

“PAC - PNEUMONIA DA COMUNIDADE: NOVIDADES E CONTROVÉRSIAS”

José M. D. Poças

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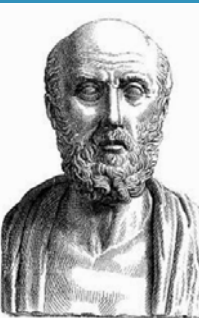
Of peripneumony, Hippocrates wrote:

Peripneumonia, and pleuric affections, are to be thus observed: If the fever be acute, and if there be pains on either side, or in both, and if expiration be if cough be present, and the sputa expectorated be of a blond or livid color, or likewise thin, frothy, and florid, or having any other character different from the common.

"When pneumonia is at its height, the case is beyond remedy if he is not purged, and it is bad if he has dyspnoea, and urine that is thin and acrid, and if sweats come out about the neck and head, for such sweats are bad, as proceeding from the suffocation, rales, and the violence of the disease which is obtaining the upper hand, unless there be a copious evacuation of thick urine, and the sputa be concocted; when either of these comes on spontaneously, that will carry off the disease."

Hippocrates noted that death from pneumonia usually occurs on the seventh day.

OS ENSINAMENTOS QUE O PAI DA MEDICINA SABIAMENTE NOS LEGOU



400 B.C: Hippocrates defines pneumonia

Narrative review

Controversies in diagnosis and management of community-acquired pneumonia

Sarah Sparham, Patrick GP Charles

Prina et al. *Critical Care* (2016) 20:267
DOI 10.1186/s13054-016-1442-y

Critical Care

REVIEW

Open Access

New aspects in the management of pneumonia

Elena Prina¹, Adrian Ceccato^{1,3} and Antoni Torres^{1,2,4*}



F1000Research

F1000Research 2016, 5(F1000 Faculty Rev):300 Last updated: 09 MAR 2016



REVIEW

Advances in the prevention, management, and treatment of community-acquired pneumonia [version 1; referees: 2 approved]

Mathias W. Pletz¹, Gernot G. Rohde², Tobias Welte³, Martin Kolditz⁴, Sebastian Ott⁵

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EXPERT REVIEW OF CLINICAL PHARMACOLOGY, 2017
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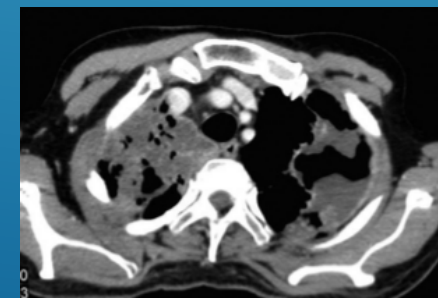
REVIEW

Tools for outcome prediction in patients with community acquired pneumonia

Faheem Khan^a, Mark B Owens^a, Marcos Restrepo^b, Pedro Povoa^{c,d} and Ignacio Martin-Loeches^{a,e}

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PRIORIZAR A ABORDAGEM DE UM VASTO E COMPLEXO TEMA, ASSUMIDO OPÇÕES...



▶ Incidência

- ▶ 400.000.000 casos/ano
 - ▶ 60% > 65 anos
- ▶ 1,5% dos Doentes no SU
 - ▶ 1/2 doentes geriátricos
- ▶ 10-20% necessitam de internamento em C. Intermédios / Intensivos
 - ▶ 1ª causa p/ DI de admissão aos CI (10%)
- ▶ Redução c/ Vacina Pneumocócica: 15-30%

▶ Mortalidade

- ▶ 3.500.000 - 4.000.000 / Ano
 - ▶ 1- 50%
 - ▶ 1/2 em crianças < 5 anos
 - ▶ 1% s/ critérios de gravidade em clínica de ambulatório
 - ▶ 5-20% c/ critério de gravidade em enfermaria hospitalar
 - ▶ Até 50% em UCI
- ▶ Maior Tx de Mortalidade p/ DI (1-15%)

EPIDEMIOLOGIA



Bacterial Pneumonia in Older Adults



Thomas J. Marrie, MD, FRCPC^{a,*}, Thomas M. File Jr, MD, MSC^{b,c}

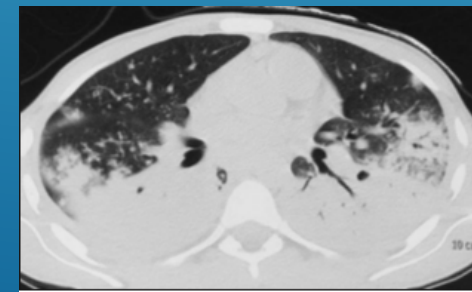
Box 1

Comorbid illnesses among 1343 patients hospitalized with pneumonia in the Pneumonia Patient Outcomes Research Team study

Comorbidity	Patients (%)
COPD	33.9
Coronary artery disease	26.0
Alcoholism or intravenous drug use	25.0
Cancer	17.8
Congestive heart failure	16.8
Neuromuscular disease	16.3
Diabetes mellitus	14.7
Immunosuppression	12.1
Renal disease	10.4
Dementia	10.0
Seizure disorder	5.6
None	14.4

Data from Fine MJ, Stone RA, Singer DE, et al. Processes and outcomes of care for patients with community-acquired pneumonia. Results from the Pneumonia Patient Outcomes Research Team (PORT) study. Arch Intern Med 1999;159:970-80.

POPULAÇÕES DE MAIOR RISCO: O IMPORTANTE IMPACTO DO FACTOR IDADE





Community-Acquired Pneumonia in HIV-Positive Patients: an Update on Etiologies, Epidemiology and Management

André Almeida^{1,2} · Matteo Boattini^{1,2}



Community-acquired lower respiratory tract infections in HIV-infected patients on antiretroviral therapy: predictors in a contemporary cohort study

Cristiane C. Lamas^{1,2} · Lara E. Coelho¹ · Beatriz J. Grinsztejn¹ · Valdilea G. Veloso¹

- ▶ **PAC no Doente com infecção VIH+**
 - ▶ A infecção bacteriana mais frequente
 - ▶ Segunda causa de morte (20% do total)
 - ▶ 20% das causas de internamento hospitalar

OUTRO IMPORTANTE GRUPO DE RISCO: O CASO PARTICULAR DO DOENTE COM INFEÇÃO VIH



Prevalence of Atypical Pathogens in Patients With Cough and Community-Acquired Pneumonia: A Meta-Analysis

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 Anella Perry Dale, MPH
 Thy Nho Thu, BS
 Dak Soo Han, RN
 Mark H. Ebell, MD, MS
 Department of Epidemiology and Biostatistics, College of Public Health, University of Georgia, Athens, Georgia

Intensive Care Med (2016) 42:1374–1386
 DOI 10.1007/s00134-016-4394-4

REVIEW

Community-acquired pneumonia related to intracellular pathogens



Catia Cillóniz¹, Antoni Torres^{1*}, Michael Niederman², Menno van der Eerden³, James Chalmers^{4,5}, Tobias Welte⁶ and Francesco Blasi⁷

Bacterial Pneumonia in Older Adults

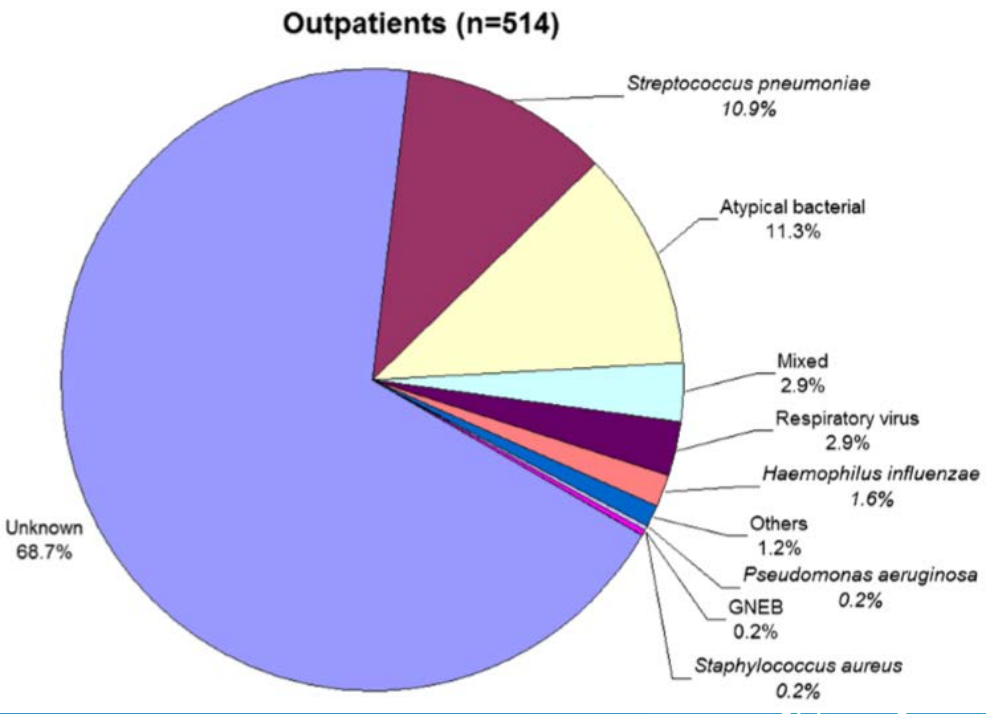


Thomas J. Marrie, MD, FRCPC^{a,*}, Thomas M. File Jr, MD, MSc^{b,c}

Table 1
 Cause of community-acquired pneumonia in Western European countries from 2005 to 2012

	Studies (N)	Range (%)
Gram-positive bacteria		
<i>Streptococcus pneumoniae</i>	19	12–85
<i>Streptococcus viridians</i>	1	1.7
Gram-negative bacilli		
Gram-negative enteric bacilli		
<i>Haemophilus influenzae</i>	15	1.1–29.4
<i>Pseudomonas aeruginosa</i>	10	0.9–16
<i>Pseudomonas spp</i>	1	0.2–3.2
<i>Klebsiella pneumoniae</i>	5	0.3–5.0
<i>Moraxella catarrhalis</i>	5	0.3–2.3
<i>Escherichia coli</i>	3	0.6–2.1
Atypical bacteria		
<i>Mycoplasma pneumoniae</i>	10	0.7–61.3
<i>Legionella pneumophila</i>	12	1.7–20.1
<i>Legionella spp</i>	3	5.4–20
<i>Chlamydomphila pneumoniae</i>	9	0.1–9.9
<i>Coxiella burnetii</i>	6	0.8–3.4
Virus		
	10	1.4–28.6

Adapted from Torres A, Blasi F, Peetermans WE, et al. The etiology and antibiotic management of community-acquired pneumonia in adults in Europe: a literature review. Eur J Clin Microbiol Infect Dis 2014;33:1072.



A GRANDE VARIABILIDADE NO PESO RELATIVO DOS AGENTES DENOMINADOS DE “ATÍPICOS”!!!



OPEN ACCESS

Association of targeted multiplex PCR with resequencing microarray for the detection of multiple respiratory pathogens

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Shen et al.

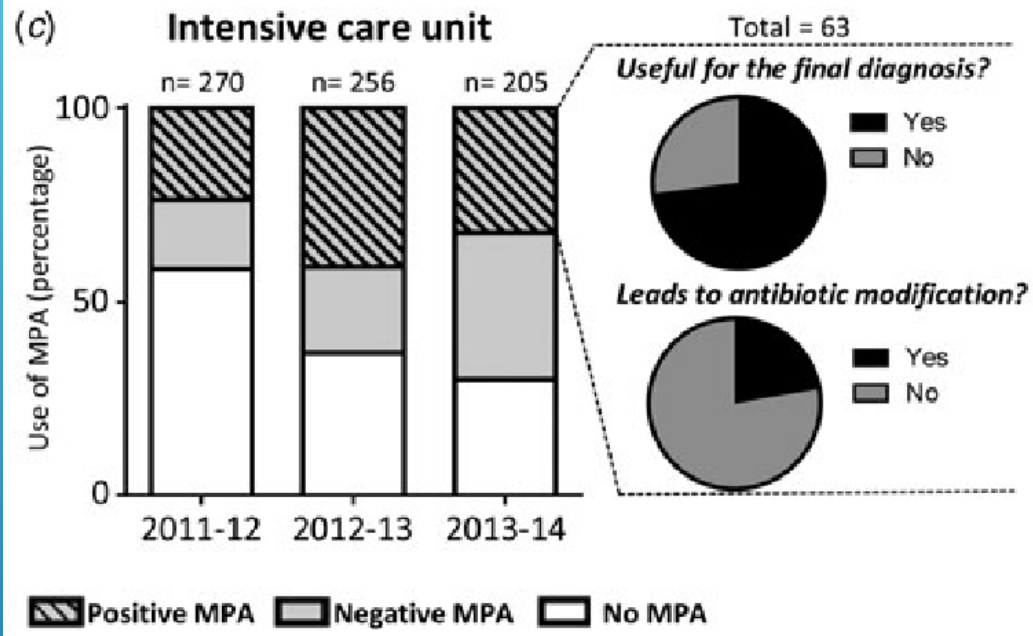
RPM-IVDC1 detection of respiratory pathogens

TABLE 6 | Sensitivity, specificity, and PPV for the RPM-IVDC1.

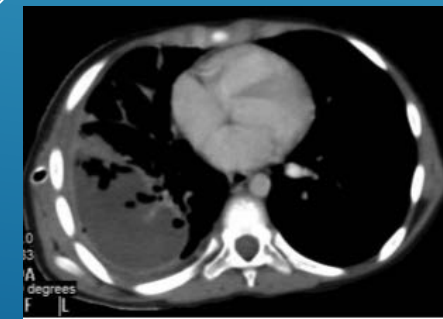
Organism	Sensitivity		Specificity		PPV	
	%	No. of samples positive/ total no. tested	%	No. of samples negative/ total no. tested	%	No. of samples positive/ total no. tested
<i>S. pneumoniae</i>	100	37/37	100	73/73	100	37/37
<i>H. influenzae</i>	92.3	12/13	97.9	95/97	85.7	12/14
<i>M. pneumoniae</i>	89.2	9/13	99.0	96/97	90.0	9/10
<i>K. pneumoniae</i>	(100) ^a	2/2	100	108/108	(100)	2/2
<i>M. catarrhalis</i>	(100)	1/1	100	109/109	(100)	1/1

^aThe numbers in parentheses were based on numbers of samples too small to perform a valid calculation.

SHORT REPORT Impact on the medical decision-making process of multiplex PCR assay for respiratory pathogens



INOVAÇÕES NAS TÉCNICAS DE DIAGNÓSTICO ETIOLÓGICO PRECISO E RÁPIDO



ARCHIVOS DE BRONCONEUMOLOGIA
www.archbronconeumol.org

Review
Review of Non-bacterial Infections in Respiratory Medicine: Viral Pneumonia[☆]

José María Galván,^a Olga Rajas,^b Javier Aspa^{b,*}

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^b Servicio de Neumología, Hospital Universitario de la Princesa, IIS-IP, Madrid, Spain

Table 1
Differential Factors Between Viral Pneumonia and Bacterial Pneumonia.

	Suggestive of viral origin	Suggestive of bacterial origin
Age	Younger than 5 and older than 65 years	Adults
Epidemic status	Seasonal or epidemic outbreaks	Throughout the year
Disease course	Slow onset	Rapid onset
Clinical profile	Most frequently rhinitis and wheezing	Most frequently high fever and tachypnea
Total leukocyte count on admission	<10×10 ⁶ c/L	>15×10 ⁶ c/L and <4×10 ⁶ c/L
C-reactive protein on admission	<20 mg/L	>60 mg/L
Serum procalcitonin on admission	<0.1 µg/L	>0.5 µg/L (>1 µg/L with greater specificity)
Chest X-ray	Bilateral, interstitial infiltrates	Lobar alveolar infiltrates
Response to antibiotic treatment	Slow response or no response	Rapid

Adapted from Ruuskanen et al.³

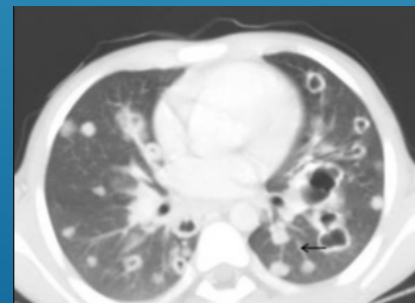
Table 2

Viruses Related with Community-Acquired viral Pneumonia in Children and Adults.

Syncytial respiratory virus
Rhinovirus
Influenza A, B and C virus
Human metapneumovirus
Parainfluenza virus type 1, 2, 3 and 4
Human bocavirus
Coronavirus type 229E, OC43, NL63, HKU1, SARS and MERS-CoV
Adenovirus
Enterovirus
Varicella zoster virus, Epstein-Barr virus, human herpesvirus 6 and 7, cytomegalovirus
Hantavirus
Parechovirus
Mimivirus
Measles virus

Adapted from Ruuskanen et al.³

**PNEUMONIA “TÍPICA” (BACTERIANA) / “ATÍPICA” (VIRAL):
UMA DISTINÇÃO NEM SEMPRE FÁCIL E IMEDIATA...**



EDITORIAL

Open Access



Viral and bacterial co-infection in pneumonia: do we know enough to improve clinical care?

Kelly A. Cawcutt¹ and Andre C. Kalil^{1,2*}

Received: 23 February 2017 | Accepted: 17 May 2017
DOI: 10.1002/jmv.24895

RESEARCH ARTICLE

WILEY JOURNAL OF MEDICAL VIROLOGY

Characterization of the nasopharyngeal viral microbiome from children with community-acquired pneumonia but negative for Luminex xTAG respiratory viral panel assay detection

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Diagnosing Viral and Atypical Pathogens in the Setting of Community-Acquired Pneumonia

Grant W. Waterer, MD, PhD^{a,b,*}

KEYWORDS

• Pneumonia • Viral • Diagnostic • Point of care

KEY POINTS

- The concept of atypical pneumonia is outdated because clinically it is impossible to determine the pathogen.
- Nucleic acid detection is now the standard diagnostic method for all these pathogens, having replaced older serologic and antigen detection methods.
- Multiple pathogens are commonly detected in patients, particularly with *Legionella*, *Mycoplasma*, and *Chlamydia*.

Clinics Review Articles

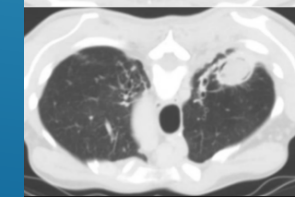
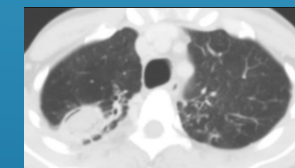
CLINICS IN CHEST MEDICINE

Viral and Atypical Pneumonia in Adults

EDITORS
Charles S. Dela Cruz
Richard G. Wunderink

MARCH 2017

QUAIS AS IMPLICAÇÕES CLÍNICAS DAS DUPLAS INFEÇÕES (VIRAIS E BACTERIANAS) QUE AFETAM CERCA DE 12-25% DOS DOENTES???



Review

Viral and Bacterial Interactions in the Upper Respiratory Tract

Astrid A. T. M. Bosch, Giske Biesbroek, Krzysztof Trzcinski, Elisabeth A. M. Sanders, Debby Bogaert*

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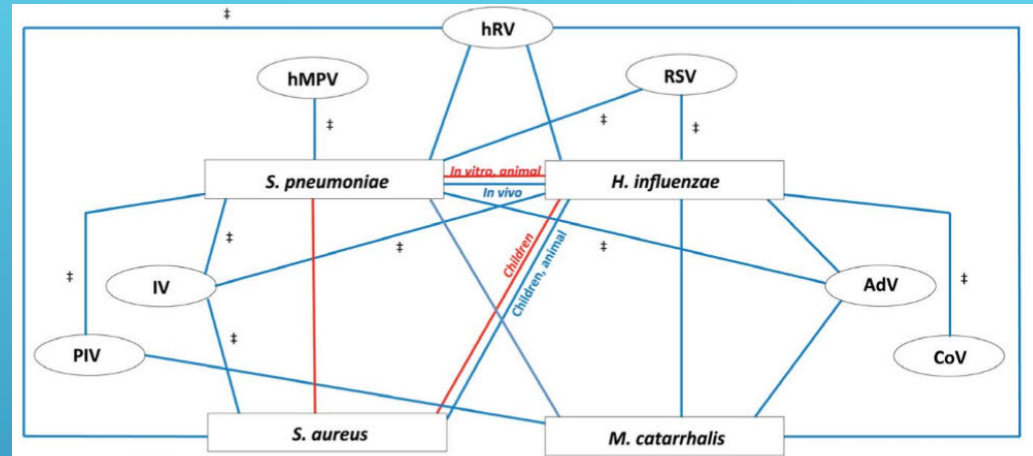
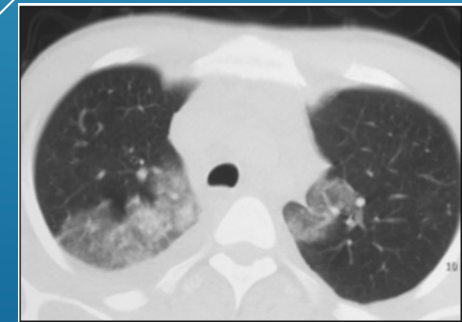


Figure 3. Proposed model of bacterial and viral interactions. This model represents the cumulative dynamics of bacterial and viral interactions occurring within the nasopharyngeal niche during asymptomatic episodes as observed in all cumulative literature references. All available information on the four main potential pathogenic bacteria (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus*, and *Moraxella catarrhalis*) and seven common respiratory viruses (rhinoviruses (hRV), respiratory syncytial virus (RSV), adenoviruses (AdV), coronavirus (CoV), influenza viruses (IV), para-influenza viruses (PIV), and human metapneumovirus (hMPV)) are depicted. Red lines represent a negative association of co-colonization (competition), blue lines represent a positive association of co-colonization (synergism). For all depicted associations, evidence is available from human (surveillance) studies, except for those indicated with ‡, where evidence is only available from in vitro and/or animal studies.
doi:10.1371/journal.ppat.1003057.g003

FISIOPATOLOGIA DA INFEÇÃO DUPLA I



Review

Viral–bacterial interactions in the respiratory tract

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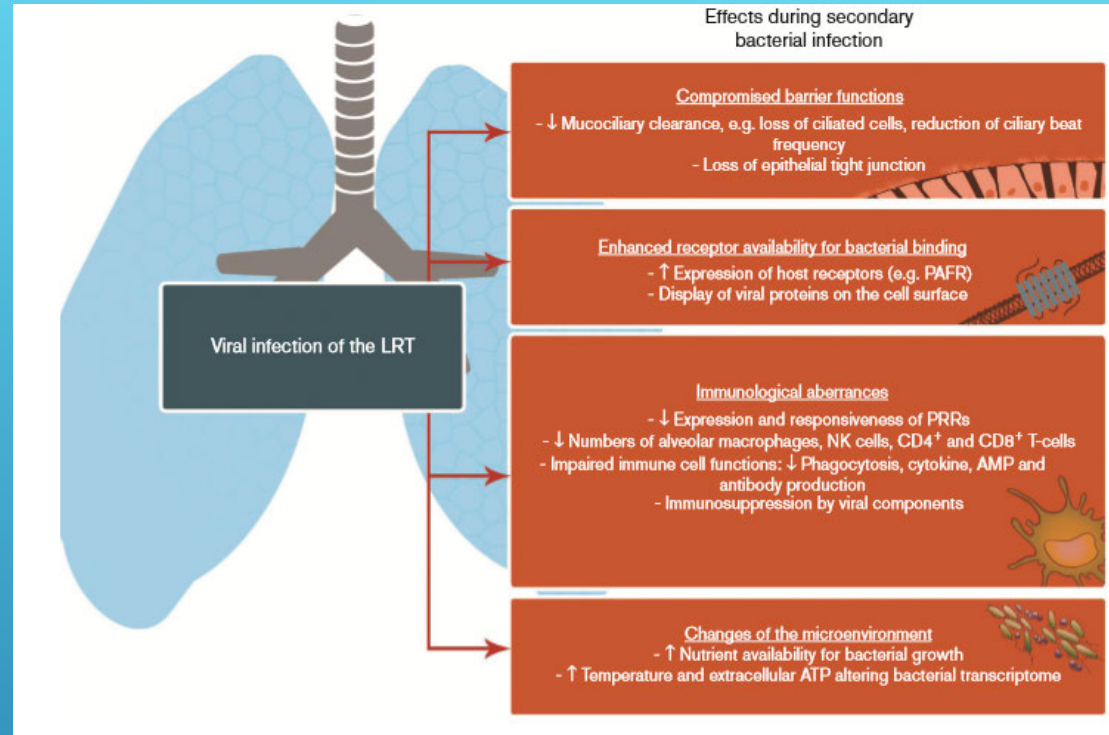


Fig. 1. Effects of viral infections of the LRT on susceptibility and response to secondary bacterial infection. PAFR, Platelet activating factor receptor; PRR, pathogen recognition receptor; AMP, antimicrobial peptides.

FISIOPATOLOGIA DA INFEÇÃO DUPLA II





CrossMark

Viral infection in community-acquired pneumonia: a systematic review and meta-analysis

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Affiliations: ¹Division of Pulmonary, Critical Care and Sleep Medicine, University of Louisville, Louisville, KY, USA. ²Division of Infectious Diseases, University of Louisville, Louisville, KY, USA.

Correspondence: Rodrigo Cavallazzi, Division of Pulmonary, Critical Care and Sleep Medicine, University of Louisville, 401 E Chestnut Street, Suite 310, Louisville, KY, 40202, USA. E-mail: rodrigo.cavallazzi@louisville.edu

ABSTRACT The advent of PCR has improved the identification of viruses in patients with community-acquired pneumonia (CAP). Several studies have used PCR to establish the importance of viruses in the aetiology of CAP.

We performed a systematic review and meta-analysis of the studies that reported the proportion of viral infection detected *via* PCR in patients with CAP. We excluded studies with paediatric populations. The primary outcome was the proportion of patients with viral infection. The secondary outcome was short-term mortality.

Our review included 31 studies. Most obtained PCR *via* nasopharyngeal or oropharyngeal swab. The pooled proportion of patients with viral infection was 24.5% (95% CI 21.5–27.5%). In studies that obtained lower respiratory samples in >50% of patients, the proportion was 44.2% (95% CI 35.1–53.3%). The odds of death were higher in patients with dual bacterial and viral infection (OR 2.1, 95% CI 1.32–3.31).

Viral infection is present in a high proportion of patients with CAP. The true proportion of viral infection is probably underestimated because of negative test results from nasopharyngeal or oropharyngeal swab PCR. There is increased mortality in patients with dual bacterial and viral infection.

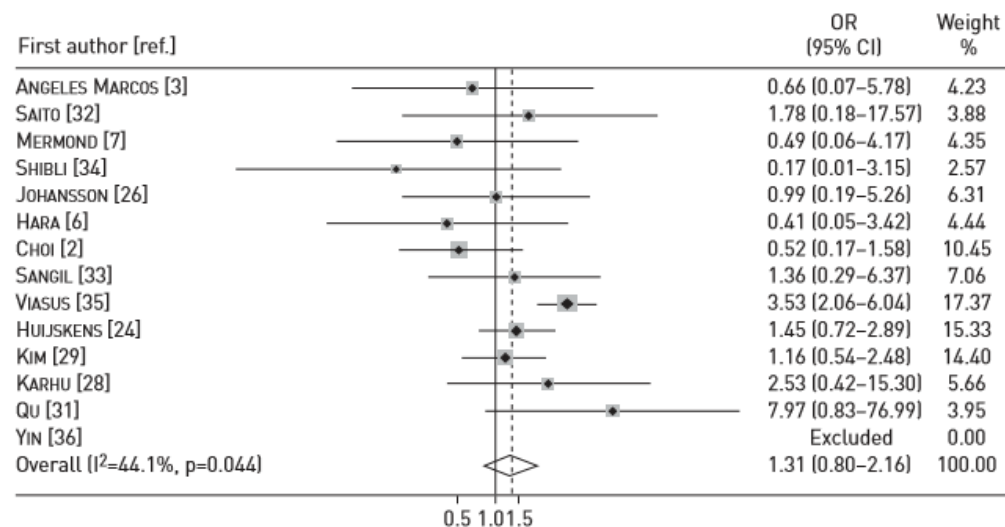
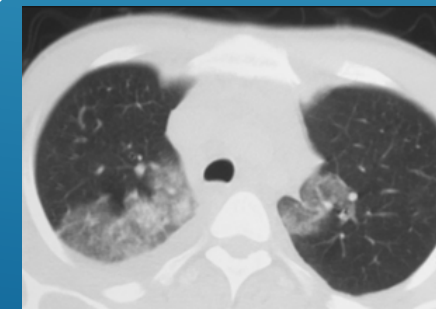


FIGURE 3 Forest plot displaying the odds ratio (OR) of death in the presence of viral infection in patients with community-acquired pneumonia. Weights are from random-effects analysis.

QUAIS AS IMPLICAÇÕES PROGNÓSTICAS DAS INFEÇÕES DUPLAS?



Deaths from Bacterial Pneumonia during 1918–19 Influenza Pandemic

John F. Brundage* and G. Dennis Shanks†

Commentary

Kevan L. Hartshorn

From the Department of Medicine, Boston University School of Medicine, Boston, Massachusetts

New Look at an Old Problem

Bacterial Superinfection after Influenza

1918 Spanish flu:



UMA HIPÓTESE A TER EM CONTA PARA EXPLICAR A EXCESSIVA MORTALIDADE DA PANDEMIA DE 1918



- ▶ Biomarcadores (valores mais elevados nas infecções mistas, virais e bacterianas, comportando pior prognóstico)

- ▶ “Point of care diagnosis”: Kit de PCR
- ▶ Lactato
- ▶ D-Dímeros
- ▶ ProCalcitonina
- ▶ ProAdrenomedulina
- ▶ Peptídeos Natriuréticos
- ▶ Copeptina
- ▶ Neopterin
- ▶ Proendotelina

- ▶ Escalas de Prognóstico

- ▶ PSI (PORT)
- ▶ CURB 65
- ▶ PS-CURXO 80 (SCAP)

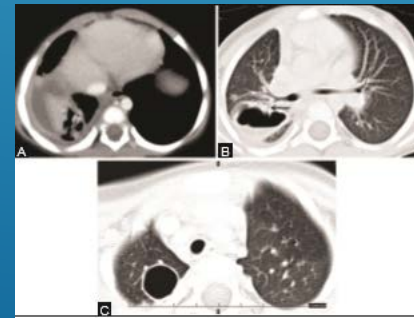
- ▶ Fatores genéticos

- ▶ Apótipos do gene “FER”

- ▶ Possível utilidade na prática clínica

- ▶ Diagnóstico empírico em ambulatório
- ▶ Distinção entre infecção bacteriana e viral
- ▶ Precocidade no início da terapêutica (opção pelo uso de ABs)
- ▶ Suspensão do(s) AB(s)
- ▶ Necessidade de internamento hospitalar
- ▶ Necessidade de transferência p/ CI
- ▶ Alta clínica para ambulatório
- ▶ Avaliação do grau de gravidade e no Prognóstico
- ▶ “Política de ABs” (Stewardship)

BIOMARCADORES DE DIAGNÓSTICO E FATORES CLÍNICOS DE PROGNÓSTICO



Jessica Martin

October 06, 2017

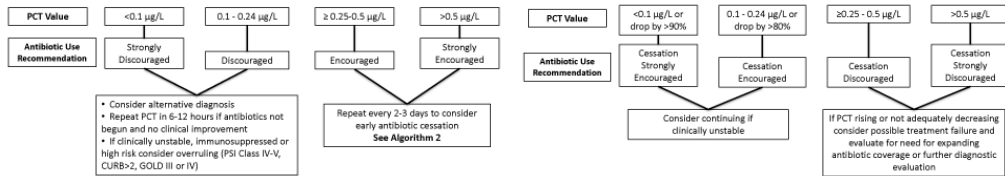
Efficacy of Procalcitonin-Guided Antimicrobial Stewardship Initiative for Diagnosing Pneumonia

Algorithm 1: LRTI Initial PCT Value

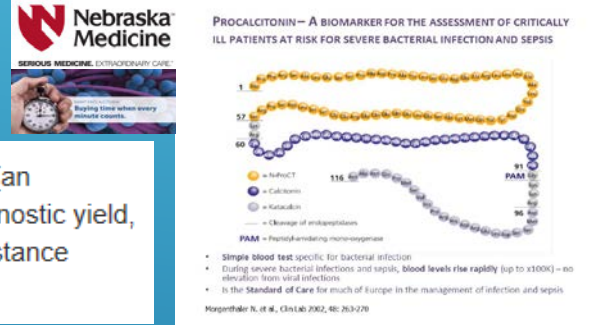
Algorithm 2: LRTI PCT Value Follow Up

LRTI Initial Antibiotic Use Algorithm

LRTI PCT Follow up Algorithm

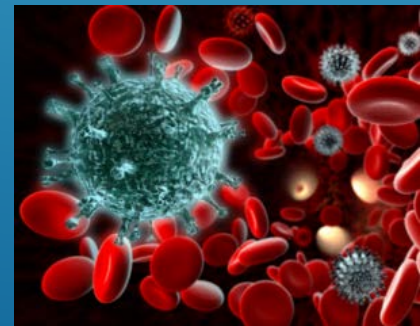


The investigators concluded that "implementation of a [procalcitonin] algorithm through [an antimicrobial stewardship program] is a novel and efficacious addition to improving diagnostic yield, targeting appropriate therapy, and reducing length of stay. The impact on antibiotic resistance remains to be determined."



Implementation of a procalcitonin diagnostic algorithm improves diagnostic yield and reduces hospital length of stay in bacterial pneumonia.

PROCALCITONINA: O NOVO BIOMARCADOR MAIS INVESTIGADO



Characteristic	Points Assigned*
Demographic Factor	
Age	
• Men	Add age (years)
• Women	Add age (years) - 10
Nursing home resident	+10
Coexisting Illnesses	
Neoplastic disease [†]	+30
Liver disease [‡]	+20
Congestive heart failure [§]	+10
Cerebrovascular disease	+10
Renal disease [¶]	+10
Physical Examination Findings	
Altered mental status*	+20
Respiratory rate ≥ 30 /min	+20
Systolic blood pressure < 90 mmHg	+20
Temperature $< 35^\circ\text{C}$ or $\geq 40^\circ\text{C}$	+15
Pulse ≥ 125 /min	+10
Laboratory and Radiographic Findings	
Arterial pH < 7.35	+30
Blood urea nitrogen ≥ 30 mg/dL (11 mmol/L)	+20
Sodium < 130 mmol/L	+20
Glucose ≥ 250 mg/dL (14 mmol/L)	+10
Hematocrit $< 30\%$	+10
Partial pressure of arterial oxygen < 60 mmHg**	+10
Pleural effusion	+10

*A total point score for a given patient is obtained by adding the patient's age in years (age minus 10 for females) and the points for each applicable patient characteristic. Points assigned to each predictor variable were based on coefficients obtained from the logistic regression model used in step 2 of the prediction rule.

[†]Any cancer, except basal or squamous cell cancer of the skin, that was either active at the time of presentation or diagnosed within 1 year of presentation.

[‡]A clinical or histologic diagnosis of cirrhosis or other form of chronic liver disease, such as chronic active hepatitis.

[§]Systolic or diastolic ventricular dysfunction documented by history and physical examination, as well as chest radiography, echocardiography, MUGA scanning, or left ventriculography. A clinical diagnosis of stroke, transient ischemic attack, or stroke documented by MRI or CT scan.

[¶]A history of chronic renal disease or abnormal blood urea nitrogen and creatinine values documented in the medical record.

**Disorientation (to person, place, or time, not known to be chronic), stupor, or coma.

**In the pneumonia PORT cohort study, an oxygen saturation value $< 90\%$ on pulse oximetry or intubation before admission was also considered abnormal.

PORT Scoring System
 Total Score < 70 = Risk Class II
 Total Score 71-90 = Risk Class III
 Total Score 91-130 = Risk Class IV
 Total Score > 130 = Risk Class V
 PORT and CURB 65 scores used to determine the point of care for treatment—home vs hospital vs ICU
 Adapted from PSI/PORT Score: Pneumonia Severity Index for CAP. Fine MJ. Available at: <https://www.mdcalc.com/psi-port-score-pneumonia-severity-index-cap/>. Accessed January 17, 2019.

Table 1. CURB-65 Scoring

Clinical Feature	Points
Confusion (defined as a Mental Test Score of ≤ 8 , or disorientation in person, place, or time)	1
Uremia: blood urea > 7 mmol/L (~ 19 mg/dL)	1
Respiratory rate: ≥ 30 breaths/minute	1
Blood pressure: systolic < 90 mm Hg or diastolic ≤ 60 mm Hg	1
Age ≥ 65 years	1
Total points	

Table 2. Treatment Options Based on CURB-65 Score

Score	Group	Treatment Options
0 or 1	Group 1; mortality low (1.5%)	Low risk; consider home treatment
2	Group 2; mortality intermediate (9.2%)	Consider hospital-supervised treatment (either short-stay inpatient or hospital-supervised outpatient)
≥ 3	Group 3; mortality high (22%)	Manage in hospital as severe pneumonia; consider admission to intensive care unit, especially with CURB-65 score of 4 or 5

SCAP or PS-CURXO 80

Major criteria	Minor criteria
P: pH < 7.30 (13 points)	C: Confusion (5 points)
	U: BUN > 30 mg/dl (5 points)
	R: Breaths per minute > 30 (9 points)
S: Systolic blood pressure < 90 mm Hg (11 points)	X: multilobar/bilateral in chest X-rays (5 points)
	O: PaO ₂ < 54 or PaO ₂ /FIO ₂ < 250 mm Hg (6 points)
	80: age ≥ 80 (5 points)

Define severe CAP if patient has at least a major or two minor criteria.

Low-risk groups (0-1): with less than 10 points

Medium-risk group (0-1): with 10-19 points

High-risk groups (3-4): with more than 20 points

Predicts the risk of poor outcome (development of SS-SSh, need for MV or treatment failure) and need for ICU

SMART-COP

S Systolic BP < 90 mm Hg (PAS < 90 mm Hg): 2 points

M Multilobar involvement: 1 point

A Albumin < 3.5 g/dl: 1 point

R RR adjusted for age: 1 point

T Tachycardia ≥ 125 : 1 point

C Confusion: 1 point

O Oxygenation adjusted for age: 2 points

P pH < 7.35 : 2 points

Age rpm	< 50 years	> 50 years
	≥ 25 /min	≥ 30 /min

Age	< 50 years	> 50 years
PaO ₂	< 70 mm Hg	< 60 mm Hg
Sat O ₂	$\leq 93\%$	$\leq 90\%$
PaO ₂ /FIO ₂	< 333	< 250

From 0-2 points: **low risk** of need for intensive VPS or VS

From 3-4 points: **moderate risk** (1 of 8) of need for intensive VPS or VS

From 5-6 points: **high risk** (1 of 3) of need for intensive VPS or VS

If ≥ 7 points: **very high risk** (2 of 3) of need for intensive VPS or VS

SCAP: Severity community-acquired pneumonia; SS: severe sepsis; SSh: septic shock; MV: mechanical ventilation; ICU: Intensive Care Unit; SBP: systolic blood pressure; RR: respiratory rate; bpm: breaths per minute; PaO₂: arterial oxygen pressure; SatO₂: oxygen saturation; PaO₂/FIO₂: respiratory quotient (arterial oxygen pressure/fraction of inspired oxygen); VPS: vasopressor support; VS: ventilator support
 Adapted from citations 10 and 11

AS DIFERENTES ESCALAS DE AVALIAÇÃO UTILIZADAS NA PRÁTICA CLÍNICA



REVIEW

Open Access

New aspects in the management of pneumonia

Elena Prina¹, Adrian Ceccato^{1,3} and Antoni Torres^{1,2,4*}



Table 2. High-risk identification in the emergency department (including assessment of the ATS/IDSA minor criteria).

Clinical assessment, supplemented by evaluation of the following criteria:

- Presence of acute respiratory failure
 - Respiratory rate of 30/min or more
 - Arterial oxygen partial pressure/fractional inspired oxygen (paO_2/FiO_2) of 250 or less
 - Oxygen saturation of less than 90%
 - Multi-lobar infiltrate
- Presence of acute extra-pulmonary organ dysfunction
 - Systolic blood pressure of less than 90 mm Hg/hypotension requiring aggressive fluid resuscitation
 - Elevated lactate
 - Temperature of less than 36°C
 - New-onset mental confusion
 - Acute renal failure/blood urea nitrogen of more than 20 mg/dL
 - Leucocytes of less than 4000/ μ L
 - Thrombocytes of less than 100,000/ μ L
- Presence of instable comorbidity
 - Especially acute cardiovascular complication

ATS/IDSA, American Thoracic Society/Infectious Diseases Society of America.



REVIEW

Advances in the prevention, management, and treatment of community-acquired pneumonia [version 1; referees: 2 approved]

Mathias W. Pletz¹, Gernot G. Rohde², Tobias Welte³, Martin Kolditz⁴, Sebastian Ott⁵

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²Department of Respiratory Medicine, Hannover Medical School, Hannover, Germany

³Department of Respiratory Medicine, Maastricht University Medical Center, Maastricht, Netherlands

⁴Division of Pulmonology, University Hospital Carl Gustav Carus, Dresden, Germany

⁵Department of Pulmonary Medicine, Inselspital, University Hospital, Bern, Switzerland

Table 1. Low-risk identification in the outpatient setting.

Clinical assessment, supplemented by evaluation of the following criteria:

- Respiratory rate of less than 30 per min
- Diastolic/systolic blood pressure of at least 61 mm Hg/90 mm Hg
- No new-onset mental confusion
- Oxygen saturation of at least 90% on room air
- No (potentially) decompensating comorbidity
- No poor functional status ("chronically bedridden")

CRITÉRIOS DE GRAVIDADE



RESEARCH ARTICLE

Open Access



Clinical failure with and without empiric atypical bacteria coverage in hospitalized adults with community-acquired pneumonia: a systematic review and meta-analysis

Khalid Eljaaly^{1,2*}, Samah Alshehri^{1,2}, Ahmed Aljabri^{1,2}, Ivo Abraham², Mayar Al Mohajer³, Andre C. Kalil⁴ and David E. Nix^{2,3}

Abstract

Background: Both typical and atypical bacteria can cause community-acquired pneumonia (CAP); however, the need for empiric atypical coverage remains controversial. Our objective was to evaluate the impact of antibiotic regimens with atypical coverage (a fluoroquinolone or combination of a macrolide/doxycycline with a β -lactam) to a regimen without atypical antibiotic coverage (β -lactam monotherapy) on rates of clinical failure (primary endpoint), mortality, bacteriologic failure, and adverse events, (secondary endpoints).

Methods: We searched the PubMed, EMBASE and Cochrane Library databases for relevant RCTs of hospitalized CAP adults. We estimated risk ratios (RRs) with 95% confidence intervals (CIs) using a fixed-effect model, but used a random-effects model if significant heterogeneity (I^2) was observed.

Results: Five RCTs with a total of 2011 patients were retained. A statistically significant lower clinical failure rate was observed with empiric atypical coverage (RR, 0.851 [95% CI, 0.732–0.99; $P = 0.037$]; $I^2 = 0\%$). The secondary outcomes did not differ between the two study groups: mortality (RR = 0.549 [95% CI, 0.259–1.165, $P = 0.118$], $I^2 = 61.434\%$) bacteriologic failure (RR = 0.816 [95% CI, 0.523–1.272, $P = 0.369$], $I^2 = 0\%$), diarrhea (RR = 0.746 [95% CI, 0.311–1.790, $P = 0.512$], $I^2 = 65.048\%$), and adverse events requiring antibiotic discontinuation (RR = 0.83 [95% CI, 0.542–1.270, $P = 0.39$], $I^2 = 0\%$).

Conclusions: Empiric atypical coverage was associated with a significant reduction in clinical failure in hospitalized adults with CAP. Reduction in mortality, bacterial failure, diarrhea, and discontinuation due to adverse effects were not significantly different between groups, but all estimates favored atypical coverage. Our findings provide support for the current guidelines recommendations to include empiric atypical coverage.

Keywords: Community-acquired pneumonia, Antibiotics, Atypical, Macrolides, Fluoroquinolones

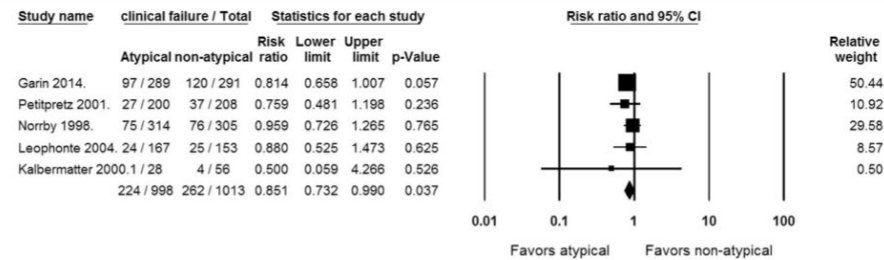


Fig. 2 Forest plot showing the risk ratios of clinical failure for patients receiving empiric antibiotic therapy with versus without atypical coverage. Vertical line, “no difference” point between the 2 groups; horizontal line, 95% confidence interval; squares, risk ratios; diamonds, pooled risk ratios. Abbreviations: CI, Confidence interval

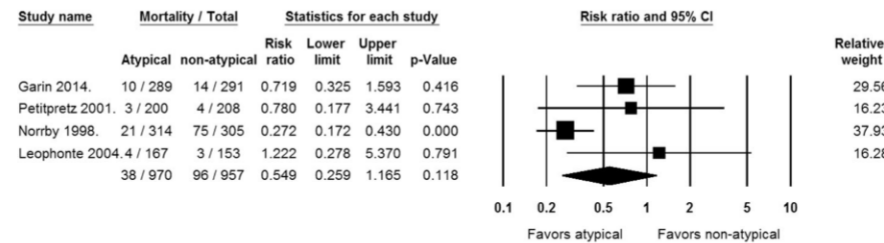


Fig. 3 Forest plot showing the risk ratios of mortality for patients receiving empiric antibiotic therapy with versus without atypical coverage. Vertical line, “no difference” point between the 2 groups; horizontal line, 95% confidence interval; squares, risk ratios; diamonds, pooled risk ratios. Abbreviations: CI, Confidence interval

TERAPÊUTICA DE ASSOCIAÇÃO PARA TODOS OS DOENTES???



Bacterial Pneumonia in Older Adults



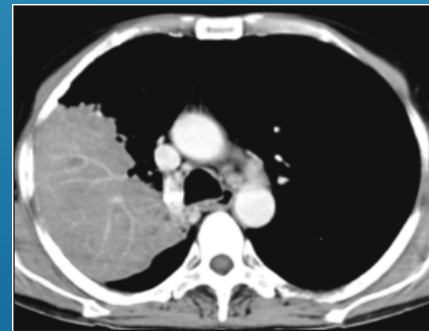
Thomas J. Marrie, MD, FRCPC^{a,*}, Thomas M. File Jr, MD, MSC^{b,c}

Box 3

Considerations when patients with pneumonia fail to improve or deteriorate during therapy

1. Reconsider the diagnosis. Many conditions can mimic pneumonia, such as pulmonary infarction, malignancy, drug reaction, and eosinophilic pneumonia.
2. Reconsider the etiologic diagnosis: Does your patient have tuberculosis or an infection with a microorganism resistant to the antibiotics you have chosen?
3. Has your patient developed nosocomial pneumonia? In areas where the potable water is contaminated with *Legionella*, consider legionellosis. If your patient has required mechanical ventilation, nosocomial pneumonia is not uncommon.
4. Has metastatic infection occurred? Bacteremic pneumonia can be complicated by endocarditis, meningitis, septic arthritis, or abscess formation in the spleen or liver.
5. Is empyema present?
6. Drug fever should be a consideration in febrile patients who are otherwise well.

O QUE PENSAR QUANDO O DOENTE NÃO MELHORA



Community-Acquired Bacterial Pneumonia: Is There Anything New?

Hans Liu, MD, FACP

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TABLE 2 Antibiotics on the horizon for community-acquired bacterial pneumonia^{36,43-51}

Agent	Omadacycline	Lefamulin	Solithromycin
Class	Tetracycline	Pleuromutilin	4th-generation macrolide
Stage of development	Early phase 3	Early phase 3	FDA issued complete response letter in December 2016 requiring further safety investigations.
Pathogens covered	Resistant Gram-positive bacteria, including <i>S pneumoniae</i> and MRSA	Multi-drug-resistant strains of <i>S pneumoniae</i> , macrolide-sensitive and macrolide-resistant <i>M pneumoniae</i>	Macrolide-resistant <i>S pneumoniae</i> and <i>M pneumoniae</i> , <i>M catarrhalis</i> ; good activity against <i>S aureus</i> , including community-acquired MRSA
Route of administration	Oral and IV	Oral and IV	Oral and IV

Abbreviations: FDA, US Food and Drug Administration; IV, intravenous; *M catarrhalis*, *Moraxella catarrhalis*; *M pneumoniae*, *Mycoplasma pneumoniae*; MRSA, methicillin-resistant *Staphylococcus aureus*; PDUFA, Prescription Drug User Fee Act; *S aureus*, *Staphylococcus aureus*; *S pneumoniae*, *Streptococcus pneumoniae*.

AVANÇOS NA TERAPÊUTICA ANTIBIÓTICA...



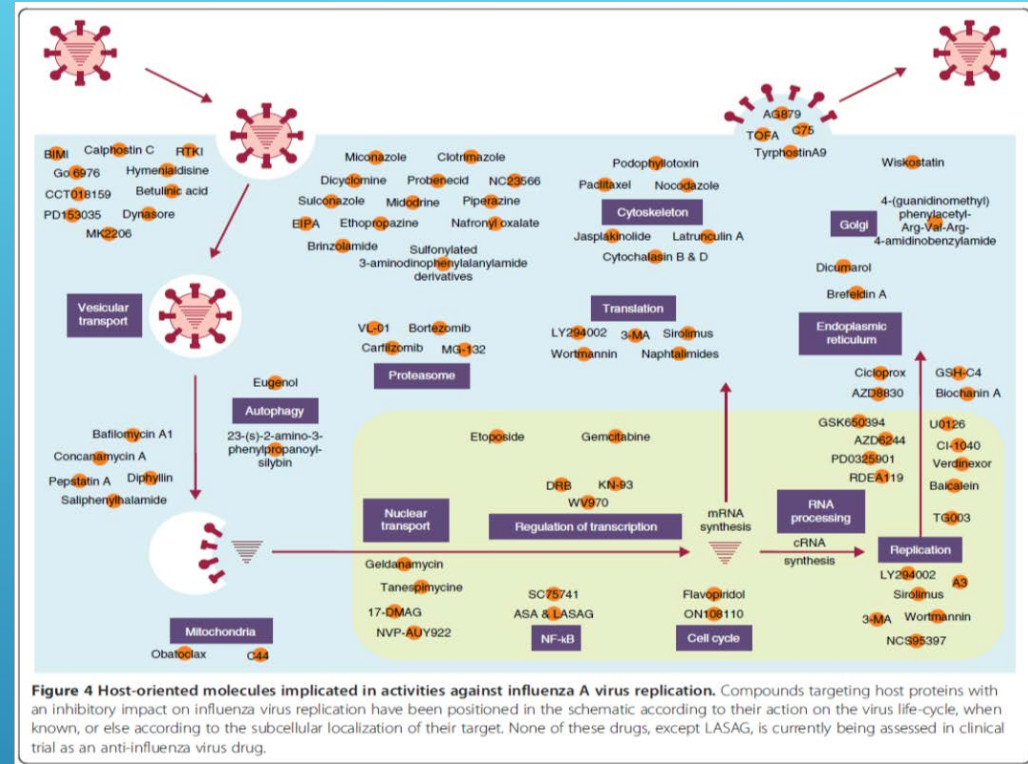
Influenza antivirals currently in late-phase clinical trial

Paulina Koszalka^{1,2} | Danielle Tilmanis¹ | Aeron C. Hurt^{1,2}

TABLE 1 Summary of influenza antivirals currently in phase II or III clinical trials

Host/Viral targeted	Name	Type of antiviral	Specific target	Administration Route	Clinical trial phase	Manufacturer/Research Group
Host targeting	DAS181-F03/ F04 ²	Sialidase	Neu5Ac α(2,3)- and Neu5Ac α(2,6)-Gal linkages of sialic acid	Oral, inhalation	I, II	Ansun Biopharma, USA
	Nitazoxanide	Thiazolide	Haemagglutinin maturation	Oral, tablet	III	Romark, USA
Viral targeting	JNJ-63623872	PB2 Inhibitor	Small molecule inhibitor of PB2	Oral, tablet	I, II	Janssen, Belgium
	T705	RNA-dependent RNA polymerase	Purine pseudobase (incorporates in viral RNA)	Oral, tablet	II, III	Toyama, Japan
	S-033188	Cap-dependent endonuclease inhibitor	Small molecule inhibitor of cap-dependent endonuclease	Oral, tablet	III	Shionogi, Japan
	CR6261	Monoclonal antibody	HA stem	Intravenous	I, II	Crucell/Janssen
	CR8020	Monoclonal antibody	HA stem	Intravenous	I, II	Crucell/Janssen
	MEDI8852	Monoclonal antibody	HA stem	Intravenous	I, II	MedImmune, USA
	MHAA4549A	Monoclonal antibody	HA stem	Intravenous	II	Genentech, USA
VIS410	Monoclonal antibody	HA stem	Intravenous	II	Visterra, USA	

²F03 and F04 refer to formulations of DAS181. DAS181-F03 and DAS181-F04 are 10 µm particles, however, F04 differs via the addition of MgSO₄.



... E NA TERAPÊUTICA ANTIVÍRICA!!!

"Revisão sobre os avanços na terapêutica anti-vírica"

José M. D. Poças

Director do Serviço de Doenças Infecciosas do CHS HSB Setúbal

RESEARCH

Open Access



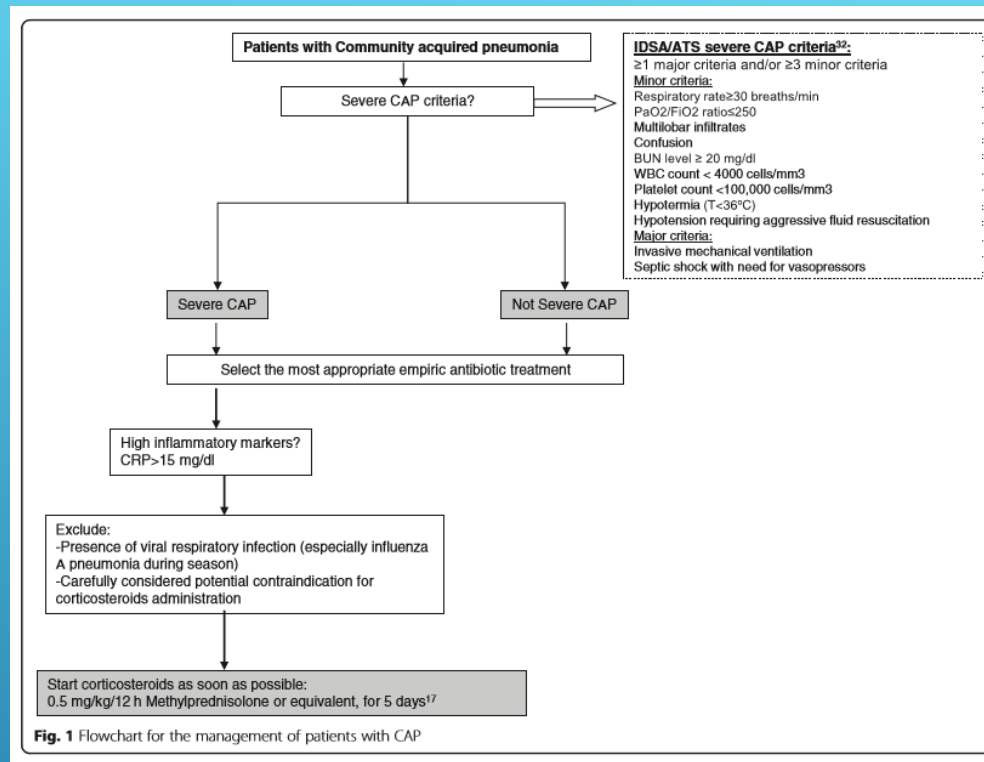
Time-dependent association of glucocorticoids with adverse outcome in community-acquired pneumonia: a 6-year prospective cohort study

Manuela Nickler¹, Manuel Ottiger¹, Christian Steuer², Alexander Kutz¹, Mirjam Christ-Crain^{3,4}, Werner Zimmerli⁵, Robert Thomann⁶, Claus Hoess⁷, Christoph Henzen⁸, Luca Bernasconi², Andreas Huber², Beat Mueller^{1,4}, and Philipp Schuetz^{1,4*} for the ProHOSP Study Group

WHAT'S NEW IN INFECTIOUS DISEASES

Adjuvant steroid therapy in community-acquired pneumonia

Caroline Bell Sisson, MMS, PA-C



O PAPEL DA TERAPÊUTICA ADJUVANTE: O EXEMPLO DOS CORTICÓIDES



- ▶ **A realidade atual estimada**
 - ▶ Tx de cobertura vacinal: 25-75%
 - ▶ Tx de cobertura dos serotipos: 33-83%
- ▶ **Os impactos de uma estratégia consequente de “oportunidade”**
 - ▶ **Económico nos países da Comunidade Europeia**
 - ▶ 10 biliões de euros / ano
 - ▶ **Epidemiológico com da vacinação contra a Pneumococo**
 - ▶ (-) 200.000 casos / ano (- 45-65% do total)
 - ▶ > 20% dos internamentos hospitalares
 - ▶ **IMPORTANTE:** Morbi-mortalidade por eventos cardio-vasculares
 - ▶ **SEM ESQUECER:** Doença pneumocócica invasiva (infecções do SNC, Sepsis e também do foro ORL)

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Narrative Review

Community-acquired pneumonia in adults: Highlighting missed opportunities for vaccination

Francesco Blasi ^{a,*}, Murat Akova ^b, Paolo Bonanni ^c, Nathalie Dartois ^d, Evelyne Sauty ^e, Chris Webber ^f, Antoni Torres ^g

^a Department of Pathophysiology and Transplantation, Università degli Studi di Milano, IRCCS Fondazione Cà Granda Ospedale Maggiore Policlinico, Milan, Italy
^b Infectious Diseases Department, Hacettepe University School of Medicine, Ankara, Turkey
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^d Pfizer Vaccines Europe, Paris, France
^e Pfizer Europe, Paris, France
^f Pfizer Vaccine Clinical Research, Maidenhead, UK
^g Pulmonology Department, Hospital Clinic, University of Barcelona, IDIBAPS, CIBERES, Barcelona, Spain

PLOS ONE

RESEARCH ARTICLE

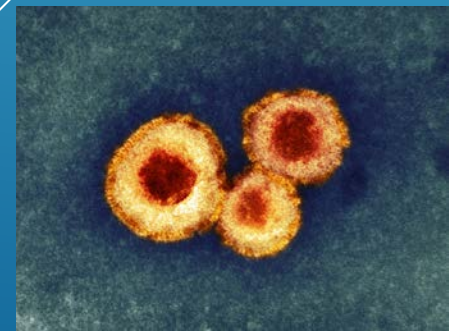
Effectiveness of pneumococcal vaccines in preventing pneumonia in adults, a systematic review and meta-analyses of observational studies

Myint Tin Tin Htar ^{1,c,*}, Anke L. Stuurman ^{2,c}, Germano Ferreira ², Cristiano Alicino ³, Kaatje Bollaerts ², Chiara Paganino ³, Ralf René Reinert ⁴, Heinz-Josef Schmitt ⁴, Cecilia Trucchi ², Thomas Vestraeten ², Filippo Ansaldi ³

¹ Pfizer: Vaccines Clinical Epidemiology, Pfizer Inc, Paris, France, ² P95 Epidemiology and Pharmacovigilance Consulting and Services, P95, Leuven, Belgium, ³ Department of Health Sciences (DiSSaI), University of Genoa, Genoa, Italy, ⁴ Pfizer: Vaccines Medical Development and Scientific Clinical Affairs, Pfizer Inc, Paris, France

© These authors contributed equally to this work.
 * Myint.TinTinHtar@pfizer.com

A IMPORTÂNCIA DA VACINA ANTIPNEUMOCÓCICA NA PREVENÇÃO



MAJOR ARTICLE

Influenza Infection and Risk of Acute Myocardial Infarction in England and Wales: A CALIBER Self-Controlled Case Series Study

Charlotte Warren-Gash,¹ Andrew C. Hayward,¹ Harry Hemingway,² Spiros Denaxas,² Sara L. Thomas,³ Adam D. Timmis,⁵ Heather Whitaker,⁴ and Liam Smeeth⁴

¹Centre for Infectious Disease Epidemiology, Research Department of Infection & Population Health, and ²Department of Epidemiology & Public Health, University College London, ³Department of Infectious Disease Epidemiology and ⁴Department of Non-Communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, ⁵Barts and the London School of Medicine and Dentistry, London; and ⁶Department of Mathematics & Statistics, Open University, Milton Keynes, United Kingdom

THE LANCET

Volume 389, Supplement 1, 23 February 2017, Page S101



Poster Abstracts

Respiratory infections as vascular triggers: self-controlled case series analysis of linked Scottish data

Dr Charlotte Warren-Gash PhD ^{a, b, c, d, e, f}, Ruth Blackburn PhD ^b, Heather Whitaker PhD ^c, Andrew Hayward MD ^b

A IMPORTÂNCIA DAS INFECÇÕES RESPIRATÓRIAS NOS EVENTOS CARDIO E CEREBROVASCULARES AGUDOS



The respiratory tract microbiome and lung inflammation: a two-way street

GB Huffnagle^{1,2,3}, RP Dickson¹ and NW Lukacs^{3,4}

The lungs are not sterile or free from bacteria; rather, they harbor a distinct microbiome whose composition is driven by different ecological rules than for the gastrointestinal tract. During disease, there is often a shift in community composition towards Gammaproteobacteria, the bacterial class that contains many common lung-associated gram-negative "pathogens." Numerous byproducts of host inflammation are growth factors for these bacteria. The extracellular nutrient supply for bacteria in the lungs, which is severely limited during health, markedly increases due to the presence of mucus and vascular permeability. While Gammaproteobacteria benefit from airway inflammation, they also encode molecular components that promote inflammation, potentially creating a cyclical inflammatory mechanism. In contrast, *Prevotella* species that are routinely acquired via microaspiration from the oral cavity may participate in immunologic homeostasis of the airways. Areas of future research include determining for specific lung diseases (1) whether an altered lung microbiome initiates disease pathogenesis, promotes chronic inflammation, or is merely a marker of injury and inflammation, (2) whether the lung microbiome can be manipulated therapeutically to change disease progression, (3) what molecules (metabolites) generated during an inflammatory response promote cross-kingdom signaling, and (4) how the lung "ecosystem" collapses during pneumonia, to be dominated by a single pathogen.

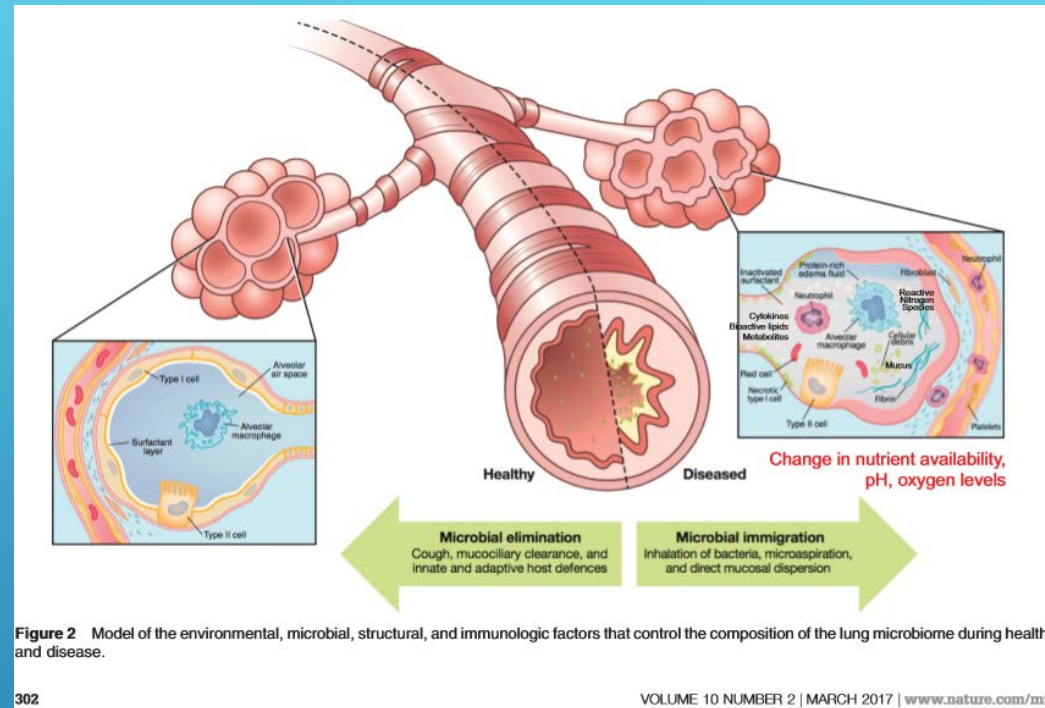
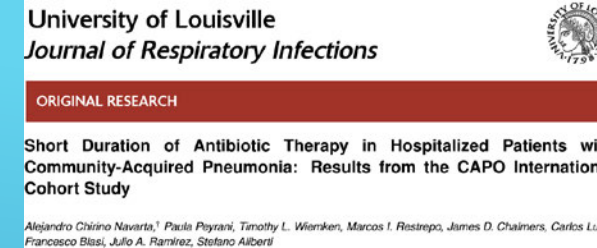


Figure 2 Model of the environmental, microbial, structural, and immunologic factors that control the composition of the lung microbiome during health and disease.

A IMPORTÂNCIA FUTURA DO ESTUDO DO MICROBIOMA RESPIRATÓRIO





▶ Incontroverso

- ▶ Instituição do AB nas 1ªh (4h)
- ▶ Colheita prévia de produtos biológicos para exame microbiológico
- ▶ Definição das estratégias de conduta clínica com base nas escalas de prognóstico
- ▶ Diagnóstico por excesso (Traqueobronquites / Pneumonias)
- ▶ “Descalação” dos Abs e o “Switch” de IV/PO
- ▶ Interesse da vacinação contra Vírus Influenza / Pneumococo
- ▶ Sessação do tabagismo

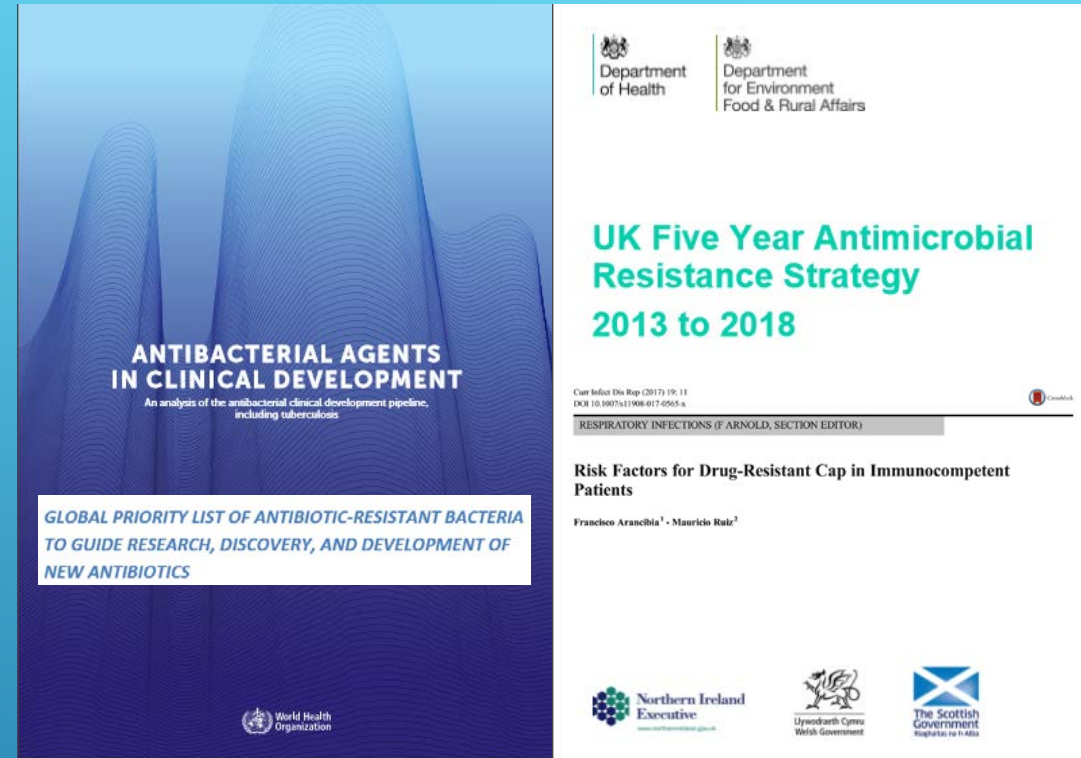
▶ Controverso

- ▶ Biomarcadores
- ▶ Técnicas de biologia molecular
- ▶ Infecções duplas (virais / bacterianas)
- ▶ Esquemas curtos de ABs (3 – 5 dias)
- ▶ Utilização sistemática da terapêutica de associação dupla em todos os casos de PAC
- ▶ Aminopenicilinas c/ ou s/ inibidor das beta-lactamases
- ▶ Terapêutica adjuvante (Corticosteroides; Estatinas; IgBH)

CONCLUSÕES



- ▶ 1)- Tem o doente febre?
- ▶ 2)- Tem o síndrome febril etiologia infecciosa?
- ▶ 3)- Que tipo de agente microbiano é a causa do quadro clínico?
- ▶ 4)- Terá a infeção uma causa mista?
- ▶ 5)- Terão o(s) microrganismos resistências primárias aos anti-microbianos?
- ▶ 6)- Qual a terapêutica mais eficaz?
- ▶ 7)- Devemos utilizar monoterapia ou terapêutica de combinação?
- ▶ 8)- Qual o tempo ideal de tratamento?
- ▶ 9)- Se não se verificarem melhorias clínicas, qual a(s) causa(s) e a terapêutica alternativa mais aconselhável?



**AS PERGUNTAS CAPITAIS PARA AS QUAIS SE EXIGEM
RESPOSTAS RÁPIDAS E FIÁVEIS DE FUTURO...**

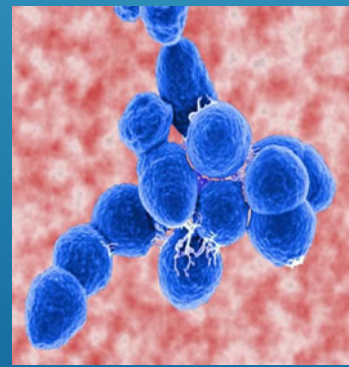
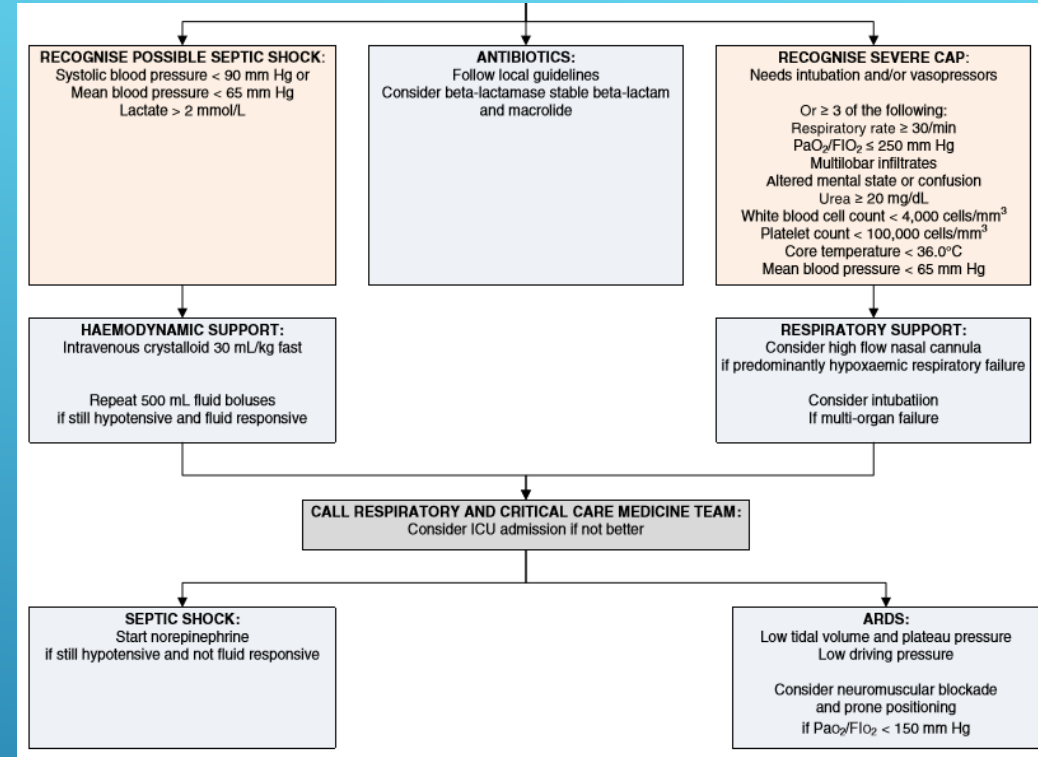
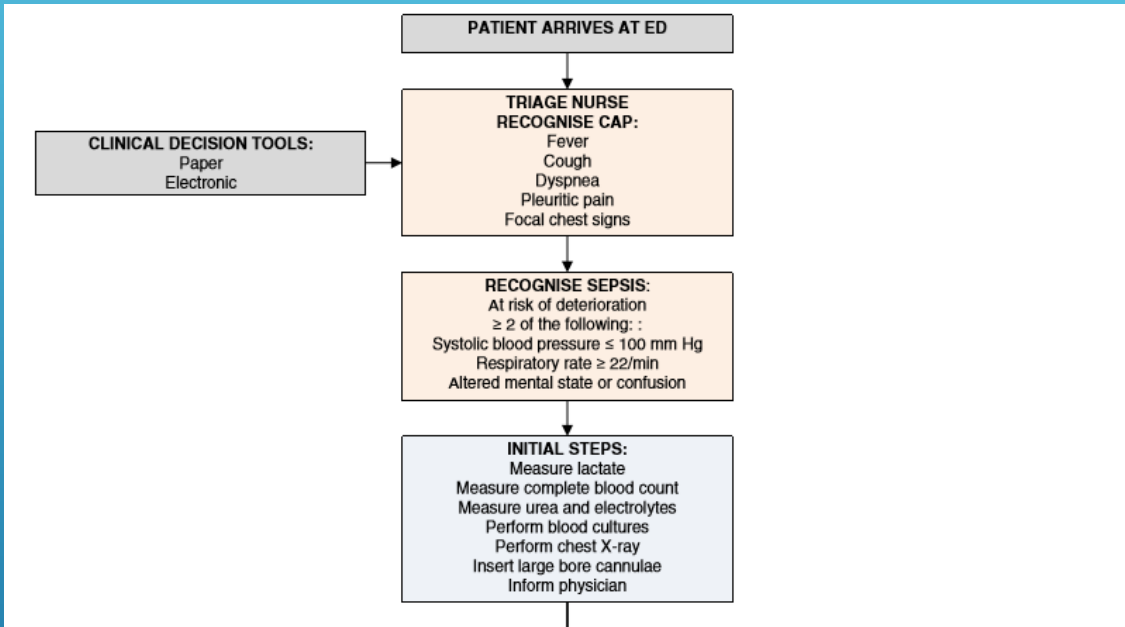


Fig. 1 Suggested approach to early and aggressive management measures for severe community-acquired pneumonia (CAP). ED emergency department, PaO_2 partial pressure of arterial oxygen, FIO_2 fraction of inspired oxygen



... ATÉ LÁ, FAÇAMOS O QUE ESTÁ ESTABELECIDO E RECOMENDADO,
AO NOSSO ALCANCE, BEM E DEPRESSA...

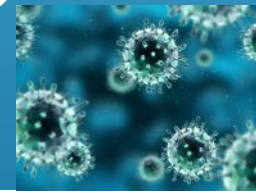


Table 1

Traditional risk definitions for CAP [22,86–89].

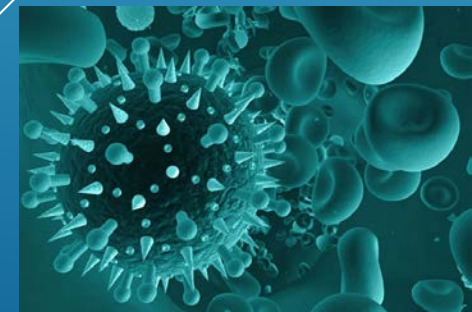
At risk	High risk
Metabolic diseases (diabetes mellitus)	Immunodeficiency (B or T cell deficiency)
Chronic respiratory disease (asthma, COPD, interstitial lung diseases)	Cerebrospinal fluid leakage, skull fracture, cochlear implant
Chronic heart, liver, renal diseases	Functional asplenia or splenectomy
Chronic alcoholism	Sickle-cell anaemia
Smoking	Nephrotic syndrome
Patients living within an institution	Transplantation (organ or bone marrow)
People with a history of (pneumococcal) pulmonary infection	Immunosuppressive therapy
	Leukaemia, lymphoma, multiple myeloma
	Neoplastic disease
	HIV infection
	Autoimmune diseases

Box 1

Eligible patients: identifying key risks for adults in the general population [84,90,91].

- Age over 65
- Current or past smoker
- High alcohol intake
- Under- or overweight
- Living or working in institutions such as schools, hospitals, prisons or care homes
- Comorbidities such as diabetes, asthma or COPD
- Previous pneumococcal infection
- Chronic immunosuppressive disease

... SEM ESQUECER AS MEDIDAS
PROFILÁTICAS APROVADAS...



Enablers and barriers to the use of antibiotic guidelines in the assessment and treatment of community-acquired pneumonia—A qualitative study of clinicians' perspectives

Antoine Sedrak^{1,2} | Mahesan Anpalahan^{2,3,4} | Karen Luetsch¹ 

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²Eastern Health, Box Hill, Victoria, Australia

³Monash University, Melbourne, Victoria, Australia

⁴North West Academic Centre, The University of Melbourne, St Albans, Victoria, Australia

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Summary

Background: Community-acquired pneumonia (CAP) is a common condition and a number of guidelines have been developed for its assessment and treatment. Adherence to guidelines by clinicians varies and particularly the prescribing of antibiotics often remains suboptimal.

Objective: The aim of this study was to elucidate potential barriers and enablers to the adherence to antibiotic guidelines by clinicians treating CAP in an Australian hospital.

Methods: Semi-structured interviews were conducted with purposively recruited senior prescribers who regularly treat CAP in an Australian hospital. Thematic analysis identified a number of themes and subthemes related to their knowledge, attitudes and behaviours associated with the use of CAP guidelines.

Results: Thematic saturation was reached after 10 in-depth interviews. Although similar barriers to the use of guidelines as previously described in the literature were confirmed, a number of novel, potential enablers were drawn from the interviews. Clinicians' acceptance and accessibility of guidelines emerged as enabling factors. Generally positive attitudes towards antimicrobial stewardship services invite leveraging what was described as the relationship-based and hierarchical nature of medical practice to provide personalised feedback and updates to clinicians.

Conclusions: Adding a social and personalised approach of antimicrobial stewardship to policy- and systems-based strategies may lead to incremental improvements in guideline adherent practice when assessing and treating CAP.



April 2017 Volume 110 Number 4

An audit of empiric antibiotic choice in the inpatient management of community-acquired pneumonia

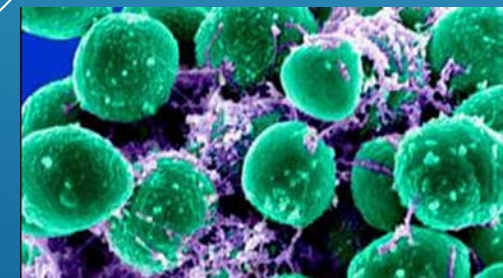
F Delaney, A Jackson

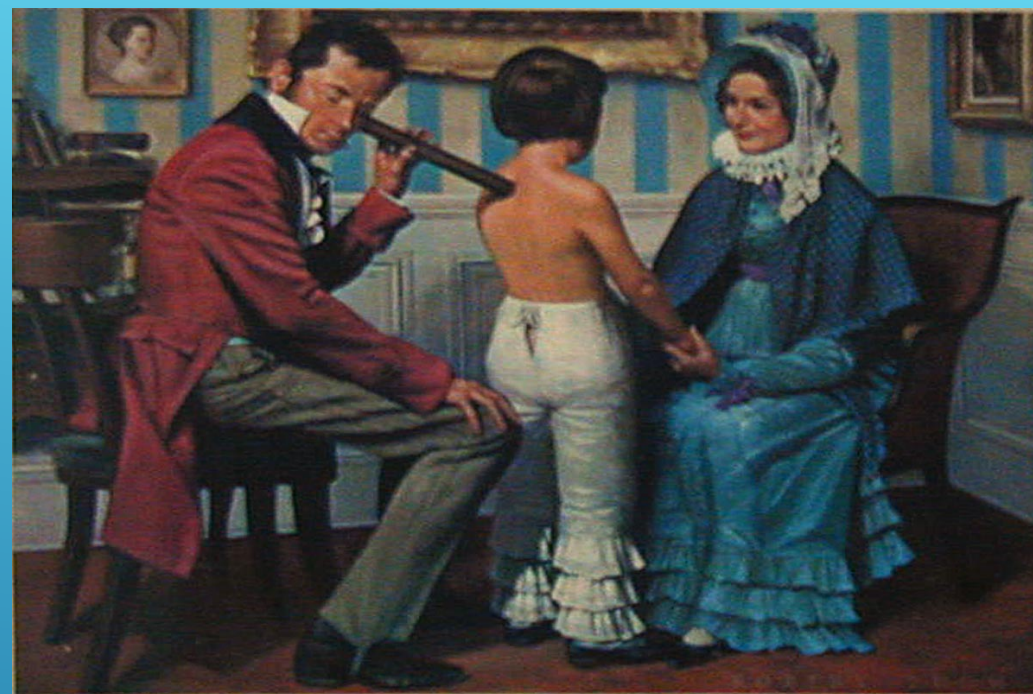
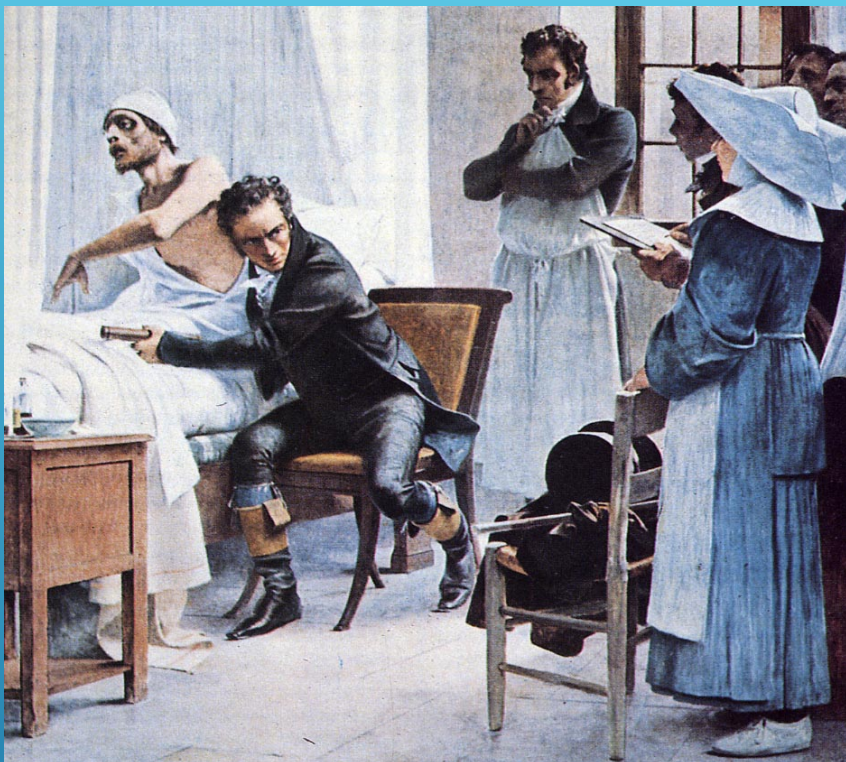
Mercy University Hospital, Grenville Place, Cork City, County Cork, Ireland

Abstract

Adherence to antimicrobial guidelines for empiric antibiotic prescribing in community-acquired pneumonia (CAP) has been reported to be worryingly low. We conducted a review of empiric antibiotic prescribing for sixty consecutive adult patients admitted to the Mercy University Hospital with a diagnosis of CAP. When analysed against local antimicrobial guidelines, guideline concordant empiric antibiotics were given in only 48% of cases, lower than the average rate in comparable studies. Concordance was 100% in cases where the CURB-65 pneumonia severity assessment score, on which the guidelines are based, was documented in the medical notes. The use of excessively broad spectrum and inappropriate antibiotics is a notable problem. This study supports the theory that lack of knowledge regarding pneumonia severity assessment tools and unfamiliarity with therapeutic guidelines are key barriers to guideline adherence, which remains a significant problem despite increased focus on antimicrobial stewardship programs in Ireland.

... E DE AUDITAR PERIODICAMENTE OS
IMPACTOS DA NOSSA PRAXIS CLÍNICA...





... SEM ESQUECER QUE É ATRAVÉS DA HISTÓRIA EPIDEMIOLÓGICA E DA SEMIOLOGIA CLÍNICA QUE DEVEMOS ORIENTAR A FORMULAÇÃO DO PRIMEIRO DIAGNÓSTICO DIFERENCIAL COMO SABIAMENTE O ANTEVIU RENE LAENNEC (1781-1826)!!!



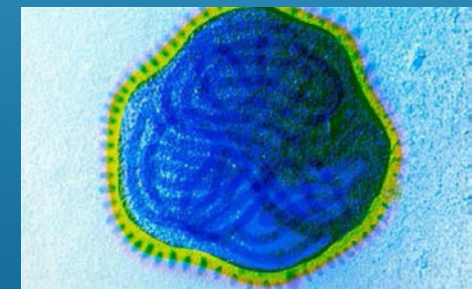
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