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Polmonite complicata: dal laboratorio alla terapia farmacologica

Dott.ssa Gaia Martelli

SOD di Pediatria – Direttore: Dott. Salvatore Cazzato
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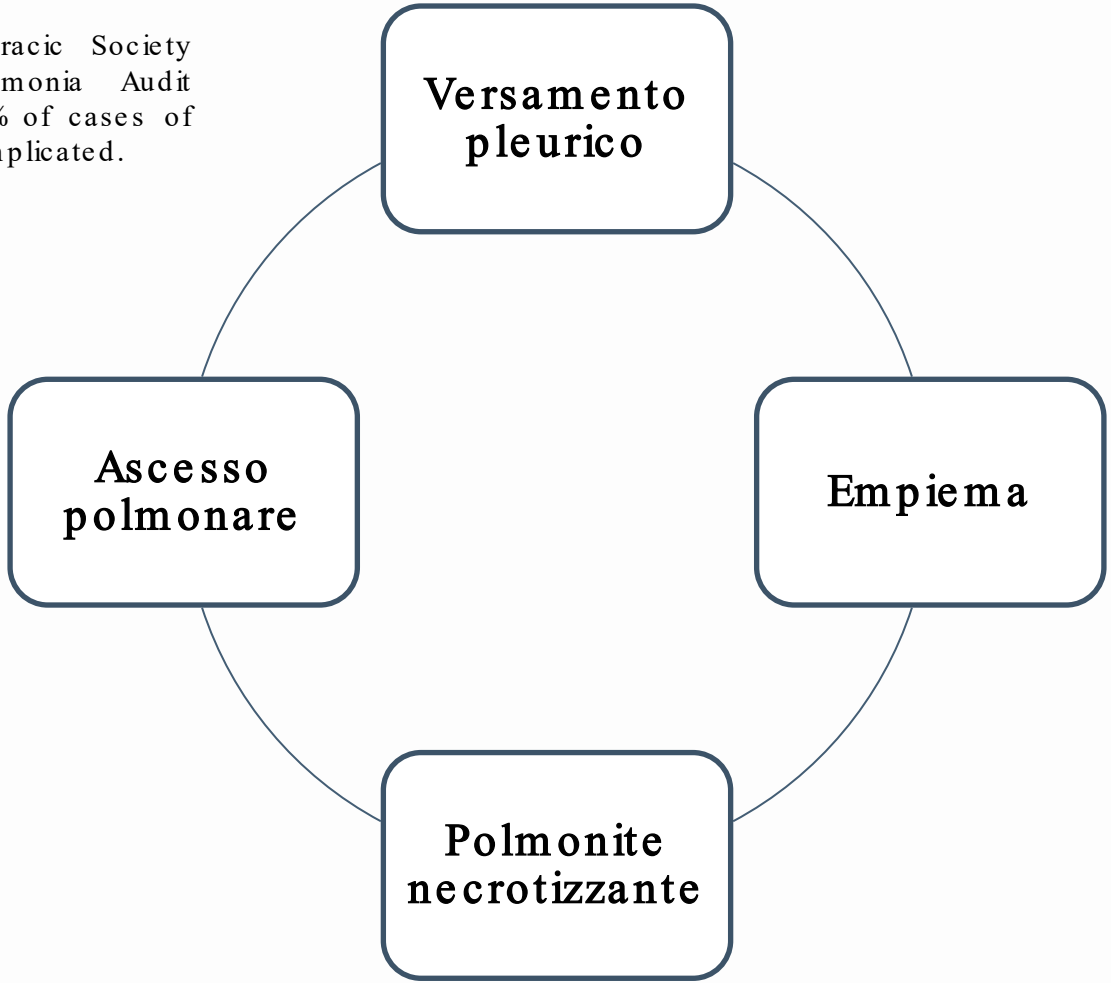
Azienda Ospedaliero-Universitaria delle Marche

The British Thoracic Society Paediatric Pneumonia Audit reported that 3% of cases of CAP become complicated.



Bradley JS et al.. Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76.

Parapneumonic effusion

- Defined as a collection of fluid in the pleural space associated with underlying pneumonia.
- In children, prospective studies of CAP in Europe and the Americas have demonstrated parapneumonic effusions in 2%–12%

Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, Kaplan SL, Mace SE, McCracken GH Jr, Moore MR, St Peter SD, Stockwell JA, Swanson JT; Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76.

Parapneumonic empyema

- Collection of pus in the pleural space associated with an underlying pneumonia.
- Pus may be defined by gross appearance, WBC count (50 000 WBCs/ microL), or positive bacterial culture.

Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, Kaplan SL, Mace SE, McCracken GH Jr, Moore MR, St Peter SD, Stockwell JA, Swanson JT; Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76.

Necrotizing pneumonia

- Extensive destruction and liquefaction of lung tissue
- Necrosis rapidly progresses to cavitation (**pneumatoceles**), which is generally peripheral and limited to a single lobe. Small cavities can coalesce and form large cysts with air-fluid levels, mimicking a lung abscess. Rupture into the pleural space can create **bronchopleural fistula**.
- Necrotising pneumonia complicates up to 7% of all cases of paediatric CAP.

Lung abscess

- A lung abscess is a thick-walled cavity that contains purulent material resulting from a pulmonary infection.
- The pathogenesis of lung abscess involves an area of initial pneumonitis that leads to necrosis, cavitation and abscess formation. **Pulmonary aspiration** may be a central factor.
- A **primary** lung abscess occurs in a previously well child with normal lungs.
- A **secondary** lung abscess occurs in children with an underlying lung abnormality, which may be congenital (cystic fibrosis, immunodeficiency or structural as in a congenital cyst adenomatoid malformation) or acquired (achalasia or a neurodevelopmental abnormality such as cerebral palsy with repeated pulmonary aspiration and suppurative lung disease).
- The presence of a factor predisposing to lung abscess will influence the likelihood of certain pathogens being isolated.

Patradoon-Ho P, Fitzgerald DA. Lung abscess in children. Paediatr Respir Rev. 2007 Mar;8(1):77-84.

Laboratorio

Infections associated with necrotising pneumonia

Bacterial:	Viruses:	Fungi*:
Streptococcus pneumoniae	Influenza	*Aspergillus spp.*
Staphylococcus aureus	Adenovirus	*Candida spp.*
Streptococcus mitis spp.	Herpes group including -Cytomegalovirus (CMV), Varicella-Zoster, Epstein-Barr Virus (EBV)	*Histoplasma capsulatum*
Streptococcus pyogenes (Group A Streptococcus)		*Coccidioides spp.*
Mycoplasma pneumoniae		*Blastomyces spp.*
Pseudomonas spp.		*Cryptococcus neoformans*
Fusobacterium spp.		

* A primary fungal cause is very rare in immunocompetent individuals but must be considered in immunosuppressed or immunodeficient patients.

Most frequent aetiologic identification of necrotizing pneumonia in 22 studies with 1408 patients.

	Subjects included on studies (*)	Positive blood culture	Positive pleural culture	Positive molecular on blood	Positive molecular on pleural fluid	Not discriminated	Total
S. pneumoniae	1280	18	65	24	78	81	266 (21 %)
S. aureus	1116	3	1	0	4	49*	57 (5 %)
Streptococcus Group A	108	0	2	2	8	(**)	12 (11 %)
M. pneumoniae#	197	0	0	0	5	73	78* (39 %)

(*)many studies included patients with different identified etiologies.
(**)some studies include other agents without any details.
(#) Methods: Paired IGM antibodies MP, PCR for MP in nasopharyngeal aspiration or in bronchoalveolar lavage.

Spencer DA, Thomas MF. Necrotising pneumonia in children. Paediatr Respir Rev. 2014 Sep;15(3):240-5; quiz 245.

Teresinha Mocelin H, Bueno Fischer G, Danezi Piccini J, de Oliveira Espinel J, Feijó Andrade C, Bush A. Necrotizing Pneumonia In Children: A Review. Paediatr Respir Rev. 2024 Feb 20:S1526-0542(24)00020-4.

Streptococcus Pneumoniae

- The most prevalent, with an identification rate between 18 and 83 %.
- Introduction of the first 7-valent conjugate pneumococcal vaccine was associated with an **initial rapid reduction** in the incidence of pneumonia and complicated disease,
- Unfortunately some of these benefits were **short lived** and there followed an increase in empyema related to serotypes not present in the vaccine.
- Following global replacement of PCV7 with 13-valent PCV (PCV13, containing additional Serotypes 1, 3, 5, 6A, 7F, and 19A), incidence and hospitalization rates for empyema reduced substantially
- An increased trend in hospital admissions was found in the late post-PCV13 period, especially due to S. pneumoniae cases.
- In Italy, S. pneumoniae serotype 3 is the most associated with NP occurring even in children with a complete vaccination schedule with PCV13

Spencer DA, Thomas MF. Necrotising pneumonia in children. Paediatr Respir Rev. 2014 Sep;15(3):240-5; quiz 245.

Teresinha Mocelin H, Bueno Fischer G, Danezi Piccini J, de Oliveira Espinel J, Feijó Andrade C, Bush A. Necrotizing Pneumonia In Children: A Review. Paediatr Respir Rev. 2024 Feb 20:S1526-0542(24)00020-4.

Staphilococcus Aureus

- The frequency and morbidity of community-acquired methicillin-resistant S. aureus (CA-MRSA) has **significantly increased** in the last decade.
- Although rare, pneumonia caused by S. aureus producing Panton-Valentine leukocidin is potentially serious, with a high mortality rate. PVL is a virulence factor produced by up to 74–100 % of CA-MRSA

Teresinha Mocelin H, Bueno Fischer G, Danezi Piccini J, de Oliveira Espinel J, Feijó Andrade C, Bush A. Necrotizing Pneumonia In Children: A Review. Paediatr Respir Rev. 2024 Feb 20:S1526-0542(24)00020-4.

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Streptococcus pyogenes (Group A Streptococcus)		*Coccidioides spp.*
Mycoplasma pneumoniae		*Blastomyces spp.*
Pseudomonas spp.		*Cryptococcus neoformans*
Fusobacterium spp.		

* A primary fungal cause is very rare in immunocompetent individuals but must be considered in immunosuppressed or immunodeficient patients.

- Rarely the sole cause of NP
- Greater risk of secondary bacterial CAP
- Viruses can decrease bacterial clearance by disrupting the respiratory epithelial barrier, impairing mucociliary function, increasing bacterial adherence by upregulating adherence proteins, and modulating immune function

Spencer DA, Thomas MF. Necrotising pneumonia in children. Paediatr Respir Rev. 2014 Sep;15(3):240-5; quiz 245.

Masters IB, Isles AF, Grimwood K. Necrotizing pneumonia: an emerging problem in children? Pneumonia (Nathan). 2017 Jul 25;9:11.

Eur Respir J 2008; 31: 1285–1291
DOI: 10.1183/09031936.00099807

Necrotising pneumonia is an increasingly detected complication of pneumonia in children

G.S. Sawicki*,+, F.L. Lu*,+, C. Valim#, R.H. Cleveland¶ and A.A. Colin*

- Studio retrospettivo osservazionale
- Bambini ospedalizzati al Children's Hospital Boston per polmonite necrotizzante da Gennaio 1990 a Febbraio 2005 (80 casi)

Su sangue:
- Leucocitosi
- Anemia
- Ipoalbuminemia
- Incremento degli indici di infiammazione (PCR, VES)

Su liquido pleurico:
- pH basso*
- Ridotto glucosio
- Elevata cellularità con predominanza neutrofilica
- Esame colturale positivo (indipendentemente da antibiotico pre-ospedalizzazione)

TABLE 2 Laboratory values of patients with necrotising pneumonia at the time of admission

	Summary statistics	Subjects
Serum laboratory values		
WBC count $\times 10^3$ cells·μL^{-1}	18.4±8.9	77
Haemoglobin g·dL^{-1}	10.4±1.6	74
Haematocrit %	30.9±4.4	75
Albumin g·dL^{-1}	2.0±1.6	40
Erythrocyte sedimentation rate mm·h^{-1}	96.7±22.9	21
C-reactive protein mg·dL^{-1}	13.3±9.3	20
Pleural fluid values		
pH	7.08±0.33	50
Glucose mg·dL^{-1}	10.0 (2.0–65.5)	44
LDH IU·L^{-1}	2810 (1413–9530)	43
Cell count $\times 10^3$ cells·μL^{-1}	9.6 (1.2–56.2)	54
Pleural neutrophils %	70±23.4	52
Culture results		
Any bacterial organism identified	38 (48)	80

Data are presented as mean±SD, n, median (interquartile range) or n (%). WBC: white blood cell; LDH: lactate dehydrogenase.

*Nei bambini, valori di pH < 7.2 sono stati associati a necessità di drenaggio pleurico

Bradley JS et al. Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76.

Sawicki GS, Lu FL, Valim C, Cleveland RH, Colin AA. Necrotising pneumonia is an increasingly detected complication of pneumonia in children. Eur Respir J. 2008 Jun;31(6):1285-91.

- Less than 10 % of blood cultures are positive, probably due to previous use of antibiotics
- Sensitivity is higher in pleural fluid culture, but culture-independent methods are a good alternative in the etiological definition of culture-negative cases (qPCR and immunochromatographic assay for antigen detection)
- **Therefore, ideally, both culture-based and molecular detection techniques should be used to determine aetiology.**
- The studies of children with NP displayed in Table 1 show positive microbiology results in 8–55% of cases

Masters IB, Isles AF, Grimwood K. Necrotizing pneumonia: an emerging problem in children? Pneumonia (Nathan). 2017 Jul 25;9:11.

Teresinha Mocelin H, Bueno Fischer G, Danezi Piccini J, de Oliveira Espinel J, Feijó Andrade C, Bush A. Necrotizing Pneumonia In Children: A Review. Paediatr Respir Rev. 2024 Feb 20:S1526-0542(24)00020-4.

- Sierologia per Mycoplasma

- Esame colturale dell'espettorato:
  - Non facilmente realizzabile in età pediatrica
  - Il riscontro di Pneumococco può avvenire anche in bambini sani

- L'isolamento di virus nelle vie respiratorie può essere utile nella comprensione della patogenesi e nelle misure di isolamento, ma non deve guidare il successivo management (rischio di sospensione di antibiotici)

Masters IB, Isles AF, Grimwood K. Necrotizing pneumonia: an emerging problem in children? Pneumonia (Nathan). 2017 Jul 25;9:11.

Received: 17 February 2022 | Revised: 5 August 2022 | Accepted: 12 October 2022

DOI: 10.1111/ped.15386

ORIGINAL ARTICLE

PEDIATRICS INTERNATIONAL WILEY

Risk factors for complicated community-acquired pneumonia in children

Gökçen Dilşa Tuğcu[1] | Beste Özsezen[1] | İrem Türkyılmaz[2] | Betül Pehlivan Zorlu[2] | Sanem Eryılmaz Polat[1] | Aslınur Özkaya Parlakay[3] | Güzin Cinel[1]

- Retrospective cohort study
- 111 patients with CAP (n= 93) and CCAP (n= 18) who visited the pediatric ward of the study hospital between January 1, 2017 and December 31, 2017.

	Community-acquired pneumonia; (*N* = 93)		Complicated community-acquired pneumonia; (*N* = 18; PPE *n* = 8, EMP *n* = 7, NP *n* = 2, and LA *n* = 1)		
	n	%	*n*	%	*p*-value
Laboratory results, (mean±SD)					
Leukocyte count ($\times 10^9$/L)	12.83±7.45		15.56±7.52		0.170
Hemoglobin level (g/dl)	10.81±1.37		10.61±2.03		0.700
Thrombocyte count($\times 10^9$/L)	361.51±128.46		351.33±205.80		0.783
C-reactive protein level (g/dl)	4.43±3.37		10.06±7.55		0.007*
Erythrocyte sedimentation rate (mm/h)	65.40±35.33		63.40±30.98		0.927

Tuğcu GD, Özsezen B, Türkyılmaz İ, Pehlivan Zorlu B, Eryılmaz Polat S, Özkaya Parlakay A, Cinel G. Risk factors for complicated community-acquired pneumonia in children. Pediatr Int. 2022 Jan;64(1):e15386.

Infection and Drug Resistance

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ORIGINAL RESEARCH

Development of a Nomogram for Predicting Massive Necrotizing Pneumonia in Children

Yonghan Luo, Yanchun Wang

Second Department of Infectious Disease, Kunming Children's Hospital, Kunming, Yunnan, People's Republic of China

- Retrospective study based on 282 children with NP admitted to Kunming Children's Hospital from January 2014 to November 2022
- The children with NP were divided into massive necrotizing pneumonia (MNP) group and non-MNP group according to the severity of the lung necrosis (>30% versus <30%).

Laboratory values	Overall (=282)	NON-MNP (=188)	MNP (=94)	P value
WBC (median [IQR]),10^9/L	12.66 [9.28, 17.09]	10.93 [8.42, 14.39]	17.01 [13.02, 22.56]	<0.001
Hb (median [IQR]), g/L	110.38 [98.00, 122.75]	115.00 [102.00, 124.25]	102.00 [92.00, 115.75]	<0.001
PLT (median [IQR]),10^9/L	453.00 [320.00, 562.75]	445.50 [323.75, 550.75]	459.00 [311.25, 606.00]	0.585
N% (median [IQR])	62.05 [51.52, 74.97]	60.85 [49.17, 72.30]	68.50 [57.45, 78.18]	0.001
L% (median [IQR])	26.40 [16.95, 38.08]	28.90 [18.88, 39.82]	21.70 [12.75, 31.84]	<0.001
CRP (median [IQR]), mg/L	52.98 [14.07, 99.03]	30.20 [7.40, 75.23]	74.44 [47.61, 176.21]	<0.001
PCT (median [IQR]), ng/mL	6.60 [0.41, 6.60]	3.96 [0.30, 6.60]	6.60 [1.19, 6.60]	0.001
AST (median [IQR]), U/L	18.00 [12.00, 35.30]	16.50 [12.00, 34.00]	23.50 [14.00, 38.75]	0.005
ALT (median [IQR]), U/L	32.00 [25.00, 49.00]	30.00 [23.75, 46.00]	39.00 [27.25, 53.00]	0.01
LDH (median [IQR]), U/L	322.50 [251.25, 395.50]	285.50 [233.75, 363.70]	393.00 [346.00, 500.50]	<0.001
Alb (median [IQR]), g/L	33.30 [29.22, 36.95]	33.55 [30.37, 38.00]	31.85 [27.62, 34.25]	<0.001
PT (median [IQR]), s	13.00 [11.90, 13.60]	13.00 [11.90, 13.60]	12.75 [12.00, 13.57]	0.555
APTT (median [IQR]), s	32.20 [26.83, 36.25]	33.25 [27.67, 37.10]	32.20 [25.90, 35.40]	0.023
FG (median [IQR]), g/L	4.53 [3.39, 5.43]	4.53 [3.35, 5.46]	4.53 [3.52, 5.29]	0.494
MP infection, (%)	62 (22.0)	46 (24.5)	16 (17.0)	0.204
Viral infection, n (%)	98 (34.8)	68 (36.2)	30 (31.9)	0.565
Bacterial infections, n (%)	46 (16.3)	32 (17.0)	14 (14.9)	0.776
Co-infection, n (%)	53 (18.8)	42 (22.3)	11 (11.7)	0.046

Infection and Drug Resistance

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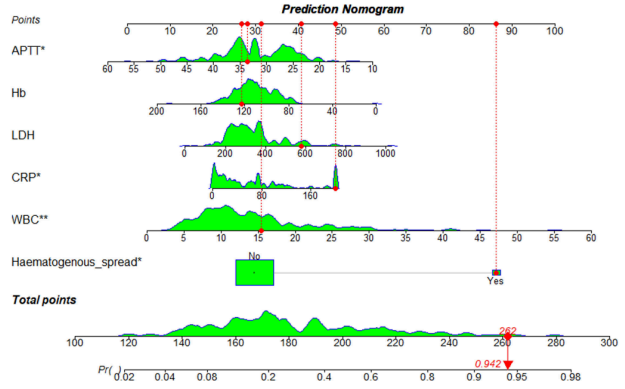


A predictive nomogram containing six independent predictors (haematogenous spread, WBC, Hb, CRP, LDH, and APTT) was established by logistic regression

	COMP-ADM, *n* = 323	COMP-HOSP, *n* = 232	PNEUMO, *n* = 6223	*p* value
Age (years)	5.78 ± 4.80	6.76 ± 5.55	3.57 ± 3.98	$P^{2,3} < .001$
Gender, male	187 (58%)	138 (59.5%)	3514 (56.5%)	$p = .59$
Ethnicity	(*n* = 4725)			
Arab	122 (49%)	93 (51%)	1561 (36%)	$p^{2,3} < .000\text{-}1$
O2 Sat (min)–ER	95.4 ± 3.76	94.7 ± 5.23	95.08 ± 4.99	$p = .55$
O2 Sat (min.)– HOSP	90.15 ± 6.43	89.54 ± 7.02	91.94 ± 6.21	$p^{2,3} < .000\text{-}1$
Fever (max)	38.7 ± 0.96	38.5 ± 0.97	38.5 ± 1.03	$p^1 = .047$
				$p^2 = .001$
WBC > 12,000[a]	187 (64%)	134 (61%)	3422 (67%)	$p = .12$
WBC < 5000[a]	14 (5%)	9 (4%)	16 (3%)	$p = .23$
CRP[b]	18.5 (5.8–6.5)	9.09 (1.44–24.4)	5.05 (1.70–12.1)	$P^{1-3} = .001$
Albumin	2.537 ± 0.71	2.751 ± 0.8	3.265 ± 0.69	$p^{2,3} < .001$
Comorbidities				
Prematurity	8 (2.5%)	13 (5.6%)	386 (6.2%)	$p^2 = .004$
Cardiac	33 (10.2%)	50 (21.6%)	454 (7.3%)	$P^{1,3} < .001$
Asthma	17 (5.3%)	10 (4.3%)	550 (8.8%)	$p^2 = .025$
				$p^3 = .012$

Note: Values are presented as mean ± *SD* or *n*(%). *p* values are statistically significant.

Abbreviations: CRP, C-reactive protein; COMP-HOSP versus PNEUMO; CS, Cesarean section; COMP-ADM, complication on admission; COMP-HOSP, complication in hospital; gr, grams; p^1, COMP-ADM versus COMP-HOSP; p^2, COMP-ADM versus PNEUMO; p^3, PNEUMO, pneumonia; O2 Sat, oxygen saturation; min, minimal; max, maximal; WBC, white blood cells.

[a]/μl.

[b]mg/dl, median (25th–75th range).

- Retrospective single-center study
- 6778 children admitted from January 2001 until March 2020 with a diagnosis of pneumonia.
- 323 arrived with complicated pneumonia (COMP-ADM), 232 developed a complication during hospitalization (COMP-HOSP) and 6223 had uncomplicated pneumonia (PNEUMO).

TABLE 2 Risk factors for the development of complicated pneumonia

	p value	OR	95% CI for OR Lower	95% CI for OR Upper
Age	0.000	1.131	1.085	1.179
Gender	0.19	0.745	0.479	1.158
Ethnicity (Arab)	0.000	2.236	1.424	3.513
O_2 Sat	0.029	0.959	0.923	0.996
Fever (max)	0.241	0.869	0.688	1.099
CRP	0.000	1.065	1.043	1.086
Cardiac disease	0.000	4.376	2.383	8.038

Abbreviations: CI, confidence interval; CRP, C-reactive protein; OR, odds ratio; O2 Sat, oxygen saturation; min, minimal; max, maximal.

Masarweh K, Gur M, Toukan Y, Bar-Yoseph R, Kassis I, Gut G, Hakim F, Nir V, Bentur L. Factors associated with complicated pneumonia in children. Pediatr Pulmonol. 2021 Aug;56(8):2700-2706.

- Prospective multi-center study
- From March 2010 to April 2012, a total of 801 children aged <18 years were admitted for CAP

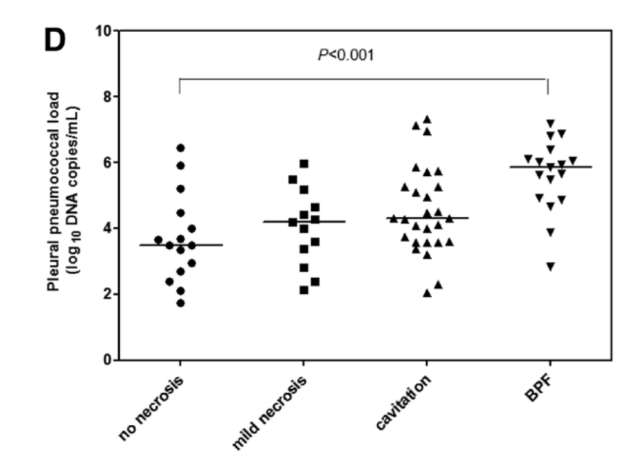


Fig. D: Relationship of different severity of lung necrosis with pleural pneumococcal load. The horizontal lines indicate median values

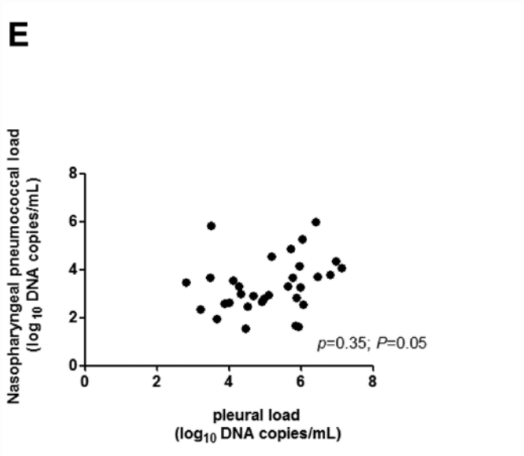


Fig. E: Correlation of nasopharyngeal pneumococcal load with pleural pneumococcal load (Spearman test).

Hsieh YC, Chi H, Chang KY, Lai SH, Mu JJ, Wong KS, Liu CC, Huang YC, Lin HC, Chang LY, Huang YC, Huang LM; Taiwan Pediatric Infectious Diseases Alliance. Increase in fitness of Streptococcus pneumoniae is associated with the severity of necrotizing pneumonia. Pediatr Infect Dis J. 2015 May;34(5):499-505.

Terapia farmacologica

- Initial therapy must be effective against *S pneumoniae* (the commonest cause of CCAP) and *S aureus*, guided by local bacteriological knowledge.
- High-dose **penicillin or ampicillin, amoxicillin–clavulanic acid, or a second-generation or third- generation cephalosporin** (eg, cefuroxime, cefotaxime, or ceftriaxone) are often used intravenously.
- Penicillin, ampicillin, and ceftriaxone are generally insufficient for coverage of *S aureus*, and should not be used in settings where this microorganism is prevalent.
- In areas where there is a high prevalence of meticillin-resistant *S aureus*, **vancomycin, linezolid or rifampicin** should be used as an additional first-line agent until culture results are available.
- When *M pneumoniae* infection is documented, treatment should also include a **macrolide**. Macrolides should never be used as the sole antibiotic in complicated pneumonia.

Spencer DA, Thomas MF. Necrotising pneumonia in children. Paediatr Respir Rev. 2014 Sep;15(3):240-5; quiz 245.

de Benedictis FM, Kerem E, Chang AB, Colin AA, Zar HJ, Bush A. Complicated pneumonia in children. Lancet. 2020 Sep 12;396(10253):786-798.

- The duration of intravenous antibiotic therapy to prescribe is controversial, and oral antibiotic therapy should be started as soon as possible
- A course of 2–3 weeks of intravenous antibiotic therapy is usually sufficient, often with a transition to oral therapy when fever has abated for at least 24–48 h, there is no respiratory distress or evidence of uncontrolled sepsis, the child is tolerating enteral feeds and has an improved mood and playfulness, and when inflammatory markers are reducing.
- Oral antibiotics are generally prescribed for around 14-21 days after intravenous therapy is stopped.

Masters IB, Isles AF, Grimwood K. Necrotizing pneumonia: an emerging problem in children? Pneumonia (Nathan). 2017 Jul 25;9:11.
de Benedictis FM, Kerem E, Chang AB, Colin AA, Zar HJ, Bush A. Complicated pneumonia in children. Lancet. 2020 Sep 12;396(10253):786-798.

Necrotizing pneumonia

- Similar antibiotic coverage is used for most patients with necrotising pneumonia.
- The effect of the antibiotics on **persistent fever** and severe clinical morbidity, which are probably driven by the **necrotising process rather than the persistence of infection**, is unknown; in fact, direct cultures of the necrotic material are commonly negative.

de Benedictis FM, Kerem E, Chang AB, Colin AA, Zar HJ, Bush A. Complicated pneumonia in children. Lancet. 2020 Sep 12;396(10253):786-798.

Lung abscess

Table I Pathogens isolated in lung abscess

Classification	Pathogen	Primary lung abscess	Secondary lung abscess
Aerobic Gram-positive cocci	*Streptococcus pneumoniae*	++++	++
	Staphylococcus aureus	+++	++
	Streptococcus pyogenes	++	
	Streptococcus milleri	+	
	Streptococcus viridans		+
Aerobic Gram-negative bacilli	*Pseudomonas aeruginosa*	++	+++
	Klebsiella pneumoniae	+	+
	Moraxella catarrhalis		+
	Acinetobacter species		
	Escherichia coli	+	
	Salmonella species		+
Anaerobic	*Bacteroides*		++
	Prevotella species		+
	Actinomyces species	+	
Fungus	*Candida albicans*		+
	Aspergillus species		+

Patradoon-Ho P, Fitzgerald DA. Lung abscess in children. Paediatr Respir Rev. 2007 Mar;8(1):77-84.

Lung abscess

- More prolonged therapy might be necessary because they are typically slow to resolve (many remain febrile for 2 weeks or more)
- Conservative treatment with IV antibiotics for 2-3 weeks, followed by 4 weeks' oral treatment.
- If fever falls to settle after 2 weeks, drainage should be considered.
- Most of anaerobic bacteria that cause lung abscess are **penicillin-sensitive** (IV therapy with high-dose of second or third-generation cephalosporin to cover anerobes, MSSA and streptococci.
- Many centers add **metronidazole or clindamycin to penicillin as first line-therapy** because of the **rise of penicillin resistance.**
- Antibiotics for the oral phase of treatment include second-generation cephalosporin, co-amoxiclav or a macrolide.
- Decompression of the abscess may be required acutely in the rare situation when the abscess is large enough to caouse significant airway compression or mediastinal shift

Patradoon-Ho P, Fitzgerald DA. Lung abscess in children. Paediatr Respir Rev. 2007 Mar;8(1):77-84.

Table 5. Selection of Antimicrobial Therapy for Specific Pathogens

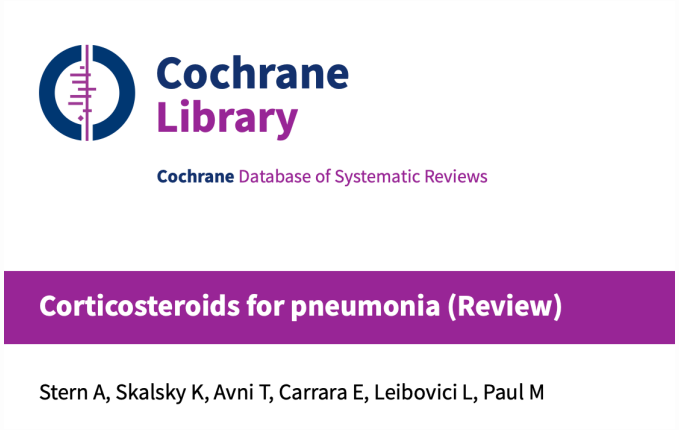
Pathogen	Parenteral therapy	Oral therapy (step-down therapy or mild infection)
Streptococcus pneumoniae with MICs for penicillin ≤2.0 μg/mL	Preferred: ampicillin (150–200 mg/kg/day every 6 hours) or penicillin (200 000–250 000 U/kg/day every 4–6 h); Alternatives: ceftriaxone (50–100 mg/kg/day every 12–24 hours) (preferred for parenteral outpatient therapy) or cefotaxime (150 mg/kg/day every 8 hours); may also be effective: clindamycin (40 mg/kg/day every 6–8 hours) or vancomycin (40–60 mg/kg/day every 6–8 hours)	Preferred: amoxicillin (90 mg/kg/day in 2 doses or 45 mg/kg/day in 3 doses); Alternatives: second- or third-generation cephalosporin (cefpodoxime, cefuroxime, cefprozil); oral levofloxacin, if susceptible (16–20 mg/kg/day in 2 doses for children 6 months to 5 years old and 8–10 mg/kg/day once daily for children 5 to 16 years old; maximum daily dose, 750 mg) or oral linezolid (30 mg/kg/day in 3 doses for children <12 years old and 20 mg/kg/day in 2 doses for children ≥12 years old)
S. pneumoniae resistant to penicillin, with MICs ≥4.0 μg/mL	Preferred: ceftriaxone (100 mg/kg/day every 12–24 hours); Alternatives: ampicillin (300–400 mg/kg/day every 6 hours), levofloxacin (16–20 mg/kg/day every 12 hours for children 6 months to 5 years old and 8–10 mg/kg/day once daily for children 5–16 years old; maximum daily dose, 750 mg), or linezolid (30 mg/kg/day every 8 hours for children <12 years old and 20 mg/kg/day every 12 hours for children ≥12 years old); may also be effective: clindamycin[a] (40 mg/kg/day every 6–8 hours) or vancomycin (40–60 mg/kg/day every 6–8 hours)	Preferred: oral levofloxacin (16–20 mg/kg/day in 2 doses for children 6 months to 5 years and 8–10 mg/kg/day once daily for children 5–16 years, maximum daily dose, 750 mg), if susceptible, or oral linezolid (30 mg/kg/day in 3 doses for children <12 years and 20 mg/kg/day in 2 doses for children ≥12 years); Alternative: oral clindamycin[a] (30–40 mg/kg/day in 3 doses)
Group A *Streptococcus*	Preferred: intravenous penicillin (100 000–250 000 U/kg/day every 4–6 hours) or ampicillin (200 mg/kg/day every 6 hours); Alternatives: ceftriaxone (50–100 mg/kg/day every 12–24 hours) or cefotaxime (150 mg/kg/day every 8 hours); may also be effective: clindamycin, if susceptible (40 mg/kg/day every 6–8 hours) or vancomycin[b] (40–60 mg/kg/day every 6–8 hours)	Preferred: amoxicillin (50–75 mg/kg/day in 2 doses), or penicillin V (50–75 mg/kg/day in 3 or 4 doses); Alternative: oral clindamycin[a] (40 mg/kg/day in 3 doses)

Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, Kaplan SL, Mace SE, McCracken GH Jr, Moore MR, St Peter SD, Stockwell JA, Swanson JT; Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76.

Pathogen	Parenteral therapy	Oral therapy (step-down therapy or mild infection)
Haemophilus influenza, typeable (A-F) or nontypeable	Preferred: intravenous ampicillin (150-200 mg/kg/day every 6 hours) if β-lactamase negative, ceftriaxone (50–100 mg/kg/day every 12-24 hours) if β-lactamase producing, or cefotaxime (150 mg/kg/day every 8 hours); Alternatives: intravenous ciprofloxacin (30 mg/kg/day every 12 hours) or intravenous levofloxacin (16-20 mg/kg/day every 12 hours for children 6 months to 5 years old and 8-10 mg/kg/day once daily for children 5 to 16 years old; maximum daily dose, 750 mg)	Preferred: amoxicillin (75-100 mg/kg/day in 3 doses) if β-lactamase negative) or amoxicillin clavulanate (amoxicillin component, 45 mg/kg/day in 3 doses or 90 mg/kg/day in 2 doses) if β-lactamase producing; Alternatives: cefdinir, cefixime, cefpodoxime, or ceftibuten
Mycoplasma pneumoniae	Preferred: intravenous azithromycin (10 mg/kg on days 1 and 2 of therapy; transition to oral therapy if possible); Alternatives: intravenous erythromycin lactobionate (20 mg/kg/day every 6 hours) or levofloxacin (16-20 mg/kg/day every 12 hours; maximum daily dose, 750 mg)	Preferred: azithromycin (10 mg/kg on day 1, followed by 5 mg/kg/day once daily on days 2–5); Alternatives: clarithromycin (15 mg/kg/day in 2 doses) or oral erythromycin (40 mg/kg/day in 4 doses); for children >7 years old, doxycycline (2–4 mg/kg/day in 2 doses; for adolescents with skeletal maturity, levofloxacin (500 mg once daily) or moxifloxacin (400 mg once daily)
Stapyhylococcus aureus, methicillin susceptible (combination therapy not well studied)	Preferred: cefazolin (150 mg/kg/day every 8 hours) or semisynthetic penicillin, eg oxacillin (150–200 mg/kg/day every 6–8 hours); Alternatives: clindamycin[a] (40 mg/kg/day every 6–8 hours) or >vancomycin (40–60 mg/kg/day every 6–8 hours)	Preferred: oral cephalexin (75–100 mg/kg/day in 3 or 4 doses); Alternative: oral clindamycin[a] (30–40 mg/kg/day in 3 or 4 doses)
S. aureus, methicillin resistant, susceptible to clindamycin (combination therapy not well-studied)	Preferred: vancomycin (40–60 mg/kg/day every 6–8 hours or dosing to achieve an AUC/MIC ratio of >400) or clindamycin (40 mg/kg/day every 6–8 hours); Alternatives: linezolid (30 mg/kg/day every 8 hours for children <12 years old and 20 mg/kg/day every 12 hours for children ≥12 years old)	Preferred: oral clindamycin (30–40 mg/kg/day in 3 or 4 doses); Alternatives: oral linezolid (30 mg/kg/day in 3 doses for children <12 years and 20 mg/kg/day in 2 doses for children ≥12 years)
S. aureus, methicillin resistant, resistant to clindamycin (combination therapy not well studied)	Preferred: vancomycin (40–60 mg/kg/day every 6-8 hours or dosing to achieve an AUC/MIC ratio of >400); Alternatives: linezolid (30 mg/kg/day every 8 hours for children <12 years old and 20 mg/kg/day every 12 hours for children ≥12 years old)	Preferred: oral linezolid (30 mg/kg/day in 3 doses for children <12 years and 20 mg/kg/day in 2 doses for children ≥12 years old); Alternatives: none; entire treatment course with parenteral therapy may be required

Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C, Kaplan SL, Mace SE, McCracken GH Jr, Moore MR, St Peter SD, Stockwell JA, Swanson JT; Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis. 2011 Oct;53(7):e25-76.

Role of corticosteroids?



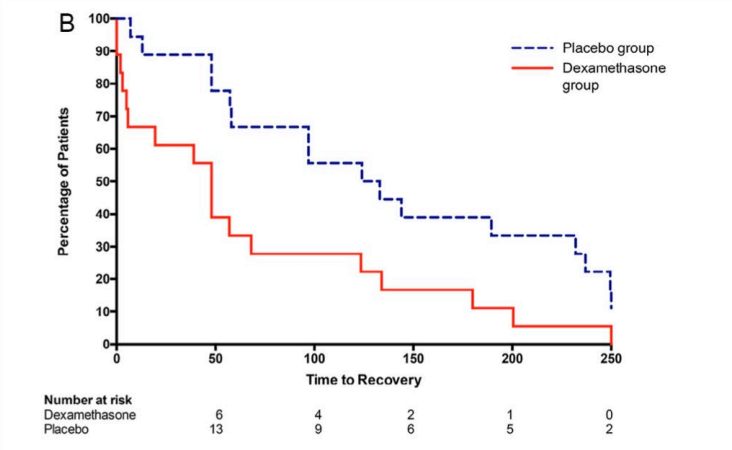
- 17 RCTs comprising a total of 2264 participants: 13 RCTs included 1954 adult participants, and four RCTs included 310 children.
- All trials limited inclusion to inpatients with community-acquired pneumonia (CAP)

- Among children with bacterial non-severe CAP, corticosteroids reduced **early clinical failure rates,** based on two small, clinically heterogeneous trials, and reduced **morbidity, but non mortality**
- Corticosteroid therapy was associated with more adverse events, especially hyperglycaemia

THE JOURNAL OF PEDIATRICS • www.jpeds.com ORIGINAL ARTICLES

Dexamethasone for Parapneumonic Pleural Effusion: A Randomized, Double-Blind, Clinical Trial

Alfredo Tagarro, PhD, MD[1,2], Enrique Otheo, MD[3,4], Fernando Baquero-Artigao, MD[5], María-Luisa Navarro, PhD, MD[6], Rosa Velasco, MD[7], Marta Ruiz, MD[8], María Penín, MD[9], David Moreno, PhD, MD[10], Pablo Rojo, PhD, MD[11], and Rosario Madero, PhD,[12] on behalf of the CORTEEC Study Group*



- Multicenter, randomized, double blind, placebo-controlled clinical trial of 60 children from 1 month to 14 years of age with community-acquired pneumonia (CAP) *and* pleural effusion.
- Patients were randomly assigned to the DXM (n = 30) or placebo (n = 30) group
- The aim was to investigate whether the treatment of DXM (0.25 mg/kg/dose every 6 hours for 48 hours) with antibiotic therapy decreased the time to recovery of parapneumonic pleural effusion compared with placebo.

- The median time to recovery was **68 hours** (2.8 days) **shorter** in the patients receiving DXM
- There were no significant differences in complications or adverse events attributable to the study drugs, except for hyperglycemia.

Tagarro A, Otheo E, Baquero-Artigao F, Navarro ML, Velasco R, Ruiz M, Penín M, Moreno D, Rojo P, Madero R; CORTEEC Study Group. Dexamethasone for Parapneumonic Pleural Effusion: A Randomized, Double-Blind, Clinical Trial. J Pediatr. 2017 Jun;185:117-123.e6.

Role of corticosteroids?

Systemic corticosteroids cannot be recommended for patients with CCAP and more studies are necessary.

- Oxygen
- Fluid and electrolyte replacement (hyponatraemia) → isotonic intravenous fluid was associated with a lower risk of hyponatraemia
- Nutritional status should be monitored during and after hospitalisation for children with CCAP (hypoalbuminaemia)

Domande?

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