.0)	4
Adenovirus	1 (1.1)	0	4 (2.6)	3	2 (2.0)	1	7 (2.1)	4
Episodes with viruses	68/85 (80.0)	20/68 (29.4)	122/150 (81.3)	36/122 (29.5)	78/99 (78.8)	14/78 (17.9)	268/334 (80.2)	70/268 (26.1)

- % among the total number of CAP investigated;
- ^ % of the total number of infections in which the single virus was identified

Agents of Community Acquired Pneumonia in Children

(from Jain S, et al. NEJM 2015)



MARCATORI CAPACI DI DIFFERENZIARE CAP VIRALI E BATTERICHE

(from Principi N, Esposito S. Int J Mol Sci 2017)

Leucocitosi e neutrofilia
Velocità di eritrosedimentazione
Proteina C Reattiva (PCR)
Procalcitonina (PCT)

Soluble triggering receptor espresso dalle cellule mieloidi (sTREM)
Mid regional pro-adrenomedullin (MR-proADM)
Peptide natriuretico pro-atriale (NAP)
Numero e volume delle piastrine

White blood cell count (WBC) and absolute neutrophil count (ANC), C-reactive protein (CRP) concentration and erythrocyte sedimentation rate (ESR) in relation to the aetiology of infections in the 69 children with pneumonia and serologically indicated pneumococcal or viral aetiology

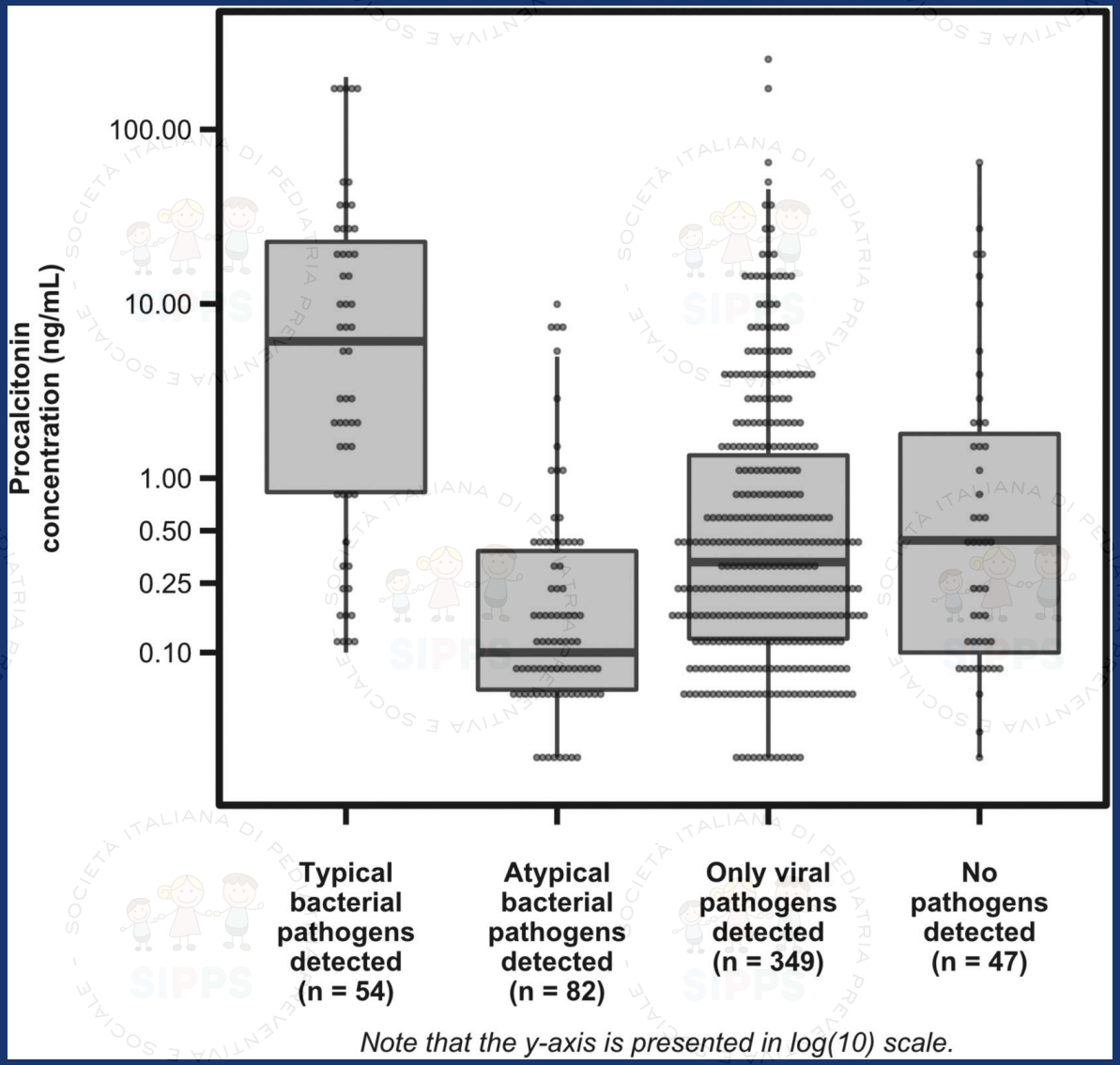
(from Korppi M, et al. Eur Resp J 1997)

Parameters	Aetiological group of infection				
	Pneumococcal (n=29)	p-value	Mixed# (n=17)	p-value	Viral‡ (n=23)
WBC $\times 10^9$ cells·L^{-1}	16.2±8.1 (13.4–19.0)	NS	12.8±6.0 (10.0–15.6)	NS	12.3±8.1 (9.5–15.1)
ANC $\times 10^9$ cells·L^{-1}	13.4±7.3* (8.7–13.7)	<0.05	6.4±3.6 (4.7–8.1)	NS	7.0±5.9 (4.4–9.6)
CRP mg·L^{-1}	89.9±102.0* (53.9–126.0)	NS	51.2±61.8 (21.4–81.0)	NS	40.9±48.8 (21.5–60.3)
ESR mm·h^{-1}	42.8±34.8* (32.0–54.8)	NS	34.3±21.9 (24.4–44.2)	NS	29.4±15.3 (23.4–35.4)

Values are presented as mean±SD, and 95% confidence intervals in parentheses. *: $p<0.05$ *vs* patients with viral infection alone. #: the viruses were RSV in 14 cases, parainfluenza in one, and adenovirus in three cases, including one dual virus infection; ‡: the viruses were RSV in 28 cases, parainfluenza in two, and adenovirus in two cases, including no dual virus infections. NS: nonsignificant; RSV: respiratiory syncytial virus.

Procalcitonin concentrations among children hospitalized with CAP stratified by patterns of microbiological detection

(from Stockmann C, et al. J Pediatr Infect Dis Soc, 2018)



Trattamento antibiotico della CAP lieve o moderata

- **BAMBINI 3 MESI – 5 ANNI**:

Amoxicillina 90 mg/kg/die in 3 somministrazioni

- Pneumococco è il batterio più spesso in causa
- Amoxicillina è un farmaco sicuro e ben tollerato e di costo contenuto
- L'eventuale presenza di *S. pneumoniae* aminopenicillino-resistente non modifica sostanzialmente l'efficacia
- Può essere discusso il dosaggio e il frazionamento

La grande maggioranza degli studi clinici randomizzati e controllati dimostra che l'efficacia delle aminopenicilline, inclusa amoxicillina, non è inferiore a quello di antibiotici a spettro allargato

Sp penicillin resistance and CAP outcome

(Cardoso MRA et al. Arch Dis Child 2008)

Treatment outcome	Susceptible	Intermediate	Resistant	Total	P
All children (n = 240)					0.75*
Success	94 (78)	49 (77)	46 (82)	189 (79)	
Failure	26 (22)	15 (23)	10 (18)	51 (21)	
Children without pleural effusion on admission (n = 111)					0.87*
Success	48 (86)	29 (91)	20 (87)	97 (87)	
Failure	8 (14)	3 (9)	3 (13)	14 (13)	
Children with pleural effusion on admission (n = 129)					0.37*
Success	46 (72)	20 (63)	26 (79)	92 (71)	
Failure	18 (28)	12 (37)	7 (21)	37 (29)	

*Fisher's exact test.

Trattamento antibiotico della CAP lieve o moderata

- Bambini > 5 anni,
  Amoxicillina 90 mg/kg/die in 3 somministrazioni

➢ La terapia con macrolide può essere considerato nel caso di bambini che non abbiano mostrato un miglioramento clinico dopo 48 ore di terapia antibiotica con amoxicillina ma che persistano in buone condizioni generali e non necessitino di ospedalizzazione

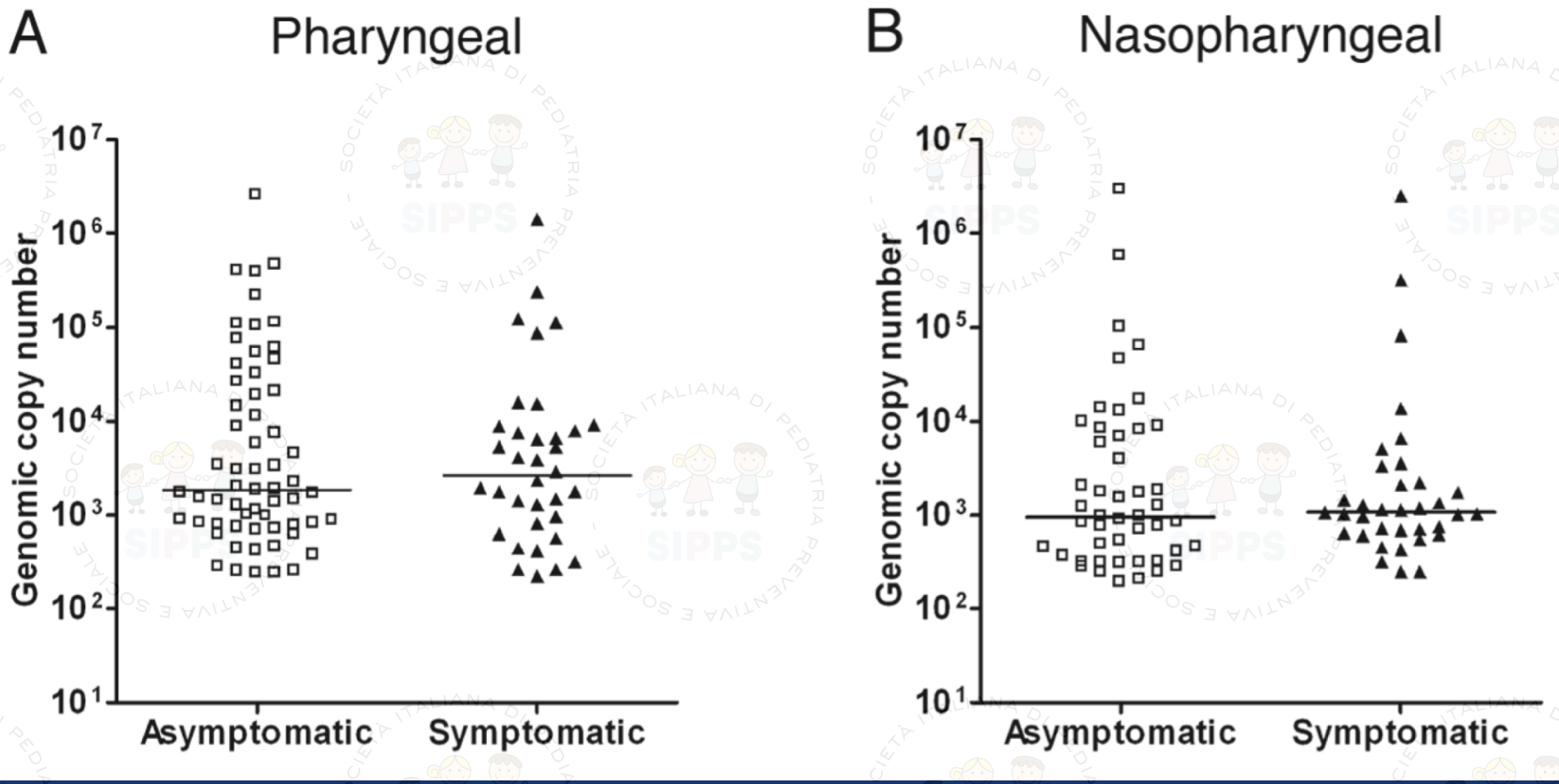
Incidence rates of acute Mycoplasma pneumoniae infection on the basis of serological and PCR findings.

(from Principi N, et al. Clin Infect Dis 2001)

Positive rest result, diagnosis	Proportion (%) of patients with infection, by age group			
	2–4 y	5–7 y	>7 y	All
Serological				
Acute bronchitis	12/62 (19.3)	8/34 (23.5)	9/17 (52.9)	29/113 (25.6)
Wheezing	12/53 (22.6)	4/15 (26.6)	7/14 (50.0)	23/82 (28.0)
Pneumonia	42/209 (20.0)	53/123 (43.0)	47/86 (54.6)	142/418 (33.9)
All	66/324 (20.4)	65/172 (37.8)	63/117 (53.8)	194/613 (31.6)
PCR				
Acute bronchitis	8/62 (12.9)	6/34 (17.6)	6/17 (35.3)	20/113 (17.7)
Wheezing	7/53 (13.2)	3/15 (20.0)	4/14 (28.6)	14/82 (17.1)
Pneumonia	33/209 (15.8)	36/123 (29.3)	39/86 (45.3)	108/418 (25.8)
All	48/324 (14.8)	45/172 (26.2)	49/117 (41.9)	142/613 (23.2)
Serological and/or PCR				
Acute bronchitis	14/62 (22.5)	10/34 (29.4)	12/17 (70.5)	36/113 (31.8)
Wheezing	12/53 (22.6)	5/15 (33.3)	7/14 (50.0)	24/82 (29.2)
Pneumonia	43/209 (20.5)	56/123 (45.5)	51/86 (59.3)	150/418 (35.8)
All	69/324 (21.3)	71/172 (41.3)	70/117 (59.8)	210/613 (34.3)

Pharyngeal (A) and nasopharyngal (B) Mycoplasma pneumoniae DNA loads in symptomatic and asymptomatic patients

(from Spuesens EBM, et al. PLOS Medicine 2013)



Principali ragioni che supportano l'uso dell'amoxicillina per la terapia della CAP anche nel bambino grande

- Buona parte delle forma da Mycoplasma guarisce spontaneamente

- Gli studi clinici randomizzati e controllati che confrontino amoxicilina e macrolidi nella terapia della CAP del bambino grande sono pochi ma sembrano sistematicamente indicare che i macrolidi non sono superiori all'amoxicillina come farmaci di scelta iniziale

SAFE USE OF SELECTED CEPHALOSPORINS IN PENICILLIN-ALLERGIC PATIENTS: A META-ANALYSIS

(from Pochicero M and Casey JR -Otolaryngology–Head and Neck Surgery 2007;136: 340-347

A significant increase in allergic reactions to
cephalothin (odds ratio [OR]2.5; 95% confidence interval [CI] 1.1 to 5.5),
cephaloridine (OR 8.7; CI 5.9 to 12.8), and
cephalexin (OR 5.8; CI 3.6 to 9.2), and
all first generation cephalosporins plus cefamandole
(OR 4.8; CI 3.7 to 6.2)
were observed in penicillin allergic patients;
no increase was observed with
second generation cephalosporins (OR 1.1; CI, 0.6 to 2.1) or
third generation cephalosporins (OR 0.5; CI 0.2 to 1.1).

Clinical challenges, skin testing, and monoclonal antibody studies point to the paramount importance of similarities in side chain structure to predict cross-allergy between cephalosporins and penicillins

Cross-reactivity between penicillins and cephalosporins based on side chain similarity

(from Pichichero M,. Diag Microbiol Infect Dis 2007)

7-Position side chain						
Similar side chain/ cross-reactivity possible within group[a,b]	Similar side chain/ cross-reactivity possible with group	Similar side chain/ cross-reactivity possible with group	Completely dissimilar side chains/unlikely cross-reactivity with each other[b,c]			
Cephaloridine(1st) Cephalothin (1st) Penicillin G	Cefaclor (2nd) Cephradine (1st) Cephalexin (1st) Cefadroxil (1st) Amoxicillin Ampicillin	Cefepime (4th) Ceftizoxime (3rd) Cefpirome (4th) Cefotaxime (3rd) Cefpodoxime (3rd) Ceftriaxone (3rd)	Cefoperazone (3rd) Cefotetan (2nd) Cefazolin (1st) Cefuroxime (2nd) Cefdinir (3rd) Cefditoren (3rd)	Cefixime (3rd) Cefprozil (2nd) Cefmetazole (2nd) Ceftibuten (3rd) Ceftazidime (3rd) Cefoxitin (2nd)		
3-Position side chain						
Similar side chain/ cross-reactivity possible within group[b,d]	Similar side chain/ cross-reactivity possible within group	Similar Side chain/ cross-reactivity possible within group	Similar side chain/ cross-reactivity possible within group	Similar side chain/ cross-reactivity possible within group	Similar side chain/ cross-reactivity possible within group	Dissimilar side chain/unlikely cross-reactivity with each other[b,e]
Cefadroxil (1st) Cephalexin (1st)	Cefmetazole (2nd) Cefoperazone (3rd) Cefotetan (2nd)	Cefotaxime (3rd) Cephalothin (1st)	Ceftibuten (3rd) Ceftizoxime (3rd)	Cefuroxime (2nd) Cefoxitin (2nd)	Cefdinir (3rd) Cefixime (3rd)	Cefpodoxime (3rd) Cefprozil (2nd) Ceftibuten (3rd) Ceftriaxone (3rd) Cefepime (4th) Cefpirome (4th) Cefazolin (1st) Cefaclor (2nd) Ceftazidime (3rd)

Clinical cure after short- (5 days) or long-term (10 days) of amoxicillin therapy in outpatient children with CAP

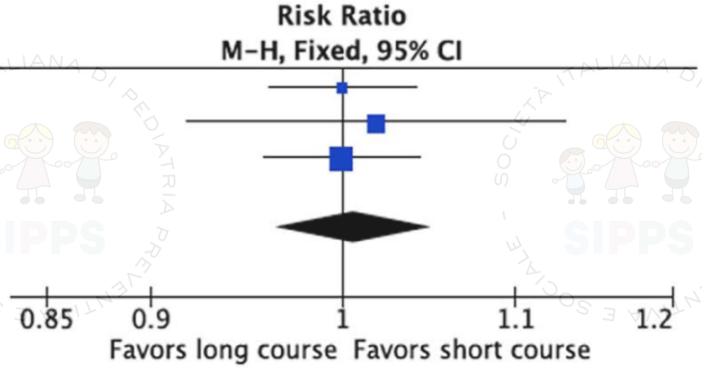
(from Marques IR, et al. Eur J Pediatr 2022)

a

Study or Subgroup	Short course Events	Total	Long course Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Greenberg 2014	42	42	56	56	15.7%	1.00 [0.96, 1.04]
Pernica 2021	108	126	106	126	34.2%	1.02 [0.92, 1.13]
Williams 2022	154	160	156	162	50.1%	1.00 [0.96, 1.04]
Total (95% CI)		**328**		**344**	**100.0%**	**1.01 [0.96, 1.05]**
Total events	304		318			

Heterogeneity: $Chi^2 = 0.24$, df = 2 (P = 0.89); $I^2 = 0\%$

Test for overall effect: Z = 0.29 (P = 0.77)

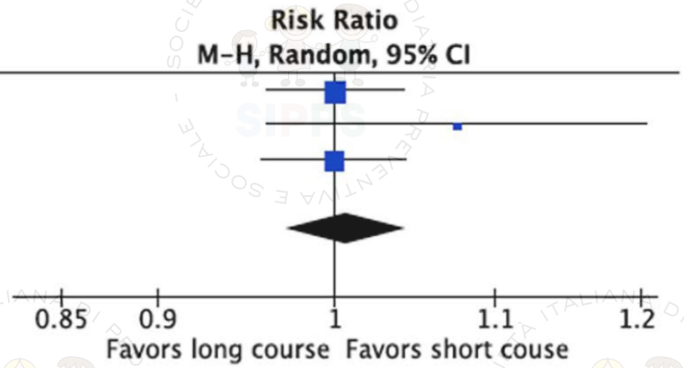


b

Study or Subgroup	Short course Events	Total	Long course Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Greenberg 2014	42	42	56	56	47.1%	1.00 [0.96, 1.04]
Pernica 2021	88	98	76	91	9.1%	1.08 [0.96, 1.20]
Williams 2022	154	160	156	162	43.8%	1.00 [0.96, 1.04]
Total (95% CI)		**300**		**309**	**100.0%**	**1.01 [0.97, 1.04]**
Total events	284		288			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.71$, df = 2 (P = 0.26); $I^2 = 26\%$

Test for overall effect: Z = 0.35 (P = 0.72)



a Clinical cure of children 6 month to 10 years old.
b Clinical cure analysis restricted to children aged 6–71 months

PRINCIPAL BACTERIA CAUSING CHILDHOOD CAP BY AGE

(From Principi N & Esposito S, Thorax 2011)

Bacteria	Age group			
	Birth to 1 month	1 to 3 months	3 months to 5 years	5 to 18 years
Streptococcus pneumoniae	+	+++	++++	+++
*Haemophilus influenzae**	+	+	+	±
Streptococcus pyogenes		+	+	+
Staphylococcus aureus	++	++	+	+
Streptococcus agalactiae	+++	+		
Escherichia coli	++	+		
Mycoplasma pneumoniae		+	++	++++
Chlamydiophyla pneumoniae		+	+	++
Chlamydia trachomatis	+	++		
Bordetella pertussis	±	++	+	+

Sembra tutto facile.

In realtà, se tutte le CAP di territorio fossero trattate con antibiotici seguendo queste raccomandazioni, è molto probabile che ci sarebbe egualmente un alto numero di errori prescrittivi, probabilmente per eccessivo uso di antibiotici.

Per ridurre questo rischio bisogna:

1) essere quanto più possibile certi della diagnosi di CAP

2) cercare di differenziare le forme virali dalle batteriche

Terapia antibiotica dell' OTITE MEDIA ACUTA

2019 – LG italiana – OMA non complicata *

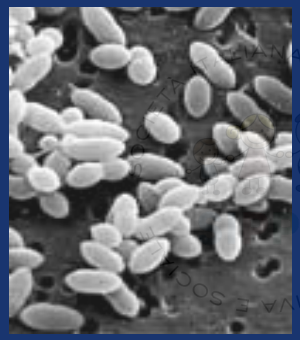
Lateralità	Bilaterale		Monolaterale	
Severità Sintomi	Grave	Lieve	Grave	Lieve
Età < 6 mesi	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Antibiotico Immediato** *(raccomandazione positiva forte)*
Età 6 – 24 mesi	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Antibiotico Immediato** *(raccomandazione positiva debole)*
Età > 24 mesi	**Antibiotico Immediato** *(raccomandazione positiva forte)*	**Attesa Vigile** *(raccomandazione positiva forte)*	**Attesa Vigile** *(raccomandazione positiva debole)*	**Attesa Vigile** *(raccomandazione positiva forte)*

*** NO OTORREA, NO RICORRENZA RECENTE, NO COMPLICANZE**

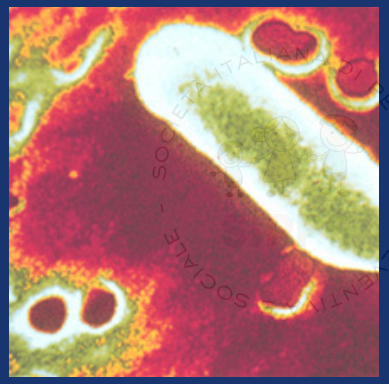
LG OMA 2019

Raccomandazione n° 6. La vigile attesa deve essere valutata nel singolo caso e condivisa con i genitori e può essere applicata solo nel caso in cui sia garantita la possibilità di follow-up entro 48 - 72 ore. **(Raccomandazione positiva forte)**

Patogeni in otite media acuta

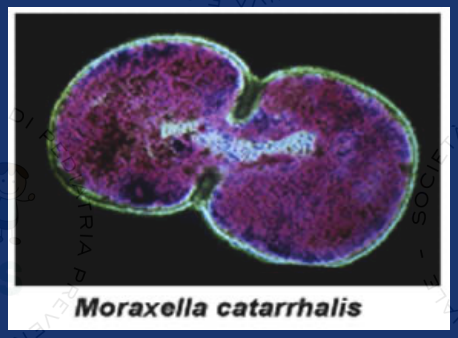


Streptococco Pneumoniae 32%



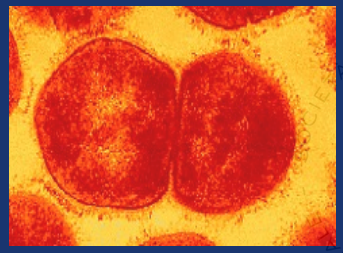
Moraxella Catarrhalis 16%

Haemophilus Influenzae 22%



Moraxella catarrhalis

Streptococco Pyogenes 5%



LG OMA 2019

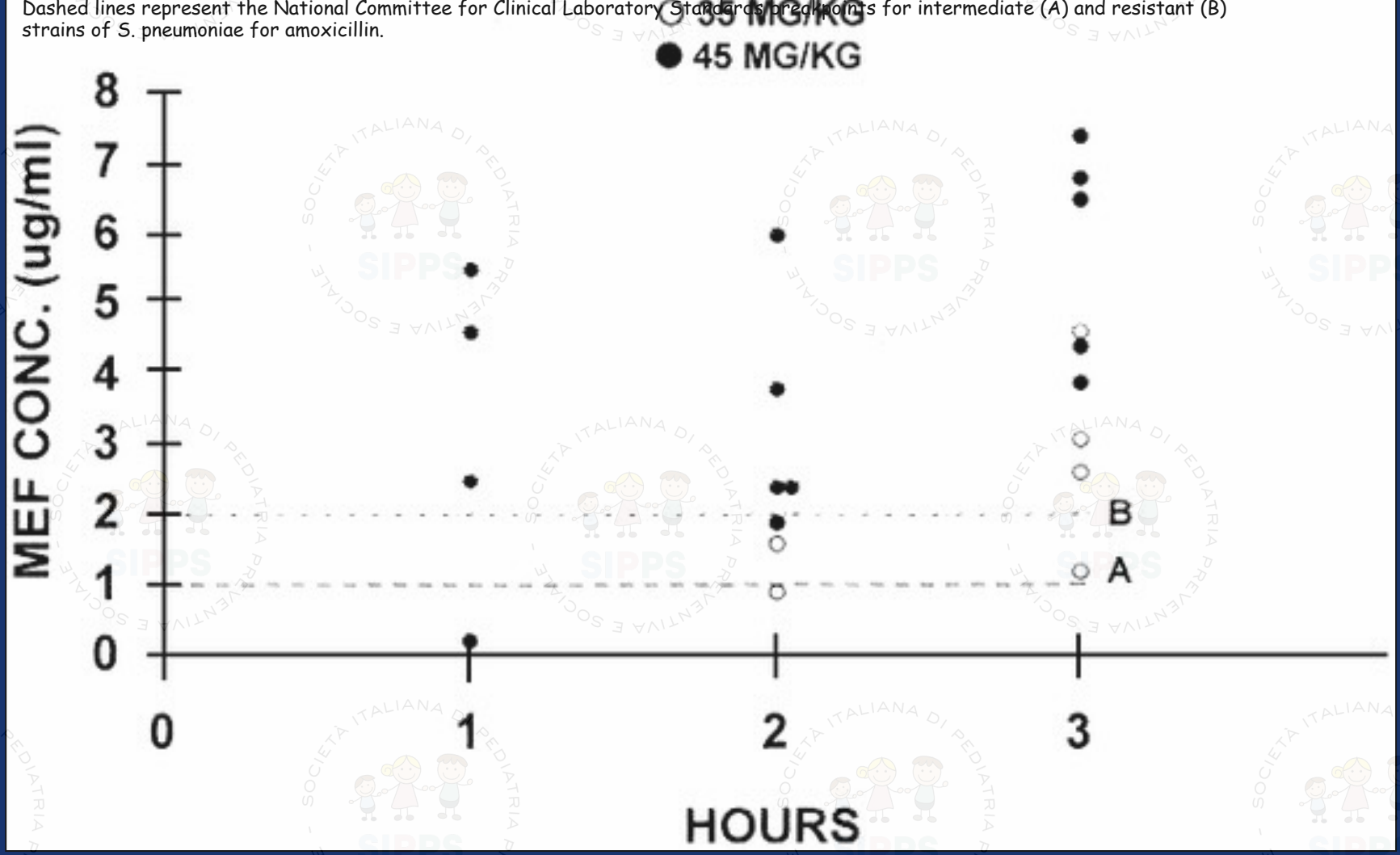
Caratteristiche Episodio	Terapia Raccomandata
Sintomi lievi No otorrea No ricorrenza No fattori R*	**Amoxicillina** (80-90 mg/kg/die in 3 dosi)
Sintomi gravi o congiuntivite purulenta Otorrea Ricorrenza	**Amoxicillina + acido clavulanico** (80 - 90** mg/kg/die in 3 dosi)

* fattori di rischio di maggior resistenza batterica: frequenza di comunità infantile, mancata vaccinazione antipneumococcica, provenienza da aree geografiche con elevata prevalenza di isolamento di batteri resistenti

MIDDLE EAR FLUID CONCENTRATIONS OF AMOXICILLIN AFTER LARGE DOSAGES IN CHILDREN WITH ACUTE OTITIS MEDIA.

Seikel, Kathleen; Shelton, Sharon; McCracken, George Pediatric Infectious Disease Journal. 16(7):710-711, July 1997.

Dashed lines represent the National Committee for Clinical Laboratory Standards breakpoints for intermediate (A) and resistant (B) strains of S. pneumoniae for amoxicillin.



LG OMA 2019

Durata – Raccomandazione

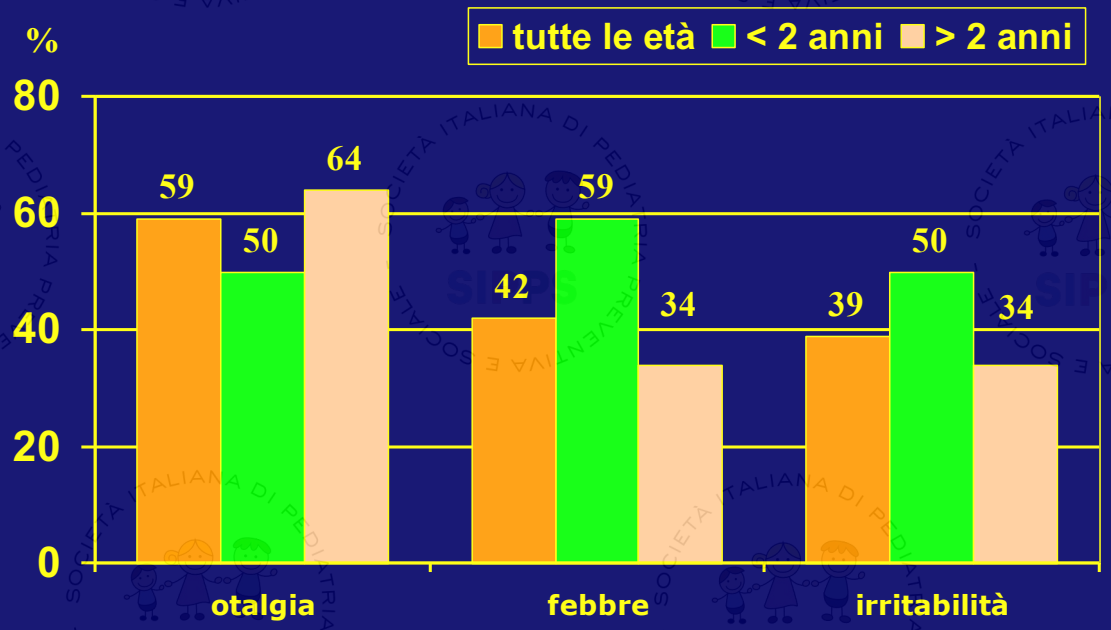
Raccomandazione n° 11. La durata della terapia antibiotica con amoxicillina o amoxicillina-acido clavulanico deve essere di 10 giorni in bambini a rischio di evoluzione sfavorevole (minori di 2 anni e/o con otorrea spontanea). **(Raccomandazione positiva forte)**

Raccomandazione n° 12. La durata può essere ridotta a 5 giorni in bambini senza rischio di evoluzione sfavorevole (bambini di età superiore a 2 anni, senza otorrea, senza bilateralità e senza sintomatologia grave) **(Raccomandazione positiva debole)**

RISULTATI

	trattamento 5 gg	trattamento 10 gg	differenza	*p value*
fallimenti	34%	16%	18%	
AOM-SOS score gg 6-14	1,61	1,34		0,07
AOM-SOS score gg 12-14	1,89	1,2		0,001
OME post-trattamento	65%	62%		ns
n. giorni totali di antibiotico	15 ± 12	21 ± 13		<0,001
eventi avversi (diarrea)	29%	30%		ns
eventi avversi (dermatite)	34%	33%		ns
fallimenti in bambini con patologia ricorrente	28%	19%		

Otite media acuta: sintomatologia in bambini di età compresa fra 6 mesi e 7 anni



Modificato, da Kontiokari T, PIDJ 1998

Symptoms or Symptom-Based Scores Cannot Predict Acute Otitis Media at Otitis-Prone Age

Miia K. Laine, Paula A. Tähtinen, Olli Ruuskanen, Pentti Huovinen and Aino Ruohola

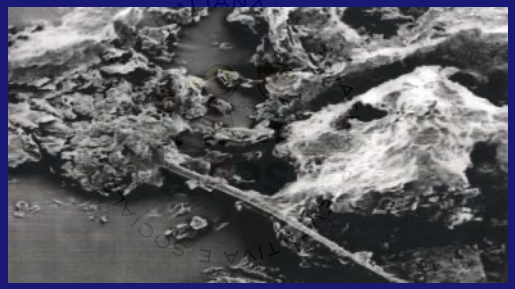
Pediatrics published online Apr 5, 2010;

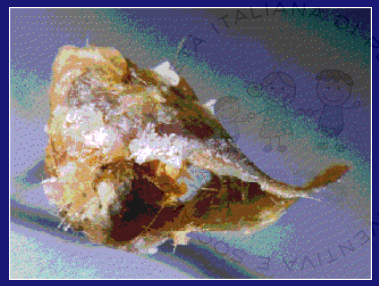
WHAT'S KNOWN ON THIS SUBJECT: Acute symptoms and scores are used as tools in the diagnosis and management of AOM. However, their predictive value for AOM is not known for young children whose parents suspect AOM.

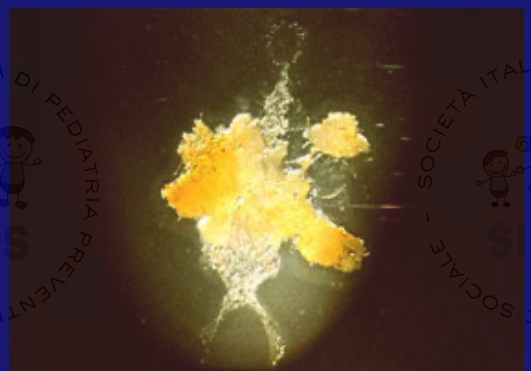
WHAT THIS STUDY ADDS: The occurrence, duration, and severity of symptoms are not predictive for AOM at otitis-prone age. Symptom-based scores cannot differentiate AOM from respiratory tract infection. Tympanic-membrane examination is crucial for the diagnosis and scoring of AOM.

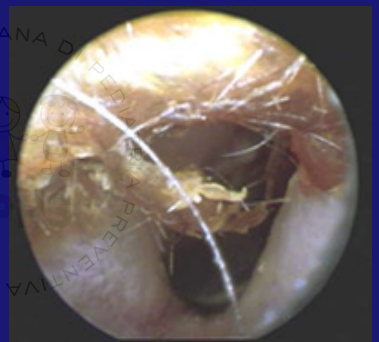
Raccomandazione

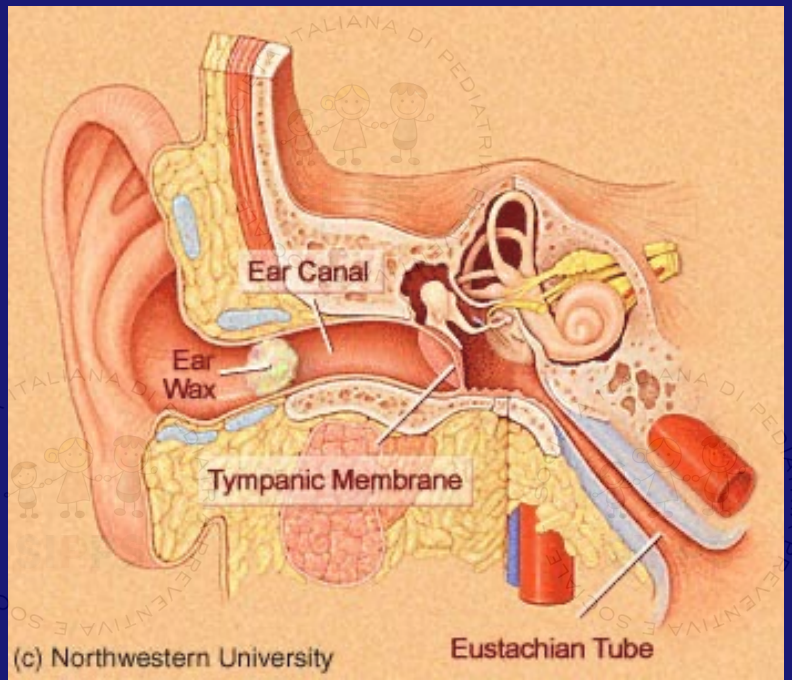
Per una otoscopia diagnostica è essenziale una visualizzazione il più completa possibile della membrana timpanica, con un canale uditivo esterno libero da cerume o corpi estranei (livello V, forza B)











La diagnosi puramente otoscopica di OMA raggiunge il maggiore grado di affidabilità quando condotta:

- con un otoscopio pneumatico
- corredato di una fonte luminosa adeguata
- di uno speculum delle dimensioni adatte e non colorato per evitare dispersioni della pressione

(LG OMA 2010: livello E: II, forza R: A, www.sip.it)

L'utilizzo della fase pneumatica deve essere evitato in caso di rilevante estroflessione della membrana timpanica o presenza di otorrea (livello VI, forza D)

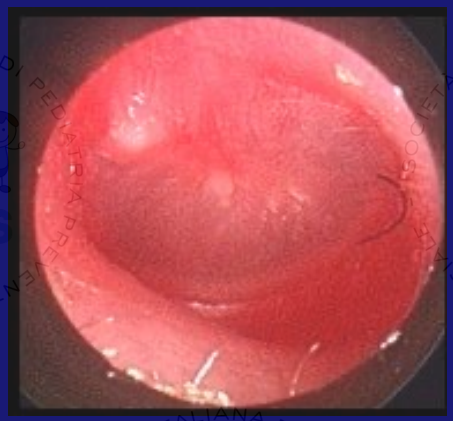
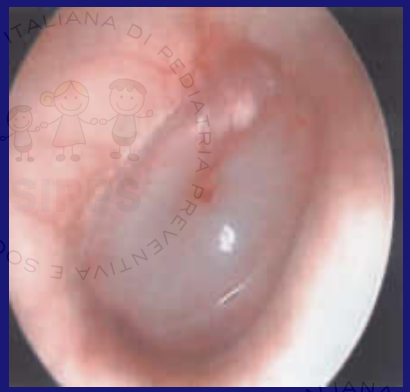
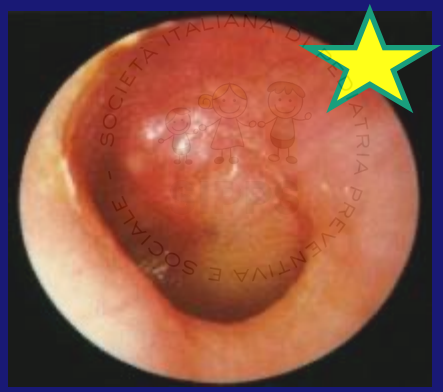
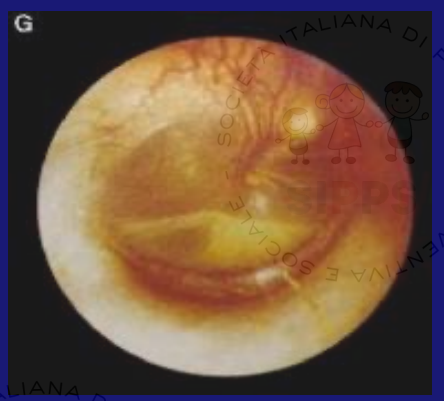
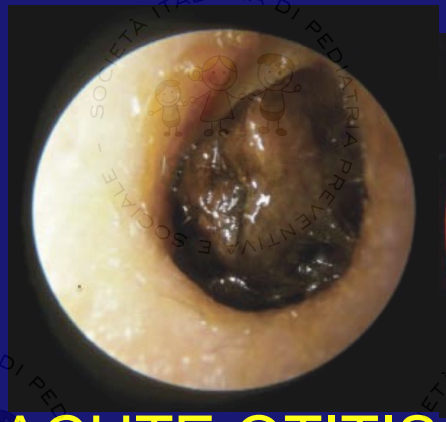
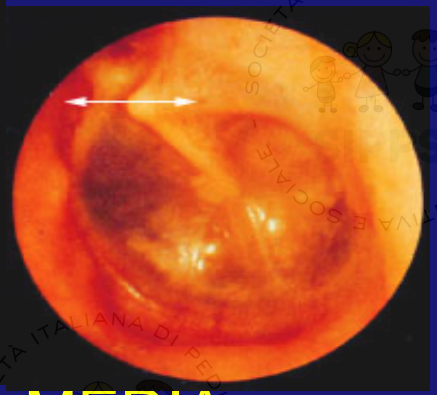
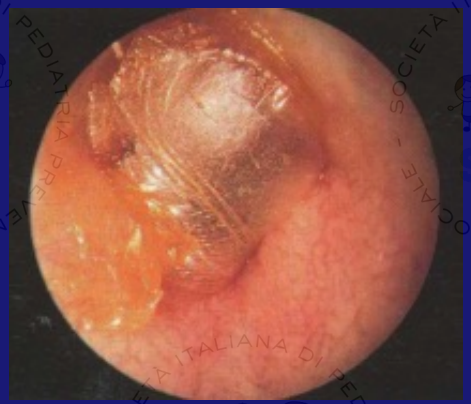
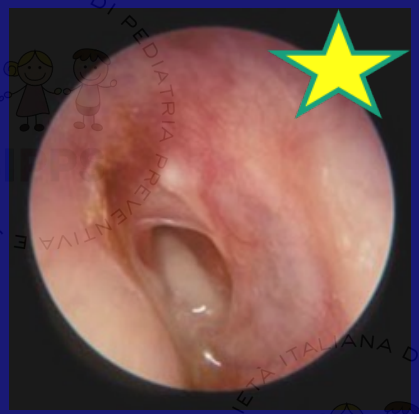
Guardare e descrivere la MT con metodo : COMPLETES

Kaleida PH. *The COMPLETES examforotitis*. Contemp. Pediatr 1997; 14: 93-101

- Color tympanic membrane (COLORE)
- Other condition (ALTRO)
- Mobility (MOBILITA')
- Position (POSIZIONE)
- Lighting (LUMINOSITA') (LATERALITA')
- Entire Surface (SUPERFICIE INTERA)
- Translucency (TRASPARENZA)
- External ear canal (CANALE ESTERNO LIBERO)
- Seal (TENUTA D'ARIA) (SEVERITA')

M.Doria 2011

OTITE MEDIA ACUTA
vera o falsa o immaginata?

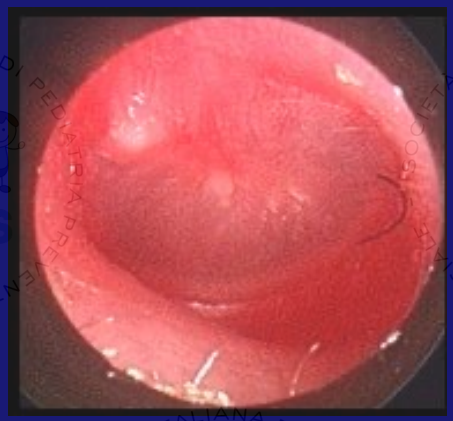
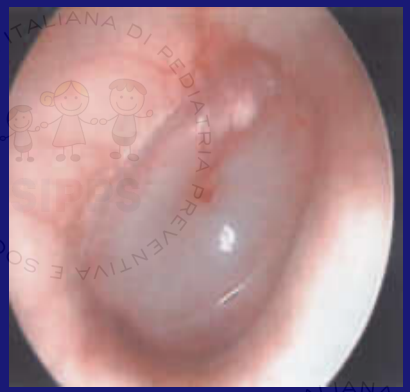
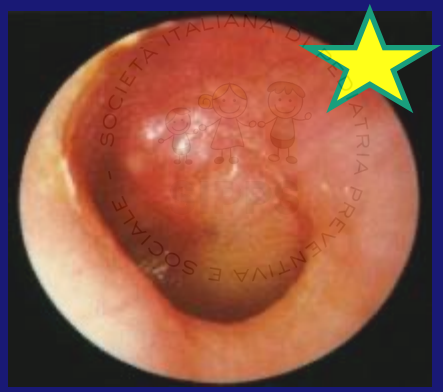
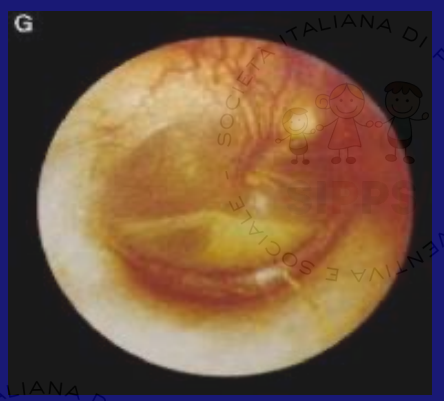
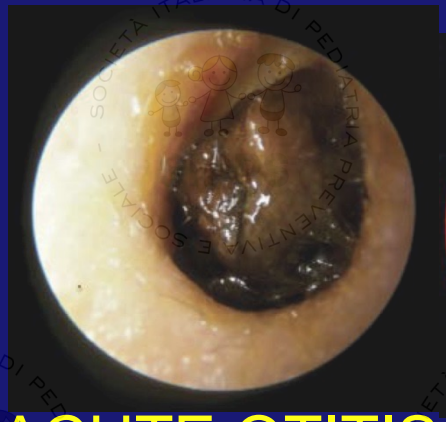
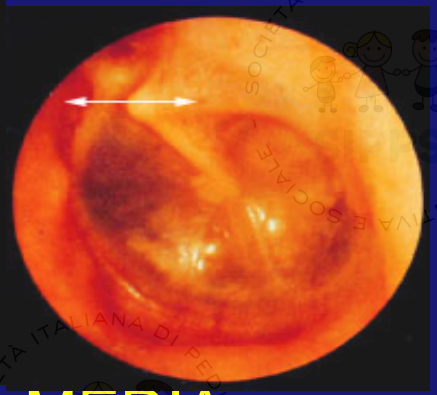
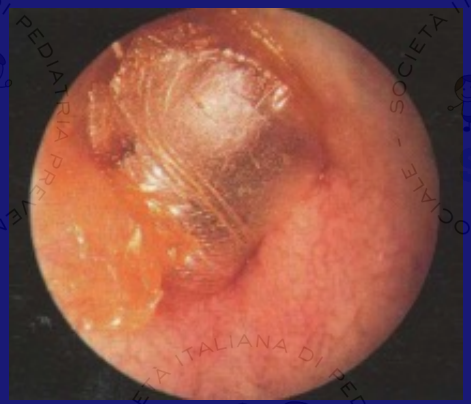
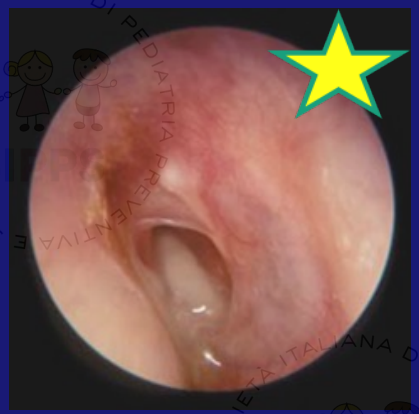









ACUTE OTITIS MEDIA

rapid onset of signs and symptoms of acute infection within the middle ear, with evidence of effusion


OTO
Next Ear Exam
Left
Right

OTITE MEDIA ACUTA
vera o falsa o immaginata?

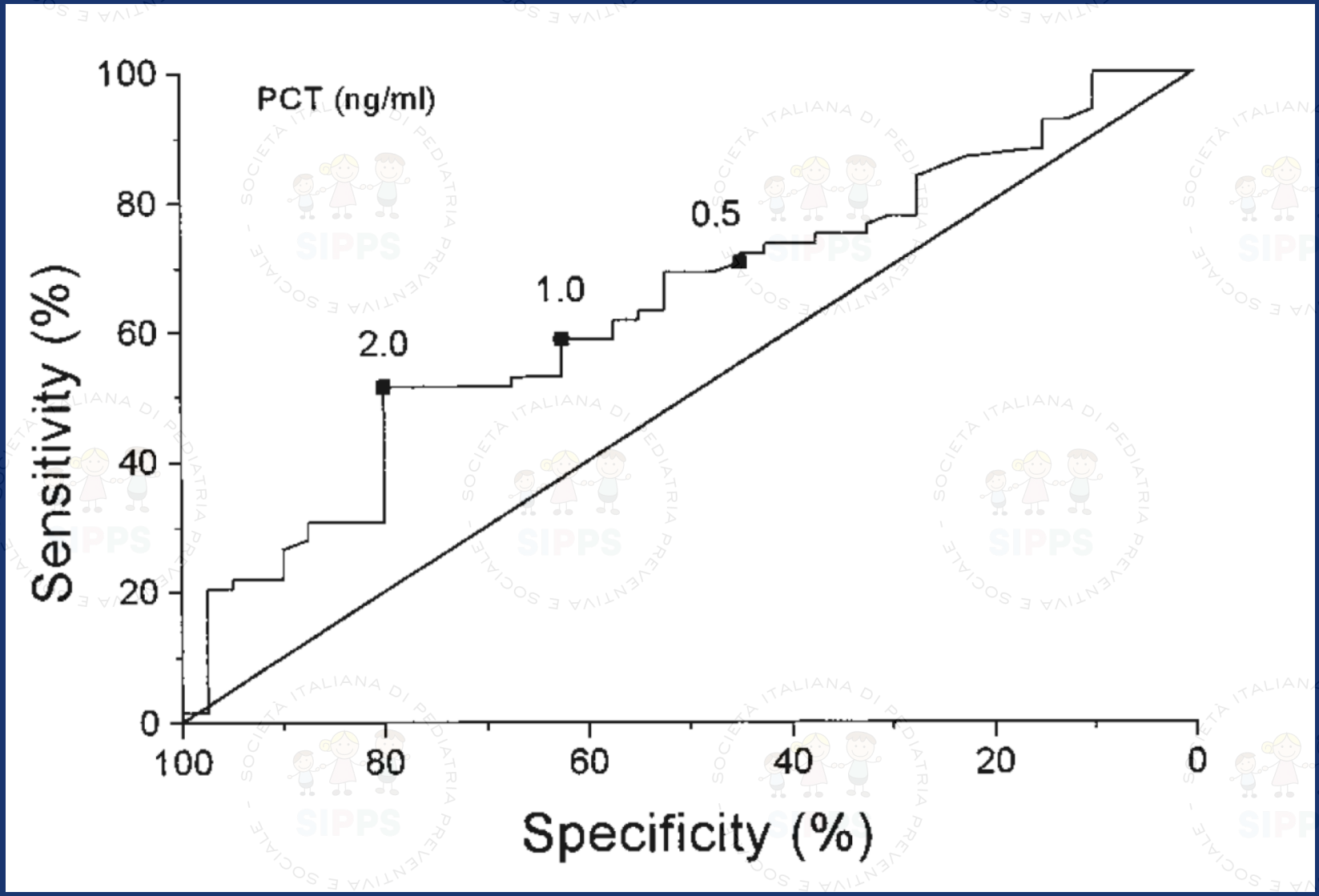









ACUTE OTITIS MEDIA

rapid onset of signs and symptoms of acute infection within the middle ear, with evidence of effusion

Procalcitonin for bacterial CAP diagnosis

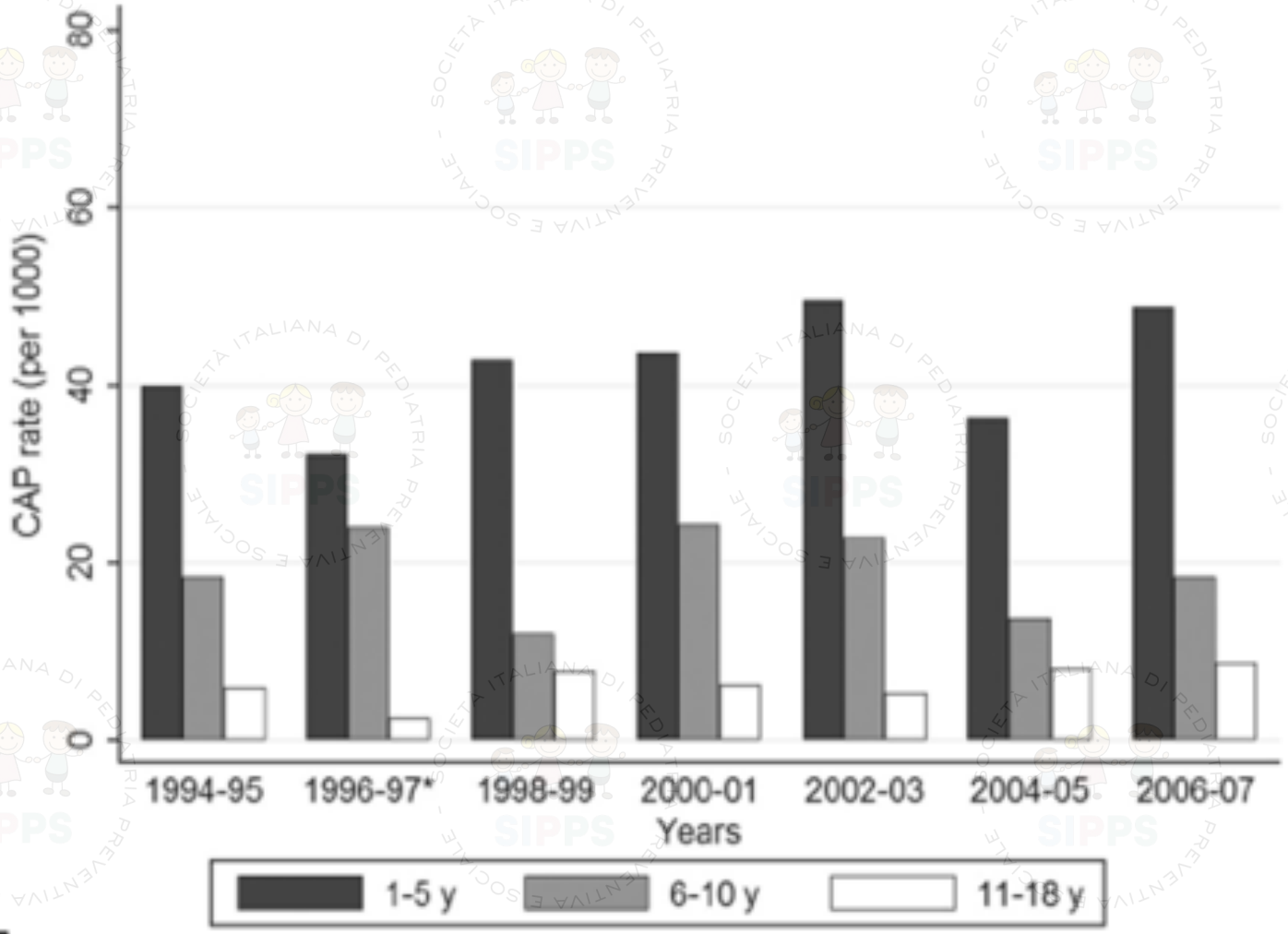
(from Toikka P, et al. Pediatr Infect Dis J 2000)



Combined evaluation of laboratory tests for bacterial CAP identification

- The highest likelihood ratio (1.74) was achieved with the combination CRP > 80 mg/L or WBC > 17.0 × 109/L or PCT > 0.84 μg/L) or ESR > 63 mm/h For this combination, the sensitivity was 61% and the specificity 65%.

- There was no combination of these markers which was sufficiently sensitive and specific to be used in clinical pediatric practice.



Two-yearly community-acquired pneumonia rates by age group. *Estimate for the 11- to 18-year-old age group contains fewer than 30 unadjusted records.

From Kronman M et al., Pediatrics 2011

Criteria for Hospitalization of Children With CAP

Respiratory Distress	Age-adjusted Tachypnea SpO2 <90–93% in room air (if FiO_2 >0.50, ICU or continuous cardiorespiratory monitoring are required to maintain saturation >92%) Cyanosis Retractions Grunting Nasal flaring
Capillary refill time >2 min Dehydration Vomiting/not feeding	
Comorbidities (eg, congenital heart disease, chronic lung disease of prematurity, chronic respiratory conditions leading to infection such as cystic fibrosis, bronchiectasis, immunodeficiency)	
Etiological agent (eg, MRSA, bacterial/viral coinfections)	
Unreliable family environment	

Espo[illegible] Sharland M, Spoulou V, Syrogiannopoulos GA, Usonis V, Vergison A, Schaad UB. Pediatr Infect Dis J. 2012 Jun;31(6):e78-85.

CRITERIA USED TO DEFINE SEVERITY OF CAP

(British Thoracic Society, Thorax 2011)

Table 6 Severity assessment

	Mild to moderate	Severe
Infants	Temperature <38.5°C	Temperature >38.5°C
	Respiratory rate <50 breaths/min	Respiratory rate >70 breaths/min
	Mild recession	Moderate to severe recession
	Taking full feeds	Nasal flaring
		Cyanosis
		Intermittent apnoea
		Grunting respiration
		Not feeding
		Tachycardia*
		Capillary refill time ≥2 s
Older children	Temperature <38.5°C	Temperature >38.5°C
	Respiratory rate <50 breaths/min	Respiratory rate >50 breaths/min
	Mild breathlessness	Severe difficulty in breathing
	No vomiting	Nasal flaring
		Cyanosis
		Grunting respiration
		Signs of dehydration
		Tachycardia*
		Capillary refill time ≥2 s

*Values to define tachycardia vary with age and with temperature.[67[II]]

Rispetto alla CAP grave che viene ospedalizzata, la CAP curata sul territorio è quella che pone il più elevato rischio di abuso e di cattivo uso degli antibiotici perché:

- Maggiore è il rischio di abuso perché:
  la diagnosi è meno certa (no radiografia, pochissimo uso dell'ecografia, scarsa utilità diagnostica dei segni e sintomi di malattia)
  la differenziazione delle forme batteriche dalle virali è estremamente difficile (poca efficacia dei test di laboratorio disponibili sul territorio)

- Maggiore è il rischio di cattivo uso perché:
  difficile, se non impossibile, l'identificazione del batterio responsabile della malattia

Test microbiologici rapidi

- *Streptococcus penumoniae* sulle urine: non utile per l'elevata dimensione dei portatori sani
- Test influenza e SARS-CoV2: buona attendibilità anche se variabile in funzione epidemiologia
- Test RSV antigenico: scarsa attendibilità

Le difficoltà di fare diagnosi di CAP e quelle di individuare l'esatta eziologia o, almeno, di diagnosticare le forme virali creano due inevitabili fenomeni:

1) complicano pesantemente l'esecuzione di studi clinici controllati capaci di valutare la necessità e l'efficacia di una qualsiasi terapia antibiotica.

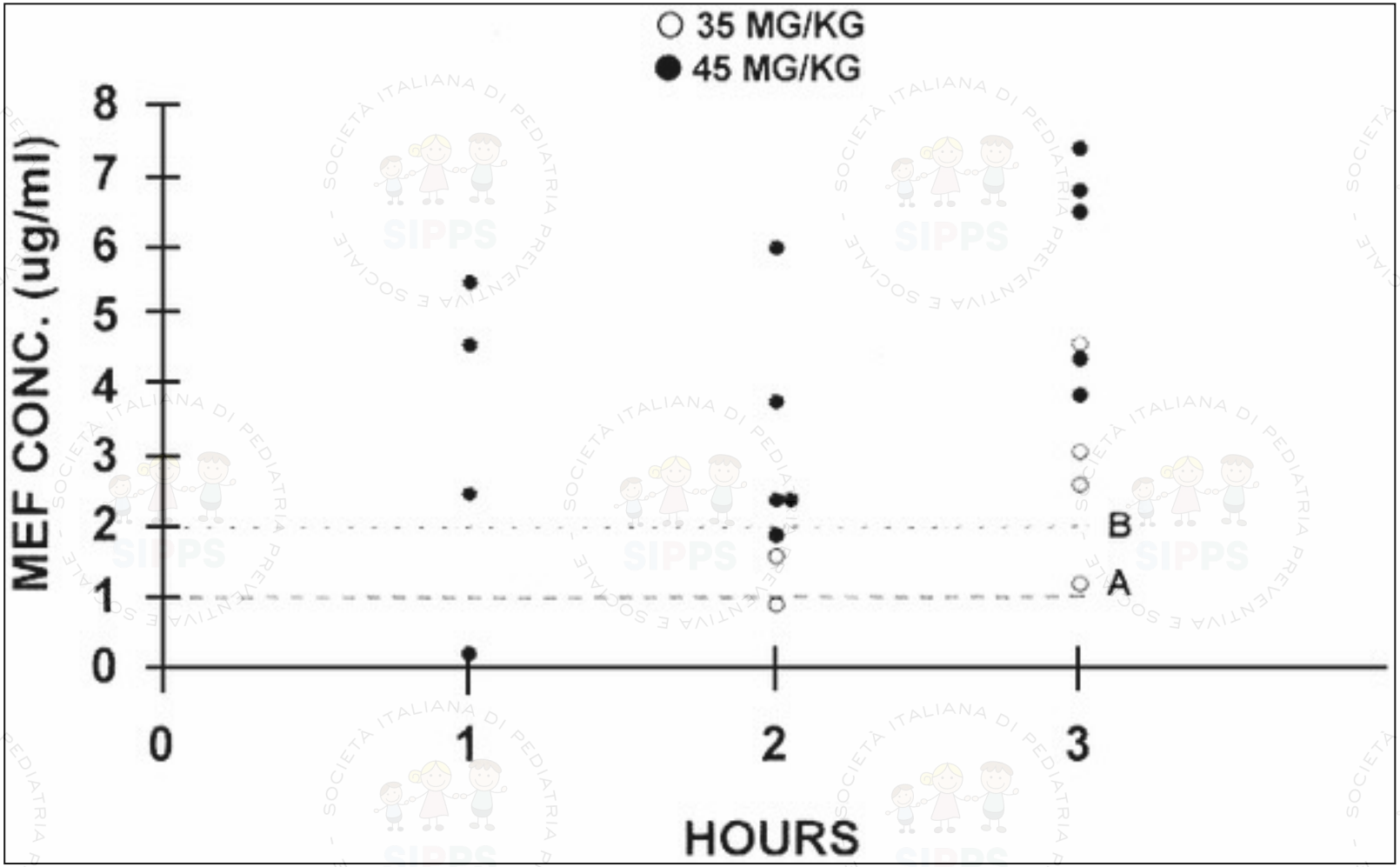
2) rendono impossibile lo stabilire raccomandazioni terapeutiche assolute e totalmente indiscutibili

Quindi, a fronte di una CAP di lieve o media entità il medico ha due possibili scelte. Trattarle tutte o cercare di selezionare i casi sfruttando al massimo le sue conoscenze cliniche, i possibili dati laboratoristici e la situazione epidemiologica locale. In ogni caso la scelta deve essere tale da limitare al massimo il cattivo uso di antibiotici

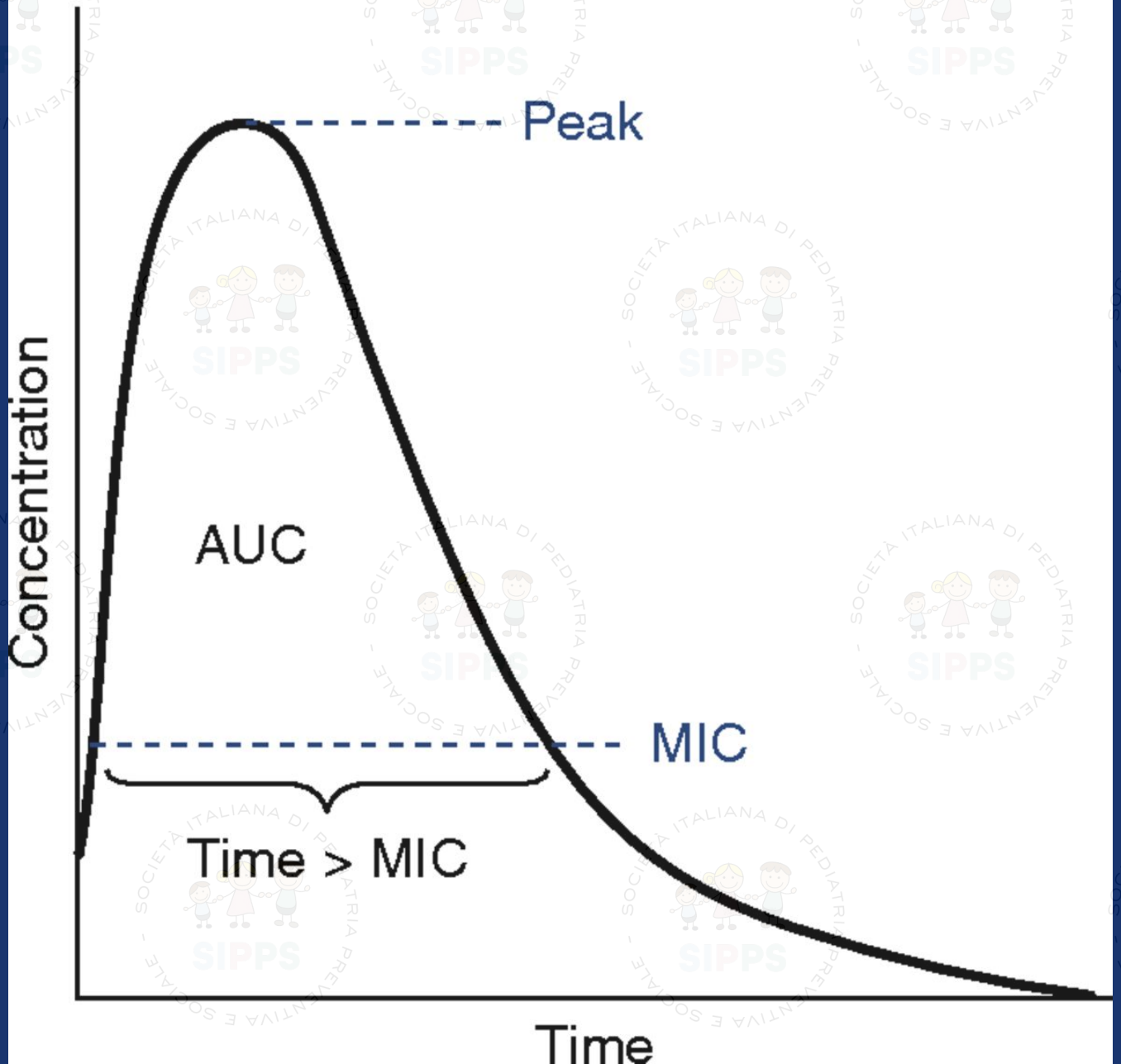
MIDDLE EAR FLUID CONCENTRATIONS OF AMOXICILLIN AFTER LARGE DOSAGES IN CHILDREN WITH ACUTE OTITIS MEDIA.

Seikel, Kathleen; Shelton, Sharon; McCracken, George Pediatric Infectious Disease Journal. 16(7):710-711, July 1997.

Dashed lines represent the National Committee for Clinical Laboratory Standards breakpoints for intermediate (A) and resistant (B) strains of S. pneumoniae for amoxicillin.



Pharmacodynamic parameters on a concentration-time curve



CONCLUSIONI

Il problema maggiore che ha il pediatra a fronte di un bambino nel quale sospetta una polmonite di lieve entità e che può rimanere a casa è quello di confermare la diagnosi e decidere se trattarlo o meno.
Una attenta valutazione della sintomatologia clinica può essere utile a sottrarre qualche caso alla terapia antibiotica
Se decide di trattare, la scelta è sempre sull'amoxicillina con qualche problema nella valutazione del dosaggio e del frazionamento giornaliero
La durata è di 5 giorni ma è richiesta una attenta osservazione per evidenziare i casi che non rispondono in modo adeguato e richiedere il cambio di terapia o il ricovero.

SPONTANEOUS RESOLUTION OF ACUTE OTITIS MEDIA

PATHOGEN	FREQUENCY (%)
Moraxella catarrhalis	80
Haemophilus influenzae	50
Streptococcus pneumoniae	20

Episodes of Rx-confirmed CAP with viruses in children aged 13-36 months

(Esposito S et al., Influenza Other Respir Viruses. 2013)

	2007-08		2008-09		2009-10		Total episodes	
VIRUS	No. (%) *	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^	No. (%)*	Coinf. No.(%)^
RSV	35 (41.1)	16	58 (38.6)	21	30 (30.3)	10	123 (36.8)	47
Rhinovirus	26 (30.5)	15	44 (29.3)	21	24 (24.2)	7	94 (28.1)	43
Bocavirus	12 (14.1)	9	15 (10.0)	11	12 (12.1)	6	39 (11.6)	26
Influenza	4 (4.7)	1	16 (10.6)	6	10 (10.1)	1	39 (11.6)	8
Metapneumo.	12 (14.1)	5	13(8.6)	4	6 (6.1)	0	31 (9.2)	9
Coronavirus	3 (3.5)	2	7 (5.8)	3	5 (5.0)	4	15 (4.5)	9
Parainfluenza (1-4)	0 (0)	0	4 (2.6)	2	6 (6.1)	2	10 (3.0)	4
Adenovirus	1 (1.1)	0	4 (2.6)	3	2 (2.0)	1	7 (2.1)	4
Episodes with viruses	68/85 (80.0)	20/68 (29.4)	122/150 (81.3)	36/122 (29.5)	78/99 (78.8)	14/78 (17.9)	268/334 (80.2)	70/268 (26.1)

- % among the total number of CAP investigated;
- ^ % of the total number of infections in which the single virus was identified

PRINCIPAL BACTERIA CAUSING CHILDHOOD CAP BY AGE

(From Principi N & Esposito S, Thorax 2011)

Bacteria	Age group			
	Birth to 1 month	1 to 3 months	3 months to 5 years	5 to 18 years
Streptococcus pneumoniae	+	+++	++++	+++
*Haemophilus influenzae**	+	+	+	±
Streptococcus pyogenes		+	+	+
Staphylococcus aureus	++	++	+	+
Streptococcus agalactiae	+++	+		
Escherichia coli	++	+		
Mycoplasma pneumoniae		+	++	++++
Chlamydiophyla pneumoniae		+	+	++
Chlamydia trachomatis	+	++		
Bordetella pertussis	±	++	+	+

Community acquired pneumonia pathogens in children by age group

(from Jain S, et al. NEJM 2015)

Pathogen	Younger than 2 years	2 to 4 years	5 to 9 years	10 to 17 years
Viral				
Adenovirus	18%	9%	4%	2%
Coronaviruses	6%	6%	3%	4%
Human metapneumovirus	14%	17%	10%	4%
Human rhinovirus	29%	25%	30%	19%
Influenza A/B	6%	5%	9%	11%
Parainfluenza virus 1 to 3	7%	8%	6%	4%
Respiratory syncytial virus	42%	29%	8%	7%
Bacterial				
Mycoplasma pneumoniae	2%	5%	16%	23%
Staphylococcus aureus	1%	1%	1%	1%
Streptococcus pneumoniae	3%	4%	4%	3%
Streptococcus pyogenes	1%	1%	< 1%	< 1%

RESEARCH LETTER

Acute Otitis Media in Children Younger Than 2 Years

Hoberman a et al

JAMA Pediatrics Published online September 2, 2013

Laterality and Severity of AOM at Entry	No. of Children With Treatment Failure/Total No. (%)					
	Pittsburgh Study[a]		Turku Study[b]		Combined Studies	
	AMOX/CLAV	Placebo	AMOX/CLAV	Placebo	AMOX/CLAV	Placebo
Unilateral nonsevere	4/39 (10)	15/42 (36)	6/33 (18)	11/23 (48)	10/72 (14)	26/65 (40)
Unilateral severe	2/29 (7)	14/28 (50)	9/48 (19)	19/42 (45)	11/77 (14)	33/70 (47)
Bilateral nonsevere	7/40 (18)	18/35 (51)	6/20 (30)	11/20 (55)	13/60 (22)	29/55 (53)
Bilateral severe	10/34 (29)	26/38 (68)	7/34 (21)	18/37 (49)	17/68 (25)	44/75 (59)