A year in review in community-acquired respiratory tract infections

Paul M. Tulkens, MD, PhD *

Cellular and Molecular Pharmacology & Center for Clinical Pharmacy
Louvain Drug Research Institute,
Catholic University of Louvain
Brussels, Belgium

http://www.facm.ucl.ac.be

* this presentation is largely inspired from a lecture and documents of Prof. A. Torres

الجمعية العلمية السعودية للطب الباطني
Saudi Society of Internal Medicine

INSPIRATION: Global Perspectives and Local Insights in Infection Management
Jeddah, Saudi Arabia, 15 November 2013

With approval of the Belgian Ethical Health Platform – visa no. 13/V1/4123/055866

Disclosures

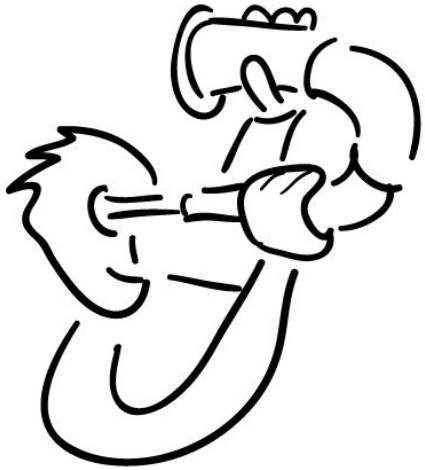
Financial support from

- the Belgian *Fonds de la Recherche Scientifique* for basic research on pharmacology antibiotics and related topics
- *Université catholique de Louvain* for personal support
- Commercial Relationships:
  - AstraZeneca, GSK, Sanofi-Aventis, Bayer HealthCare, Cempra Pharmaceuticals, The Medicines Company, Northern Antibiotics…
- Other relationships in relation to this talk
  - Belgian Antibiotic Policy Coordination Committee
  - Belgian Transparency and Reimbursement Committees
  - Participation in EMA expert meetings for novel antibiotics and as Industry supporting expert for assessment of toxicity of older ones

Slides are available at http://www.facm.ucl.ac.be → Lectures

EMA: European Medicines Agency

Looking back?



- Definitions (CAP, HCAP, HAP…)?
- Risk factors…
- Predictive factors…
- Improvements in diagnostics…
- Antibiotic combinations …
- New antibiotics?
- And what about guidelines?
- An important review
- Other questions…

CAP: community acquired pneumonia
HAP: hospital acquired pneumonia
HCAP: health care associated pneumonia

Definitions [1]

- Community-acquired pneumonia (**CAP**)
  - Patient has not been in hospital (true community)
  - No risk of HCAP
- Health-care associated pneumonia (**HCAP**)
  - Previous hospitalization (>48hrs) in the last 3 months
  - Long term care facilities
  - Domiciliary endovenous therapy
  - Chronic haemodialysis in the last 30 days
  - Domiciliary wound care
  - Close contact with a family member affected by a multidrug resistant infection
- Hospital-acquired pneumonia (**HAP**)
  - Patient hospitalized for at least 48-72h

- Different risks
- Different bacteria:
  - USA: *Pseudomonas aeruginosa* and MRSA
  - Europe: *Streptococcus pneumoniae* and less MDRM [2]... but ...
- Longer stay, severity and mortality
- Need to look for MDRM

MRSA: methicillin-*resistant Staphylococcus aureus*
MDRM: multidrug-resistant microorganism

[1] Proposed by the American Thoracic Society [ATS] /Infectious Diseases Society of America [IDSA] Statement: Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005;171:388-416.
[2] Woodhead M. Thorax. 2013 Nov;68(11):985-6.

But are those correct and useful ?

Editorial

Pneumonia classification and healthcare-associated pneumonia: a new avenue or just a cul-de-sac?

Mark Woodhead

Thorax. 2013 Nov;68(11):985-6.

- Initial US studies supported this classification. [1]
- However, several European studies did not find major differences in the spectrum of microbial causes between CAP and HCAP. [2]
- But the HCAP concept may be useful to identify patients with a worse prognosis.
- The concept may also be applicable where resistance levels are high (USA, Asian countries…) but not in Europe.

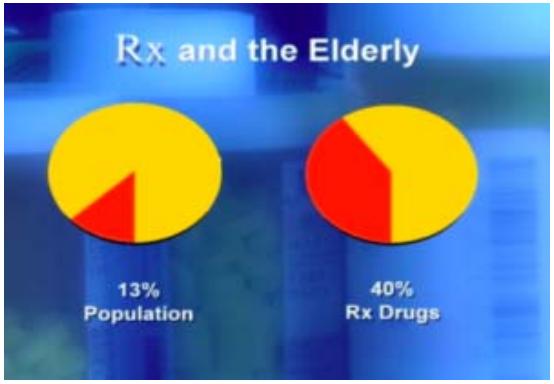
1. Kollef MH *et al*. Epidemiology and outcomes of healthcare-associated pneumonia: results from a large US database of culture positive pneumonia. *Chest* 2005;128:3854–62.
2. See e.g. Polverino E *et al.* Nursing home-acquired pneumonia: a 10-year single-centre experience. *Thorax* 2010;65:354–9

New (or well known) risk factors ?

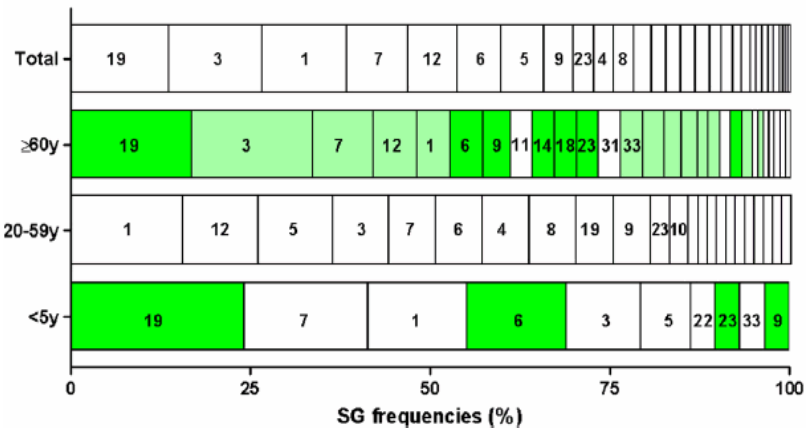
- Multi-resistant organisms
- Co-medications …
- Serotypes and resistance
- Aspiration pneumonia

"Relax – MRSA will get you before the Asian Flu"

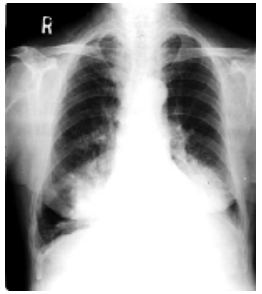
http://cooper.imb.uq.edu.au/community_background.html



Drug consumption by elderly patients in USA
https://nccnews.expressions.syr.edu/?p=40169



*S. pneumo*niae serogroups in Belgium (2007-2009)
Lismond A *et al. Int J Antimicrob Agents* 2012;39:208-16



Aspiration Pneumonia
Mineral Oil
http://www.meddean.luc.edu/

All websites accessed on 5/11/13

Multi-resistant organisms (in Europe) …

Stratifying Risk Factors for Multidrug-Resistant Pathogens in Hospitalized Patients Coming From the Community With Pneumonia

Stefano Aliberti,[1,2] Marta Di Pasquale,[2] Anna Maria Zanaboni,[3] Roberto Cosentini,[4] Anna Maria Brambilla,[4] Sonia Seghezzi,[4] Paolo Tarsia,[2] Marco Mantero,[1] and Francesco Blasi[2]

[1]Dipartimento di Medicina Clinica e Prevenzione, University of Milan-Bicocca, Clinica Pneumologica, AO San Gerardo, Monza; [2]Dipartimento Toraco-polmonare e Cardio-circolatorio, University of Milan, IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Milan; [3]Computer Science Department, University of Milan, and [4]Emergency Medicine Department, IRCCS Fondazione Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy

Aliberti S *et al. Clin Infect Dis*. 2012; 15;54:470-8.

- Observational, prospective study with 935 consecutive patients coming from the community and hospitalized with pneumonia.
- Data on admission and during hospitalization were collected.
- Logistic regression models to evaluate risk factors for acquiring MDR bacteria independently associated with the actual presence of a resistant pathogen and in-hospital mortality.

MDR: multi-drug resistant

Multi-resistant organisms (in Europe) …

Stratifying Risk Factors for Multidrug-Resistant Pathogens in Hospitalized Patients Coming From the Community With Pneumonia

rambilla,[4]

nza; [2]Dipartimento
Milan; [3]Computer
Maggiore Policlinico,

Table 4. Scoring System to Evaluate the Presence of Multidrug-Resistant Pathogens in Patients With Pneumonia From the Community Who are Hospitalized

Variable	Score
No risk factors for MDR pathogen (including comorbidities)	0
≥1 of the following: cerebrovascular disease, diabetes, COPD, antimicrobial therapy in preceding 90 days, immunosuppression, home wound care, home infusion therapy (including antibiotics)	0.5
Residence in a nursing home or extended-care facility	3
Hospitalization for ≥2 days in the preceding 90 days	4
Chronic renal failure	5

Abbreviations: COPD, chronic obstructive pulmonary disease; MDR, multidrug-resistant.

Scoring system used (as per ATS/IDSA)

Aliberti S *et al. Clin Infect Dis*. 2012; 15;54:470-8.

Multi-resistant organisms (in Europe) …

Stratifying Risk Factors for Multidrug-Resistant Pathogens in Hospitalized Patients Coming From the Community With Pneumonia

Table 4. Scoring System to Evaluate the Presence of Multidrug-Resistant Pathogens in Patients With Pneumonia From the Community Who are Hospitalized

Variable	Score
No risk factors for MDR pathogen (including comorbidities)	0
≥1 of the following: cerebrovascular disease, diabetes, COPD, antimicrobia… 90 days, immunosuppression… home infusion therapy (includ…	0.5
Residence in a nursing home or extended-care facility	
Hospitalization for ≥2 days in th…	
Chronic renal failure	

Abbreviations: COPD, chronic obstru… resistant.

Brambilla,[4]

…lonza; [2]Dipartimento …o, Milan; [3]Computer …le Maggiore Policlinico,

Scoring system us…

Table 5. Independent Predictors for In-Hospital Mortality in the Study Population

Variable	OR (95% CI)	*P* Value
Hospitalization for ≥2 days in the preceding 90 days	1.63 (1.04–2.54)	.034
Residency in a nursing home or extended-care facility	2.83 (1.54–5.21)	.001
Pneumonia severity index	2.19 (1.58–3.03)	<.001
Severe CAP	2.52 (1.61–3.93)	<.001

Abbreviations: CAP, community-acquired pneumonia; CI, confidence interval; OR, odds ratio.

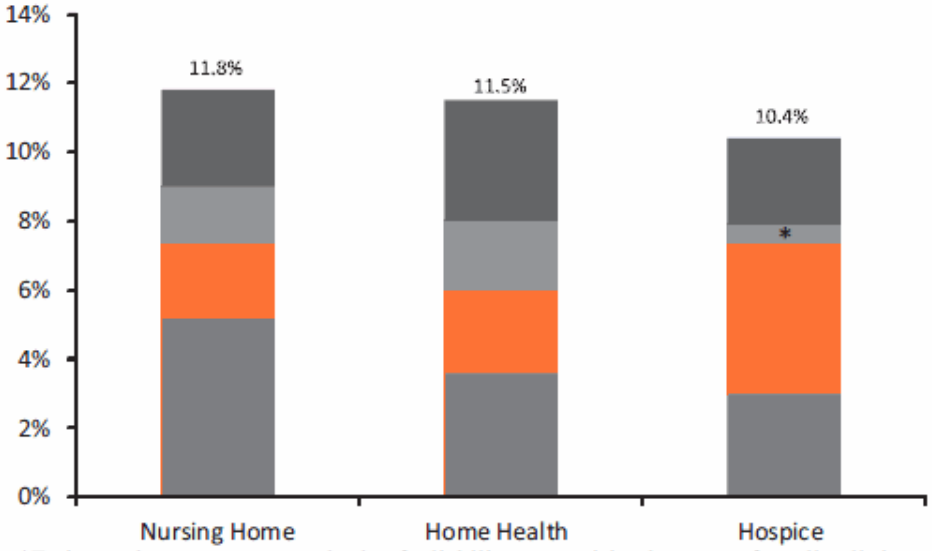
Aliberti S *et al. Clin Infect Dis*. 2012; 15;54:470-8.

The risk of health care and polymedication for the elderly

Infections in Long-Term Care Populations in the United States

Lisa L. Dwyer, MPH, Lauren D. Harris-Kojetin, PhD,* Roberto H. Valverde, MPH,* Joyce M. Frazier, MDiv,* Alan E. Simon, MD,* Nimalie D. Stone, MD, MS,† and Nicola D. Thompson, PhD†*

J Am Geriatr Soc 61:341–349, 2013.



*Estimate does not meet standards of reliability or precision because of small cell size.

Infection	Nursing Home	Home Health	Hospice
	%	%	%
Urinary tract infection	5.2	3.6	3.0
Pneumonia	2.2	2.4	4.4
Cellulitis	1.6	2.0	0.5
Other	2.8	3.5	2.5

The risk of health care and poly-medication for elderly

Infections in Long-Term Care Populations in the United States

Lisa L. Dwyer, MPH, Lauren D. Harris-Kojetin, PhD,* Roberto H. Valverde, MPH,* Joyce M. Frazier, MDiv,* Alan E. Simon, MD,* Nimalie D. Stone, MD, MS,† and Nicola D. Thompson, PhD†*

J Am Geriatr Soc 61:341–349, 2013.

Table 3. Prevalence of Infections in Nursing Home (NH) Residents, Individuals Receiving Home Health Care (HHC), and Individuals Receiving Hospice Care

Characteristic	NH Residents	Individuals Receiving HHC	Individuals Receiving Hospice Care
	Point Prevalence (95% Confidence Interval)		
Location before admission or at time of care [b]			
Private residence	9.5 (8.4–10.8)[a]	N/A	6.5 (5.0–8.4)
Assisted living, board and care, group home, residential care[c]	9.7 (7.6–12.3)[a]	N/A	—
NH, hospital skilled nursing facility, rehabilitation facility	11.3 (9.8–12.8)[a]	N/A	14.5 (11.0–18.9)
Number of medications received at time of survey interview			
<10 (reference)	11.0 (10.0–12.0)	8.9 (6.9–11.3)	11.0 (8.7–13.9)
≥10	13.0 (11.8–14.3)[a]	13.9 (11.3–17.0)[f]	9.8 (7.6–12.5)

Is serotype a main risk factor in CAP?

ORIGINAL ARTICLE

Contribution of host, bacterial factors and antibiotic treatment to mortality in adult patients with bacteraemic pneumococcal pneumonia

Pontus Naucler,[1,2] Jessica Darenberg,[3] Eva Morfeldt,[3] Åke Örtqvist,[4,5] Birgitta Henriques Normark[1,3,6]

Thorax 2013;68:571–579. doi:10.1136/thoraxjnl-2012-203106

CAP: community acquired pneumonia

Is serotype and resistance a main risk factor in CAP?

ORIGINAL ARTICLE

Contribution of host, bacterial factors a
treatment to mortality in adult patients
bacteraemic pneumococcal pneumonia

Pontus Naucler,[1,2] Jessica Darenberg,[3] Eva Morfeldt,[3] Åke Örtqv
Birgitta Henriques Normark[1,3,6]

Thorax 2013;68:571–579. doi:10.1136/thoraxjnl-2012-203106

Key messages

What is the key question?

- To what extent do host and bacterial factors contribute to mortality in bacteraemic pneumococcal pneumonia?

What is the bottom line?

- This study shows that host factors such as age, alcohol abuse, liver disease, renal disease and solid tumour contribute to mortality in patients with bacteraemic pneumococcal pneumonia, while the association between pneumococcal serotype and mortality is mitigated by adjustment for host factors.

Why read on?

- These findings suggest that host factors appear to be more important than specific serotype as determinants of mortality in patients with bacteraemic pneumococcal pneumonia, which supports targeted intervention strategies.

CAP: community acquired pneumonia

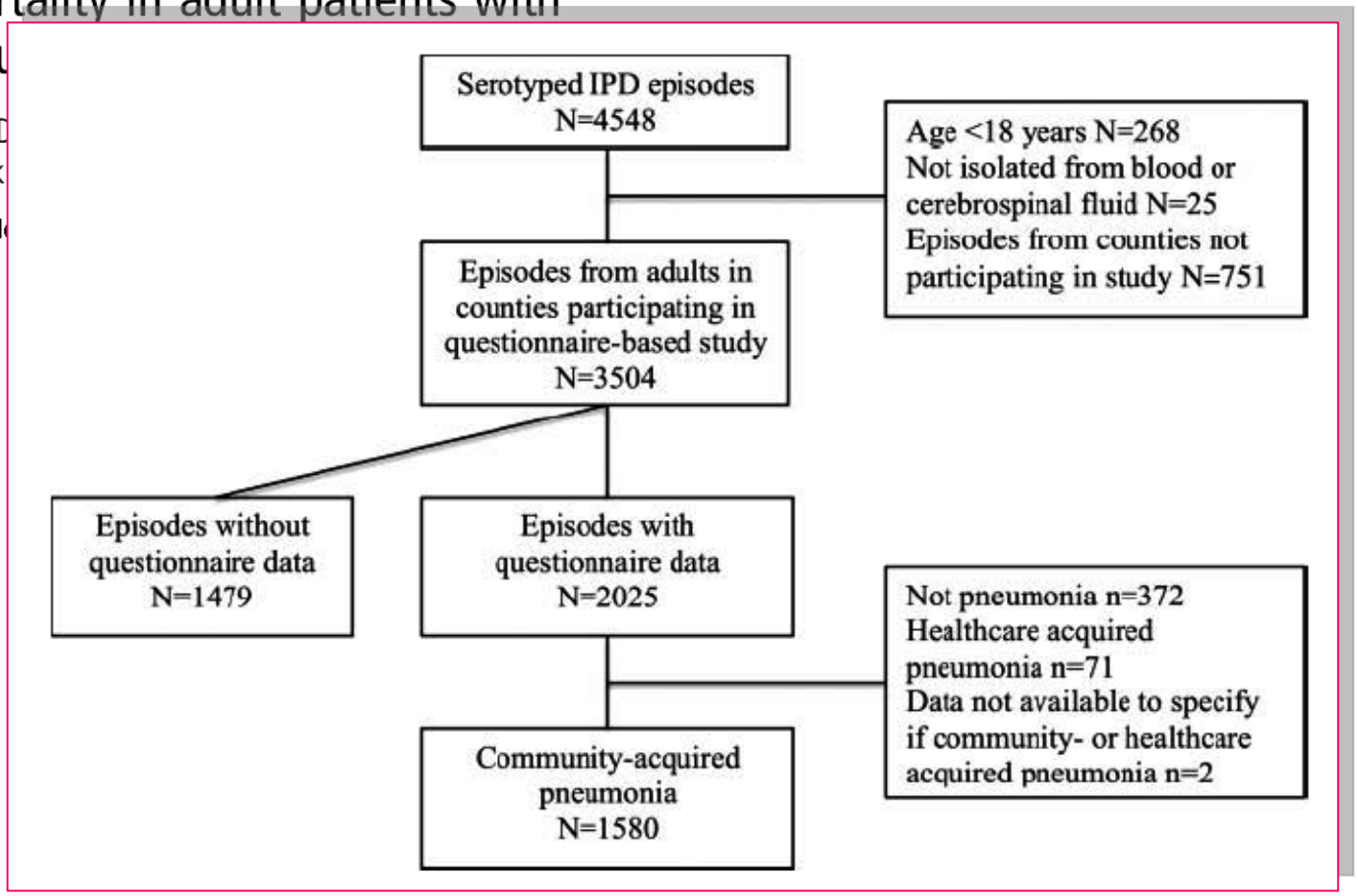
Is serotype and resistance a main risk factor in CAP?

ORIGINAL ARTICLE

Contribution of host, bacterial factors and antibiotic treatment to mortality in adult patients with bacteraemic pneu

Pontus Naucler,[1,2] Jessica D
Birgitta Henriques Normark

Thorax 2013;68:571–579. d



CAP: community acquired pneumonia

Is serotype and resistance a main risk factor in CAP?

ORIGINAL ARTICLE

Contribution of host, bacterial factors and antibiotic treatment to mortality in adult patients with bacteraemic pneumococcal pneumonia

Pontus Naucler [1,2] Jessica Darenberg [3] Eva Morfeldt [3] Åke Örtqvist [4,5]
Birgitta

Thorax 2

Not too much of a surprise

Table 1 Host factors associated with 30-day mortality in patients with bacteraemic pneumococcal pneumonia

	No of patients (column %)	No of deaths (row %)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Age				
≥85	203 (12.9)	52 (26.1)	26.74 (8.20 to 87.12)	29.43 (9.00 to 96.27)
75–84	323 (20.4)	40 (12.4)	10.69 (3.27 to 35.02)	11.30 (3.45 to 37.06)
65–74	301 (19.1)	25 (8.3)	6.85 (2.04 to 22.99)	7.10 (2.12 to 23.85)
55–64	341 (21.6)	20 (5.9)	4.71 (1.38 to 16.05)	4.84 (1.42 to 16.49)
45–54	182 (11.5)	6 (3.3)	2.58 (0.64 to 10.46)	2.59 (0.64 to 10.50)
<45	230 (14.6)	3 (1.3)	1.00 (ref)	1.00 (ref)
≥65	827 (52.3)	118 (14.3)	4.16 (2.73 to 6.32)	4.29 (2.82 to 6.54)
<65	753 (47.7)	29 (3.9)	1.00 (ref)	1.00 (ref)
Alcohol abuse				
Yes	113 (7.2)	18 (15.9)	2.39 (1.40 to 4.08)	3.82 (1.85 to 7.85)
No	1214 (76.8)	93 (7.7)	1.00 (ref)	1.00 (ref)
N/S	253 (16.0)	36 (14.2)		

CAP: community acquired pneumonia

Is s… AP?

ORIGINAL ARTI…

Contribut… treatmen… bacteraer…

Pontus Naucler… Birgitta Henriq…

Thorax 2013;68…

Table 2 Thirty-day mortality risk according to serotype and antibiotic resistance in patients

	No of patients (column %)	No of deaths (row %)	Crude OR (95% CI)	Adjusted OR† (95% CI)
Individual serotype				
9V	191 (12.1)	10 (5.2)	0.62 (0.28 to 1.40)	0.83 (0.36 to 1.93)
7F	177 (11.2)	4 (2.3)	0.26 (0.09 to 0.79)	0.51 (0.16 to 1.59)
4	158 (10.0)	8 (5.1)	0.60 (0.25 to 1.43)	0.88 (0.36 to 2.16)
3	142 (9.0)	17 (12.9)	1.54 (0.76 to 3.12)	1.85 (0.87 to 3.93)
23F	97 (6.1)	11 (11.3)	1.44 (0.65 to 3.21)	1.23 (0.54 to 2.81)
22F	79 (5.0)	7 (8.9)	1.10 (0.44 to 2.76)	1.25 (0.48 to 3.23)
6B	78 (4.9)	15 (19.2)	**2.69 (1.27 to 5.69)**	2.09 (0.96 to 4.57)
6A	76 (4.8)	10 (13.1)	1.71 (0.75 to 3.92)	1.17 (0.49 to 2.75)
19A	55 (3.5)	4 (7.3)	0.89 (0.29 to 2.75)	0.69 (0.21 to 2.22)
14	209 (13.2)	17 (8.3)	1.00 (ref)	1.00 (ref)
Other	318 (20.1)	44 (13.8)	–	–
Serotype category according to CFR‡				
High	509 (32.2)	63 (12.4)	**3.28 (1.89 to 5.70)**	1.63 (0.89 to 2.98)
Medium	484 (30.6)	35 (7.2)	**1.81 (1.00 to 3.28)**	1.27 (0.67 to 2.42)
Low	412 (26.1)	17 (4.1)	1.00 (ref)*	1.00 (ref)**
Serotype category according to invasiveness§				
Low	461 (29.2)	58 (12.6)	**4.21 (1.89 to 9.40)**	1.67 (0.70 to 4.00)
Medium	591 (37.4)	40 (6.8)	2.13 (0.94 to 4.82)	1.19 (0.49 to 2.87)
High	212 (13.4)	7 (3.3)	1.00 (ref)*	1.00 (ref)***
PCV 13 serotypes ¶				
Yes	1277 (80.8)	107 (8.4)	**0.60 (0.41 to 0.89)**	0.78 (0.51 to 1.19)
No	303 (19.2)	40 (13.2)	1.00 (ref)	1.00 (ref)
Penicillin non-susceptible††				
Yes	45 (2.9)	6 (13.3)	1.52 (0.63 to 3.65)	1.07 (0.42 to 2.74)
No	1535 (97.2)	141 (9.2)	1.00 (ref)	1.00 (ref)
Erythromycin non-susceptible††				
Yes	69 (4.4)	5 (7.4)	0.75 (0.30 to 1.90)	0.83 (0.32 to 2.16)
No	1511 (95.6)	141 (9.4)	1.00 (ref)	

Wow !

CAP: community acquired pneumonia

See notes in back-up slides

Aspiration pneumonia as a specific risk…

Official Journal of the Asian Pacific Society of Respirology
Respirology

ORIGINAL ARTICLE

Impact of aspiration pneumonia in patients with community-acquired pneumonia and healthcare-associated pneumonia: A multicenter retrospective cohort study

KOSAKU KOMIYA,[1,3] HIROSHI ISHII,[1] KENJI UMEKI,[1] SHUNJI MIZUNOE,[4] FUMITO OKADA,[2] TAKESHI JOHKOH[5] AND JUN-ICHI KADOTA[1]

[1]*Internal Medicine 2 and* [2]*Radiology, Faculty of Medicine, Oita University,* [3]*Clinical Research Center of Respiratory Medicine, Tenshindo Hetsugi Hospital,* [4]*Respiratory Medicine, Oita Prefectural Hospital, Oita, and* [5]*Radiology, Kinki Central Hospital of Mutual Aid Association of Public School Teachers, Hyogo, Japan*

Komiya K *et al. Respirology*. 2013 Apr;18(3):514-21.

SUMMARY AT A GLANCE

Aspiration pneumonia, which is defined as having risk factors for aspiration and evidence of gravity-dependent opacities on CT, was strongly associated with mortality after adjusting for the category of pneumonia, performance status and treatment failure due to resistant pathogens.

Aspiration pneumonia as a specific risk…

Official Journal of the Asian Pacific Society of Respirology
Respirology

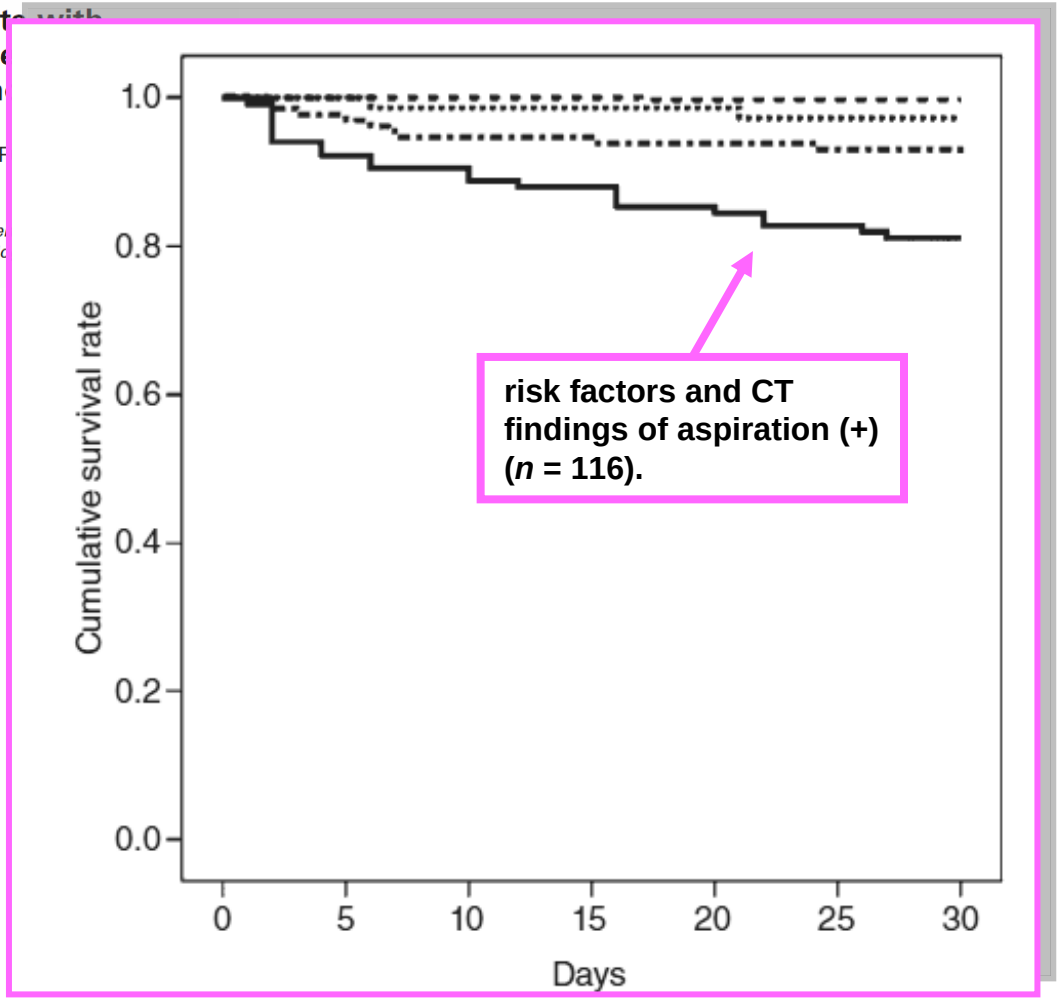
ORIGINAL ARTICLE

Impact of aspiration pneumonia in patients with community-acquired pneumonia and healthcare pneumonia: A multicenter retrospective coh

KOSAKU KOMIYA,[1,3] HIROSHI ISHII,[1] KENJI UMEKI,[1] SHUNJI MIZUNOE,[4] TAKESHI JOHKOH[5] AND JUN-ICHI KADOTA[1]

[1]*Internal Medicine 2 and* [2]*Radiology, Faculty of Medicine, Oita University,* [3]*Clinical Research Ce Tenshindo Hetsugi Hospital,* [4]*Respiratory Medicine, Oita Prefectural Hospital, Oita, and* [5]*Radiolo Mutual Aid Association of Public School Teachers, Hyogo, Japan*

Komiya K *et al. Respirology.* 2013 Apr;18(3):514-21.



CT: computed tomography

New Prognostic factors

Background:

- PSI and CURB65/CRB65 are not 100% sensitive or specific
- There is a definite percentage of patients with poor evolution that do not show initial severity, which leads to a delay in ICU admission
- These patients have two-fold mortality and it is therefore important to detect them very early

- Thrombocytosis
- Hyperglycaemia
- Vitamin D

ICU: intensive care unit

Torres A, personnal communication

Thrombocytosis as prognostic factor

CHEST Original Research
CHEST INFECTIONS

Thrombocytosis Is a Marker of Poor Outcome in Community-Acquired Pneumonia

Elena Prina, MD; Miquel Ferrer, MD, PhD; Otavio T. Ranzani, MD; Eva Polverino, MD, PhD; Catia Cillóniz, PhD; Encarnación Moreno, RN; Josep Mensa, MD; Beatriz Montull, MD; Rosario Menéndez, MD, PhD; Roberto Cosentini, MD; and Antoni Torres, MD, PhD

Prina E *et al. Chest*. 2013 Mar;143(3):767-75

- 2423 hospitalized CAP patients
- 53 thrombocytopenia (< 100,000/ mm³), 204 thrombocytosis (> 400,000/ mm³)
- More respiratory complications with thrombocytosis, more septic shock with thrombocytopenia
- Thrombocytosis added to mortality (OR 2.7), but there was a biphasic relationship

Thrombocytosis as prognostic factor

CHEST

Original Research

CHEST INFECTIONS

**Thrombocytosis Is a Marker o
Outcome in Community-Acqu
Pneumonia**

*Elena Prina, MD; Miquel Ferrer, MD, PhD; Otavio T. Ranz
Eva Polverino, MD, PhD; Catia Cillóniz, PhD; Encarnación
Josep Mensa, MD; Beatriz Montull, MD; Rosario Menéndez
Roberto Cosentini, MD; and Antoni Torres, MD, PhD*

Prina *E et al. Chest*. 2013 Mar;143(3):7

- 242
- 53 t
  (< 1
  400
- Mor
  thro
  thro
- Thr
  but

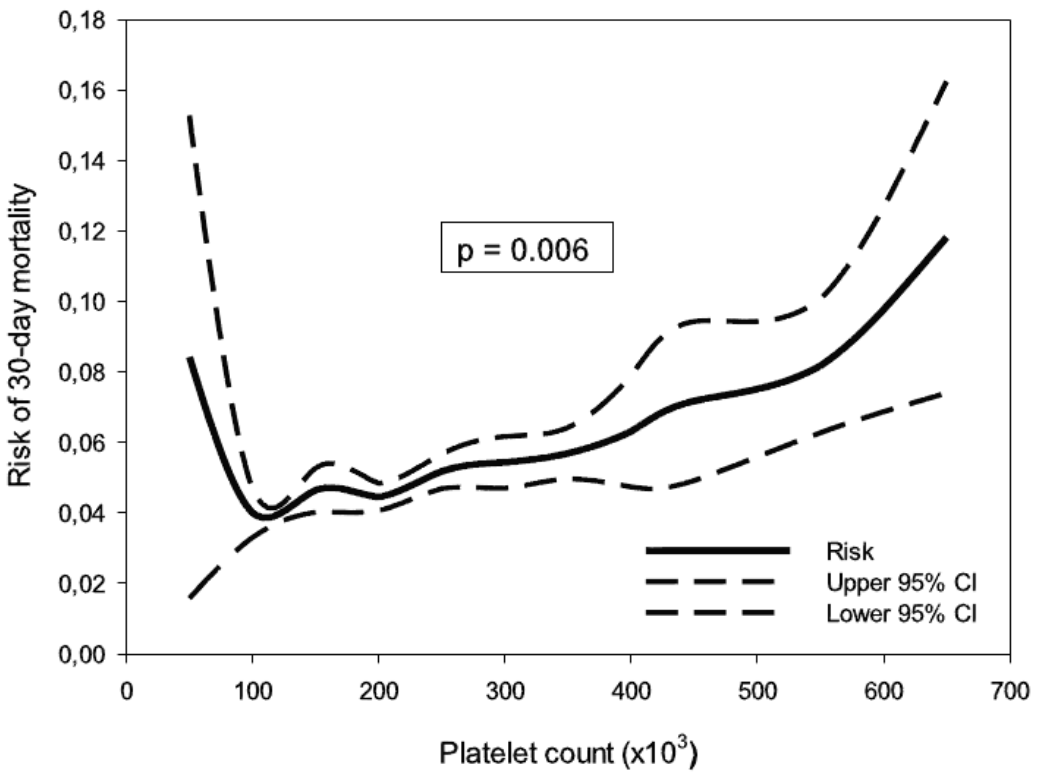


FIGURE 2. Multivariate logistic regression model to evaluate the association between platelet count as a continuous variable and mortality.

Glucose as a predictive factor…

Lepper PM *et al*. *BMJ*. 2012;344:e3397.

Serum glucose levels for predicting death in patients admitted to hospital for community acquired pneumonia: prospective cohort study


OPEN ACCESS

Philipp M Lepper *consultant physician*[1], Sebastian Ott *consultant physician*[2], Eveline Nüesch *statistician*[3 4], Maximilian von Eynatten *consultant physician*[5], Christian Schumann *consultant physician*[6], Mathias W Pletz *professor*[7], Nicole M Mealing *statistician*[3 4], Tobias Welte *professor*[8], Torsten T Bauer *professor*[9], Norbert Suttorp *professor*[10], Peter Jüni *professor*[3 4], Robert Bals *professor*[1], Gernot Rohde *professor*[11], on behalf of the German Community Acquired Pneumonia Competence Network (CAPNETZ)

Increased serum glucose level at admission without pre-existing diabetes was a predictor of death at 28 and 90 days:

- 6-10.99 mmol/L → OR 90 days mortality: 1.56 [1.22 to 2.01]
- >14 mmol/L → OR 90 days mortality: 2.37 (1.62 to 3.46)

Higher serum glucose levels were associated with increased mortality in all patients

Adding vitamin D levels to other scores

Addition of Vitamin D Status to Prognostic Scores Improves the Prediction of Outcome in Community-Acquired Pneumonia

Hilde H. F. Remmelts,[1,2,3] Ewoudt M. W. van de Garde,[4,5] Sabine C. A. Meijvis,[1] Evelyn L. G. C. A. Peelen,[6,7,8] Jan G. M. C. Damoiseaux,[9] Jan C. Grutters,[10,11] Douwe H. Biesma,[1,2] Willem Jan W. Bos,[1] and Ger T. Rijkers[12,13]

[1]Department of Internal Medicine, St Antonius Hospital, Nieuwegein; [2]Department of Internal Medicine and Infectious Diseases, University Medical Centre Utrecht; [3]Department of Internal Medicine, Gelderse Vallei Hospital, Ede; [4]Department of Clinical Pharmacy, St Antonius Hospital, Nieuwegein; [5]Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht University; [6]School for Mental Health and Neuroscience, [7]Department of Internal Medicine, Division of Clinical and Experimental Immunology, Maastricht University Medical Centre; [8]Academic MS Centre Limburg, Orbis Medical Centre, Sittard; [9]Laboratory for Clinical Immunology, Maastricht University Medical Centre; [10]Department of Pulmonology, St Antonius Hospital, Nieuwegein; [11]Division of Heart and Lungs, University Medical Centre Utrecht; [12]Department of Sciences, Roosevelt Academy, Middelburg, and [13]Department of Medical Microbiology and Immunology, St Antonius Hospital, Nieuwegein, The Netherlands

Remmelts HHF *et al. Clin Infect Dis*. 2012; 55:1488-94.

- 272 hospitalized patients with CAP.
- At admission:
  - Levels of 25-hydroxyvitamin D, leukocytes, C-reactive protein, and total cortisol
  - Pneumonia Severity Index (PSI) and CURB-65 measured on admission.
- Outcomes:
  - ➢ intensive care unit (ICU) admission
  - ➢ 30-day mortality.

CAP: community acquired pneumonia

Adding vitamin D levels to other scores

Addition of Vitamin D Status to Prognostic Scores Improves the Prediction of Outcome in Community-Acquired Pneumonia

Hilde H. F. Remmelts,[1,2,3] Ewoudt M. W. van de Garde,[4,5] Sabine C. A. Meijvis,[1] Evelyn L. G. C. A. Peelen,[6,7,8] Jan G. M. C. Damoiseaux,[9] Jan C. Grutters,[10,11] Douwe H. Biesma,[1,2] Willem Jan W. Bos,[1] and Ger T. Rijkers[12,13]

[1]Department of Internal Medicine, St Antonius Hospital, Nieuwegein; [2]Department of Internal Medicine and Infectious Diseases, University Medical Centre Utrecht; [3]Department of Internal Medicine, Gelderse Vallei Hospital, Ede; [4]Department of Clinical Pharmacy, St Antonius Hospital, Nieuwegein; [5]Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht University; [6]School for Mental Health and Neuroscience, [7]Department of Internal Medicine, Division of Clinical and Experimental Immunology, Maastricht University Medical Centre; [8]Academic MS Centre Limburg, Orbis Medical Centre, Sittard; [9]Laboratory for Clinical Immunology, Maastricht University Medical Centre; [10]Department of Pulmonology, St Antonius Hospital, Nieuwegein; [11]Division of Heart and Lungs, University Medical Centre Utrecht; [12]Department of Sciences, Roosevelt Academy, Middelburg, and [13]Department of Medical Microbiology and Immunology, St Antonius Hospital, Nieuwegein, The Netherlands

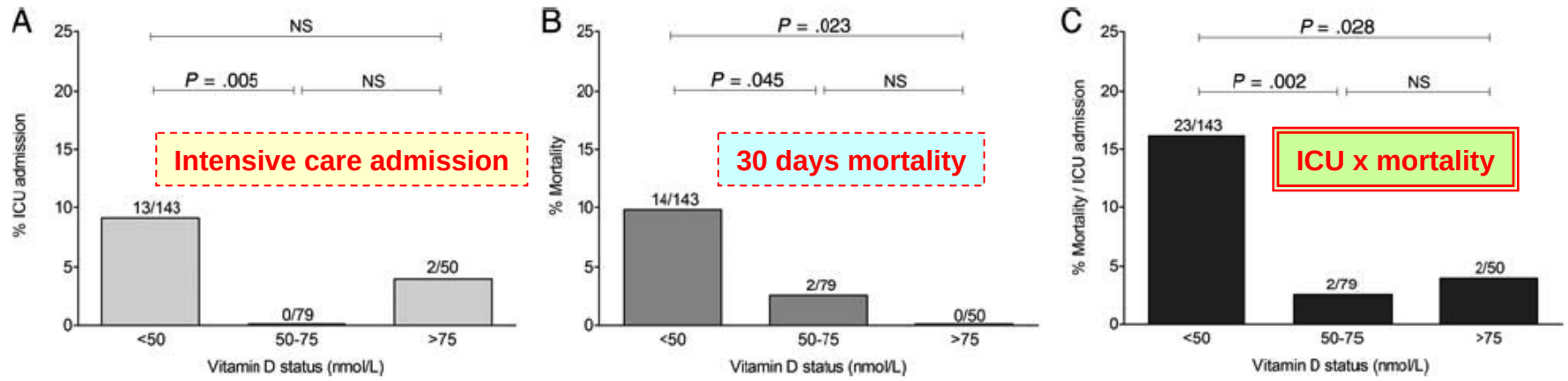


Figure 2. The rate of intensive care unit admission (*A*), 30-day mortality (*B*), and the composite endpoint mortality/ICU admission (*C*) stratified by serum 25-hydroxyvitamin D levels measured on presentation in patients with community-acquired pneumonia. Numbers above the bars indicate the number of patients with an adverse outcome. Abbreviations: ICU, intensive care unit; NS, not significant.

Remmelts HHF *et al. Clin Infect Dis*. 2012; 55:1488-94.

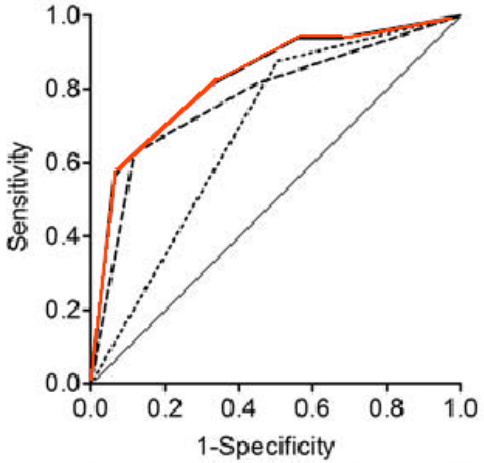
Adding vitamin D levels to other scores

Addition of Vitamin D Status to Prognostic Scores Improves the Prediction of Outcome in Community-Acquired Pneumonia

Hilde H. F. Remmelts,[1,2,3] Ewoudt M. W. van de Garde,[4,5] Sabine C. A. Meijvis,[1] Ev
Jan G. M. C. Damoiseaux,[9] Jan C. Grutters,[10,11] Douwe H. Biesma,[1,2] Willem Jan

[1]Department of Internal Medicine, St Antonius Hospital, Nieuwegein; [2]Department of Internal Medici
Centre Utrecht; [3]Department of Internal Medicine, Gelderse Vallei Hospital, Ede; [4]Department of Clini
[5]Division of Pharmacoepidemiology and Clinical Pharmacology, Utrecht University; [6]School for Mental
Internal Medicine, Division of Clinical and Experimental Immunology, Maastricht University Medical C
Medical Centre, Sittard; [9]Laboratory for Clinical Immunology, Maastricht University Medical Centre; [10]
Hospital, Nieuwegein; [11]Division of Heart and Lungs, University Medical Centre Utrecht; [12]Departmen
and [13]Department of Medical Microbiology and Immunology, St Antonius Hospital, Nieuwegein, The

- Vitamin D deficiency is associated with adverse outcome in CAP.
- Vitamin D status on presentation is a significant predictor for 30-day mortality, and more specific when combined with other biomarkers or prognostic scores.
- Vitamin D supplementation might be a promising candidate for adjuvant treatment in CAP.

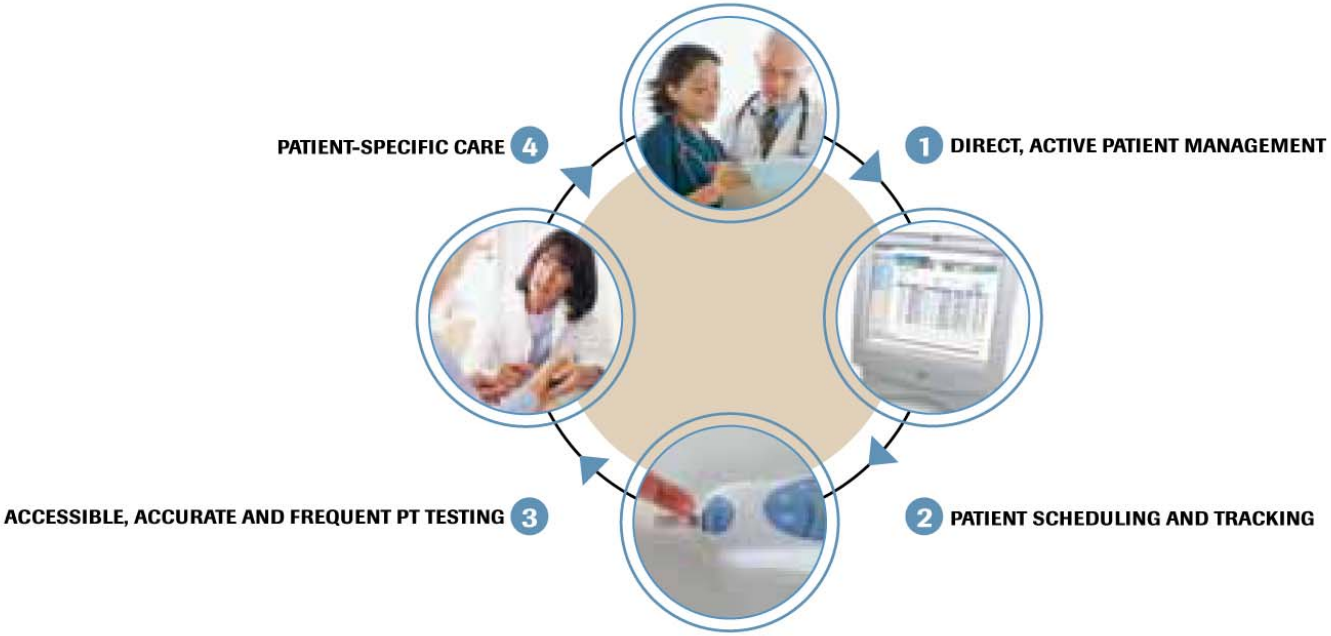


e 3. Receiver operating characteristic curve analysis of the predic-
f 30-day mortality by Pneumonia Severity Index (PSI) score, vitamin
tus, and the combined model "PSI score & vitamin D status." Data
e day of admission are shown. Abbreviations: AUC, area under the
CI, confidence interval; PSI, Pneumonia Severity Index.

CAP: community acquired pneumonia

Remmelts HHF *et al. Clin Infect Dis*. 2012; 55:1488-94.

Improvements in diagnostics …



http://www.roche-diagnostics.us/PublishingImages/coagImage1.png
accessed on 6/10/13

➢ Point of care Ultrasonography

Ultrasonographic diagnosis in children and adults

ARTICLE

JOURNAL CLUB

Prospective Evaluation of Point-of-Care Ultrasonography for the Diagnosis of Pneumonia in Children and Young Adults

Vaishali P. Shah, MD; Michael G. Tunik, MD; James W. Tsung, MD, MPH

JAMA Pediatr. 2013;167(2):119-125.
Published online December 10, 2012.
doi:10.1001/2013.jamapediatrics.107

Shah VP *et al. JAMA Pediatr*. 2013 Feb;167(2):119-25.

Ultrasonographic diagnostic in children and adults

ARTICLE

JOURNAL CLUB

Prospective Evaluation of Point-of-Ca Ultrasonography for the Diagnosis of in Children and Young Adults

Vaishali P. Shah, MD; Michael G. Tunik, MD; James W. Tsung, MD, MPH

JAMA Pediatr. 2013;167(2):119-125.
Published online December 10, 2012.
doi:10.1001/2013.jamapediatrics.107

Shah VP *et al. JAMA Pediatr*. 2013 Feb;167(2):119-25.

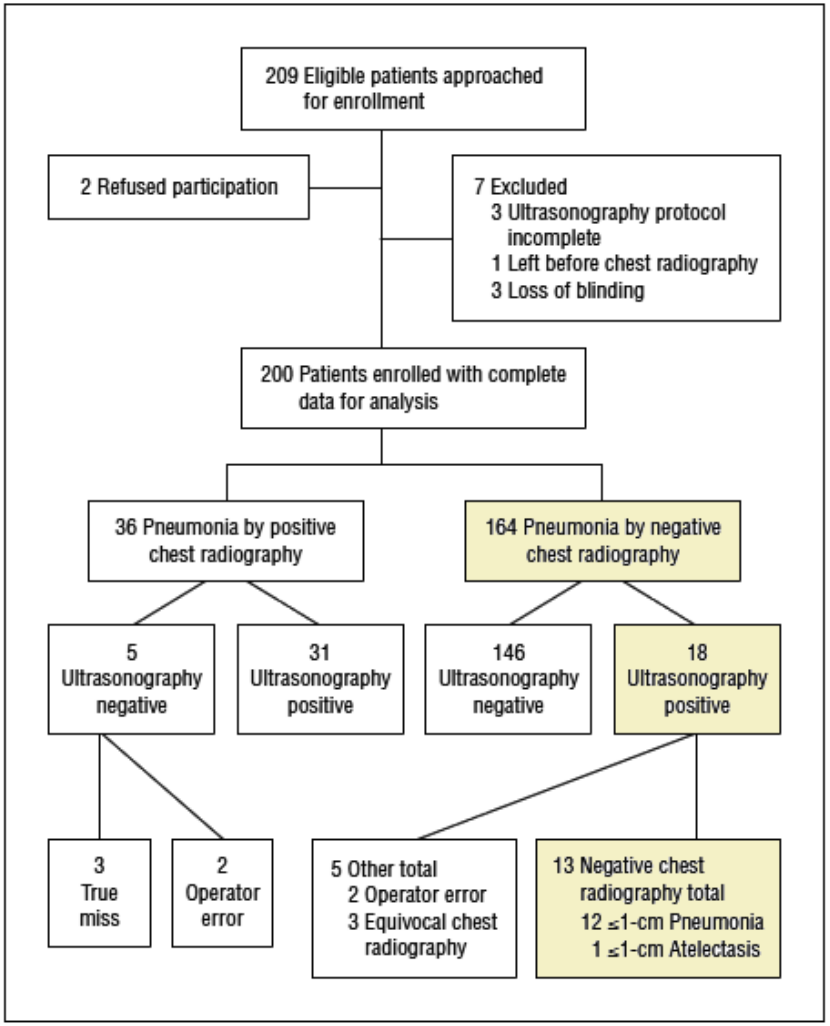


Figure 3. Standards for Reporting of Diagnostic Accuracy[17] flowchart.

Ultrasonographic diagnostic in children and adults

ARTICLE

JOURNAL CLUB

Prospective Ev
Ultrasonograp
in Children ar

Vaishali P. Shah, MD; Michael

JAMA Pediatr. 2013;167(2):119-
Published online December 10, 2
doi:10.1001/2013.jamapediatrics

Shah *VP et al. JAMA Pediatr*. 2013 Feb;167(2):119-25.

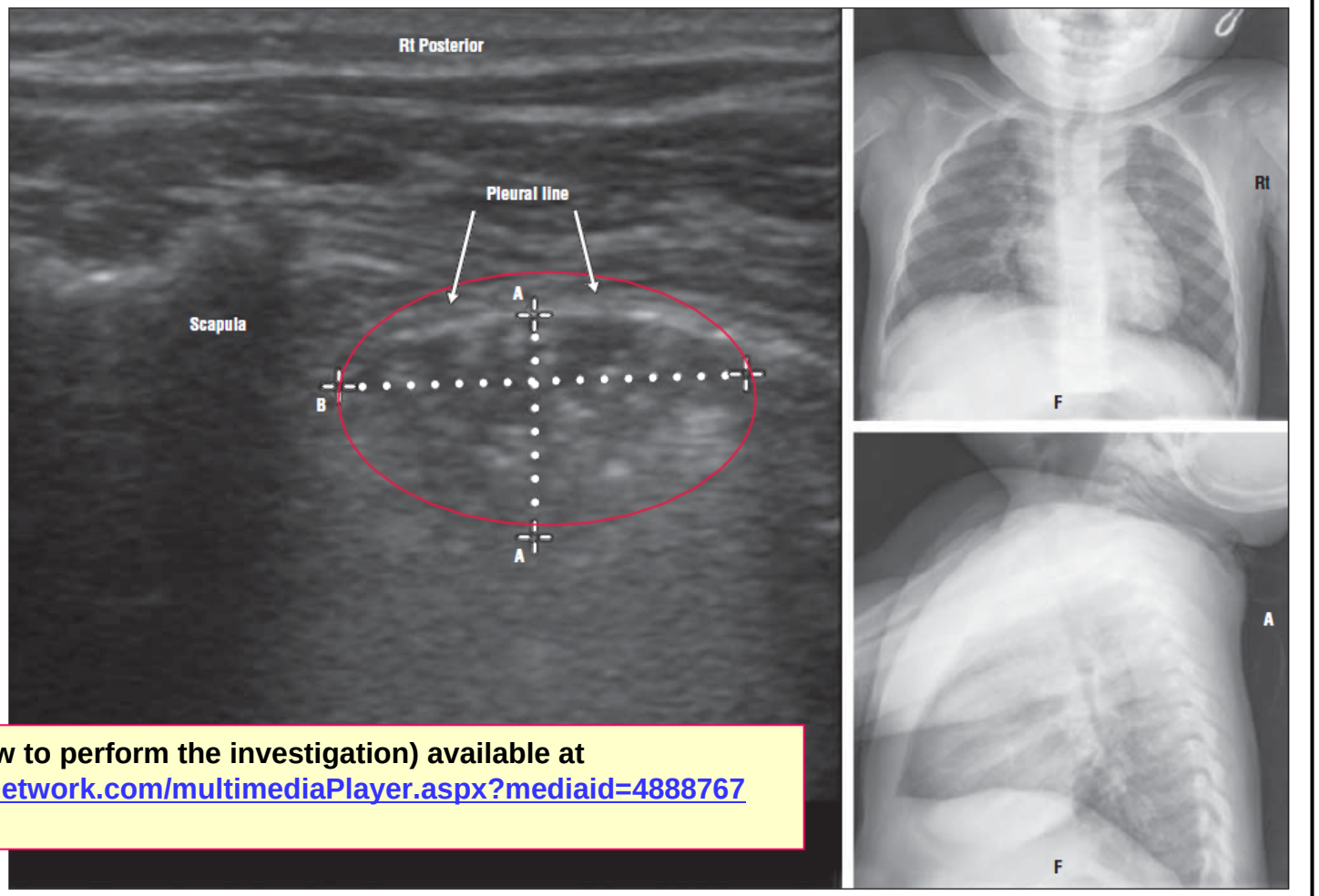


Figure 2. Lung consolidation of 1 cm or less with sonographic air bronchograms on ultrasonography not detected by chest radiography. F indicates frontal view; RT, right; and red oval, lung consolidation. A is caliper A measurement, and B is caliper B measurement.

Video (explaining how to perform the investigation) available at http://archpedi.jamanetwork.com/multimediaPlayer.aspx?mediaid=4888767 accessed on 6/10/13

Antibiotic combinations…

- The controversy about the necessity to add a macrolide to a β-lactam continues…

Medical controversies by Honoré Daumier (1837)
From '*Histoire de la médecine et des médecins*' by J.C. Sournia (Ed. Larousse, Paris, 1991)

Adding a macrolide in adults?

AUDIT, RESEARCH AND GUIDELINE UPDATE

Single versus combination antibiotic therapy in adults hospitalised with community acquired pneumonia

Chamira Rodrigo,[1] Tricia M Mckeever,[2] Mark Woodhead,[3] Wei Shen Lim,[1] on behalf of the British Thoracic Society

Rodrigo C *et al. Thorax*. 2013; 68:493-5.

- 5240 adults hospitalised with CAP from 72 secondary care trusts across England and Wales.
- The overall 30-day inpatient (IP) death rate was 24.4%.
- Combination therapy was prescribed in 3239 (61.8%) patients.

CAP: community acquired pneumonia

Adding a macrolide in adults?

AUDIT, RESEARCH AND GUIDELINE UPDATE

Single versus combination antibiotic therapy in adults hospitalised with community acquired pneumonia

Chamira Rodrigo,[1] Tricia M Mckeever,[2] Mark Woodhead,[3] Wei Shen Lim,[1]
on behalf of the British Thoracic Society

Rodrigo C *et al. Thorax*. 2013; 68:493-5.

Table 1 Multivariate analyses of the association between antibiotic therapy and clinical outcomes

Outcome measures	Total (n=5240)	β-lactam therapy (n=2001)	β-lactam/ macrolide therapy (n=3239)	Adjusted OR (95% CI)	p Value
30 day IP death rate	1281 (24.4)	536 (26.8)	745 (23.0)	0.72 (0.60 to 0.85)*	<0.001
ICU admission	419 (8)	136 (6.8)	282 (8.7)	0.94 (0.72 to 1.22)†	0.635
Need for MV	151 (2.9)	58 (2.9)	93 (2.9)	0.99 (0.71 to 1.38)†	0.508
Need for INS	130 (2.5)	42 (2.1)	88 (2.7)	0.87 (0.55 to 1.38)†	0.544
30-day IP death rate stratified by pneumonia severity					
Low severity (CURB65=0–1)	201/2247 (8.9)	95/908 (10.5)	106/1339 (7.9)	0.80 (0.56 to 1.16)‡	0.238
Moderate severity (CURB65=2)	370/1480 (25)	171/561 (30.5)	199/919 (21.7)	0.54 (0.41 to 0.72)‡	<0.001
High severity (CURB65≥3)	710/1513 (46.9)	270/532 (50.8)	440/981 (44.9)	0.76 (0.60 to 0.96)‡	0.025

IP: in-patient - MV: mechanic ventilation – INS: intropic support – CURB65: see asbtract and Lim *et al.* Thorax 2003; 58:377–82

See notes in back-up slides

Adding a macrolide in children?

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

Comparative Effectiveness of Empiric β-Lactam Monotherapy and β-Lactam–Macrolide Combination Therapy in Children Hospitalized with Community-Acquired Pneumonia

Lilliam Ambroggio, PhD, MPH[1,4], Jennifer A. Taylor, PhD, MPH[2], Loni Philip Tabb, PhD[1], Craig J. Newschaffer, PhD[1], Alison A. Evans, ScD[1], and Samir S. Shah, MD, MSCE[3,4,5]

Ambroggio L *et al. J Pediatr.* 2012;161:1097-103.

- 20743 patients hospitalized with CAP.
- 24% received b-lactam and macrolide combination therapy on admission.

CAP: community acquired pneumonia

Adding a macrolide in children?

THE JOURNAL OF PEDIATRICS • WWW.

Comparative Effectiven
and β-Lactam–Macro
Hospitalized with

Lilliam Ambroggio, PhD, MPH[1,4], Jennifer A.
Alison A. Evans

Ambroggio L *et al. J Pediatr.* 2012;161:1097-103.

- 20743 pati
- 24% recei
combinatio

Table IV. LOS according to empiric antibiotic therapy

Antibiotic category	Unadjusted relative risk (95% CI)	Adjusted relative risk (95% CI)*,†,‡
Main analysis		
Monotherapy	Reference	Reference
Combination therapy	0.91 (0.87-0.96)	0.80 (0.75-0.86)
Age category, y		
1-5	N/A	0.96 (0.86-1.06)
6-11	N/A	0.85 (0.79-0.91)
12-18	N/A	0.69 (0.49-0.98)
Monotherapy		
Aminopenicillin	Reference	Reference
Second-generation cephalosporin	1.06 (0.96-1.17)	1.01 (0.91-1.12)
Third-generation cephalosporin	1.16 (1.05-1.28)	1.03 (0.94-1.14)
Combination therapy		
Aminopenicillin + macrolide	Reference	Reference
Second-generation cephalosporin + macrolide	1.03 (0.93-1.15)	1.01 (0.90-1.13)
Third-generation cephalosporin + macrolide	0.88 (0.77-1.01)	0.91 (0.79-1.04)

LOS: length of stay

See notes in back-up slides

Adding a macrolide in children?

THE JOURNAL OF PEDIATRICS • WWW.

Comparative Effectiven
and β-Lactam–Macro
Hospitalized with

Lilliam Ambroggio, PhD, MPH[1,4], Jennifer A.
Alison A. Evans

Ambroggio *et al.* J Pediatr. 2012;161:1097-103.

- 20743 pati
- 24% recei

Table IV. LOS according to empiric antibiotic therapy

Antibiotic category	Unadjusted relative risk (95% CI)	Adjusted relative risk (95% CI)*,†,‡
Main analysis		
Monotherapy	Reference	Reference
Combination therapy	0.91 (0.87-0.96)	0.80 (0.75-0.86)
Age category, y		
1-5	N/A	0.96 (0.86-1.06)
6-11	N/A	0.85 (0.79-0.91)
12-18	N/A	0.69 (0.49-0.98)
Monotherapy		
Aminopenicillin	Reference	Reference

Authors' final words:

These findings suggest the need for a randomized clinical trial comparing β-lactam and macrolide therapies in treating children hospitalised with CAP to identify populations or subpopulations that may benefit from combination antibiotic therapy.

CAP: community acquired pneumonia

See notes in back-up slides

New antibiotics?

THEME: COMBATTING ANTIBIOTIC RESISTANCE: NEWDRUGS4BADBUGS (ND4BB)

But for today …

- Ceftaroline

Is ceftaroline a useful new antibiotic for CAP?

Diagnostic Microbiology and Infectious Disease 75 (2013) 298–303

Contents lists available at SciVerse ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Clinical Study

Assessment of ceftaroline fosamil in the treatment of community-acquired bacterial pneumonia due to *Streptococcus pneumoniae*: insights from two randomized trials☆,☆☆,☆☆☆,★,★★

Andrew F. Shorr [a,*], Marin Kollef [b], Paul B. Eckburg [c], Lily Llorens [d], H. David Friedland [d]

[a] Pulmonary and Critical Care Medicine, Washington Hospital Center, Rm 2A-68, 110 Irving St NW, Washington, DC 20010, USA
[b] Washington University School of Medicine, St Louis, MO, USA
[c] Stanford University School of Medicine, Stanford, CA, USA
[d] Cerexa, Inc. (a wholly owned subsidiary of Forest Laboratories, Inc., New York, NY), Oakland, CA, USA

Shorr AF *et al. Diagn Microbiol Infect Dis*. 2013 Mar;75(3):298-303.

CAP: community acquired pneumonia

Is ceftaroline a useful new antibiotic for CAP?

Diagnostic Microbiology

Contents lists av

Diagnostic Microbi

journal homepage: ww

Clinical Study

Assessment of ceftaroline fosamil in t
pneumonia due to *Streptococcus pneu*
trials☆,☆☆,☆☆☆,★,★★

Andrew F. Shorr [a,*], Marin Kollef [b], Paul B. Eckl

[a] Pulmonary and Critical Care Medicine, Washington Hospital Center, Rm 2A-68,
[b] Washington University School of Medicine, St Louis, MO, USA
[c] Stanford University School of Medicine, Stanford, CA, USA
[d] Cerexa, Inc. (a wholly owned subsidiary of Forest Laboratories, Inc., New York,

Shorr AF *et al. Diagn Microbiol Infect Dis*. 2013 Mar;75(3):298-303.

Table 2
Clinical and microbiological response rates in patients with *Streptococcus pneumoniae* as a baseline pathogen in the integrated FOCUS studies (mMITTE population).

Response rates by pathogen	Ceftaroline fosamil, *n*/*N* (%)	Ceftriaxone, *n*/*N* (%)	Weighted difference, % (95% CI)
Clinical cure			
All *S. pneumoniae* (baseline isolates)	59/69 (85.5)	48/70 (68.6)	$P = 0.009$
			17.0 (2.9 to 30.7)
MDRSP	4/4 (100)	2/9 (22.2)	77.8 (N/A)
Positive by urinary antigen only	25/28 (89.3)	23/31 (74.2)	15.1 (−5.7 to 34.9)
Positive by culture[a]	34/41 (82.9)	25/39 (64.1)	18.9 (−0.7 to 37.7)
Plus atypical pathogens	8/10 (80.0)	6/9 (66.7)	13.3 (−27.3 to 51.3)
Favorable[b] *microbiological response*			
All *S. pneumoniae* (baseline isolates)	60/69 (87.0)	51/70 (72.9)	$P = 0.0003$
			14.1 (0.6 to 27.4)
MDRSP	4/4 (100)	4/9 (44.4)	55.6 (N/A)
Positive by urinary antigen only	25/28 (89.3)	23/31 (74.2)	15.1 (−5.7 to 34.9)
Positive by culture[a]	35/41 (85.4)	28/39 (71.8)	13.5 (−4.8 to 31.8)

CI = confidence interval; MDRSP = multidrug-resistant *S. pneumoniae*, defined as *S. pneumoniae* strains resistant to ≥2 antimicrobial classes; mMITTE = modified microbiological intent-to-treat efficacy; N/A = not available.

[a] Includes *S. pneumoniae* isolates that were identified from a respiratory or blood specimen.

[b] Eradicated or presumed eradicated.

CAP: community acquired pneumonia

Is ceftaroline a useful new antibiotic for CAP?

Diagnostic Microbiology and Infectious Disease 75 (2013) 298–303

Contents lists available at SciVerse ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

The S/R EUCAST breakpoint for ceftriaxone is ≤0.5 / > 2 mg/L

Clinical Study

Assessment of ceftaroline fo
pneumonia due to *Streptoc*
trials☆,☆☆,☆☆☆,★,★★

Andrew F. Shorr [a,*], Marin Kollef [b]

[a] Pulmonary and Critical Care Medicine, Washington Hospi
[b] Washington University School of Medicine, St Louis, MO,
[c] Stanford University School of Medicine, Stanford, CA, USA
[d] Cerexa, Inc. (a wholly owned subsidiary of Forest Laborat

Shorr AF *et al.* *Diagn Microbiol Infect Dis*. 2013 Mar;75(3):298-303.

Table 3

Clinical response rates by baseline ceftaroline fosamil and ceftriaxone MIC for CABP isolates of *Streptococcus pneumoniae* in the integrated FOCUS studies (mMITTE population).

Baseline ceftriaxone MIC (μg/mL)	Total	
	Ceftaroline fosamil, *n*/*N* (%)	Ceftriaxone, *n*/*N* (%)
≤0.015	6/7 (85.7)	4/4 (100)
0.03	20/25 (80.0)	13/19 (68.4)
0.06	3/4 (75.0)	1/1 (100)
0.12	1/1 (100)	0/1 (0)
0.25	0	4/6 (66.7)
1	1/1 (100)	0/4 (0)
2	1/1 (100)	1/1 (100)

CABP = Community-acquired bacterial pneumonia.

CAP: community acquired pneumonia

What are the indications for ceftaroline*?

1.2 Community-Acquired Bacterial Pneumonia

Teflaro is indicated for the treatment of community-acquired bacterial pneumonia (CABP) caused by susceptible isolates of the following Gram-positive and Gram-negative microorganisms: *Streptococcus pneumoniae* (including cases with concurrent bacteremia), *Staphylococcus aureus* (methicillin-susceptible isolates only), *Haemophilus influenzae, Klebsiella pneumoniae, Klebsiella oxytoca,* and *Escherichia coli.*

4.1 Therapeutic indications

Zinforo is indicated in adults for the treatment of the following infections (see sections 4.4 and 5.1):

- Community-acquired pneumonia (CAP)

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Teflaro prescribing information (USA) available at: http://www.frx.com/pi/teflaro_pi.pdf accessed on 6/10/13

Zinforo Summary of Product Characteristics available at: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/002252/WC500132586.pdf accessed on 6/10/13

* in relation to respiratory tract infections

What is new about guidelines?

http://pharmamkting.blogspot.com/2010/10/call-for-pharma-social-media.html accessed on 5/11/13

- Do they change something in your practice?

Guidelines in paediatrics

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Influence of Hospital Guidelines on Management of Children Hospitalized With Pneumonia

Mark I. Neuman, Matt Hall, Adam L. Hersh, Thomas V. Brogan, Kavita Parikh, Jason G. Newland, Anne J. Blaschke, Derek J. Williams, Carlos G. Grijalva, Amy Tyler and Samir S. Shah

Pediatrics 2012;130;e823; originally published online October 22, 2012;
DOI: 10.1542/peds.2012-1285

Neuman MI *et al. Pediatrics*. 2012 Nov;130(5):e823-30.

43 freestanding tertiary care children's hospitals with emergency departments located in noncompeting markets of 27 states plus the District of Columbia and accounting for 15% of all pediatric hospitalizations in the United States in 2009 (677 291 of 4 508 323 admissions)

WHAT'S KNOWN ON THIS SUBJECT: There are limited data on current testing and treatment patterns for children hospitalized with pneumonia, and on whether institutional guidelines affect care.

WHAT THIS STUDY ADDS: The use of institutional clinical practice guidelines was not associated with changes in diagnostic testing, hospital length of stay, or costs for children hospitalized with pneumonia, but was associated with increased use of narrow-spectrum antibiotics.

Guidelines in paediatrics

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Influence of Hospital Guidelines on Management of Children Hospitalized With Pneumonia

Mark I. Neuman, Matt Hall, Adam L. Hersh, Thomas V. Brogan, Kavita Parikh, Jason G. Newland, Anne J. Blaschke, Derek J. Williams, Carlos G. Grijalva, Amy Tyler and Samir S. Shah

Pediatrics 2012;130;e823; originally published online October 22, 2012;
DOI

Neuman MI *et al.* *Pediatrics*. 2012 Nov;130(5):e823-30.

Guidelines seem not very useful…

TABLE 3 Outcomes of Patients Based on Presence of a Pneumonia CPG

Group	Median [IQR]	*P*	Mean Difference (95% CI)	*P*[a]
Length of hospitalization, d				
No guideline	2 [1–3]	.269	Ref	
Guideline	2 [1–3]		−0.05 (–0.29 to 0.20)	.745
Total cost, index hospitalization, $				
No guideline	10 015 [6304–15 931]	.773	Ref	
Guideline	9361 [6274–14 989]		1667 (–1747 to 5081)	.339
Total cost, episode of illness, $				
No guideline	13 265 [6477–16 281]	.553	Ref	
Guideline	9478 [6332–15 292]		1843 (–1861 to 5547)	.329

Group	Percent (95% CI)	*P*	OR (95% CI)	*P*[b]
Readmission rate, %				
No guideline	2.3 (2.0–2.6)	.367	Ref	
Guideline	2.1 (1.7–2.5)		0.89 (0.69 to 1.14)	.396

[a] *P* values comparing medians are unadjusted and aggregate (combining across hospitals).
[b] *P* values are adjusted for hospital clustering.

Guidelines in paediatrics

PEDIATRICS
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Influence of Hospital Guidelines on Management of Children Hospitalized With Pneumonia

Mark I. Neuman, Matt Hall, Adam L. Hersh, Thomas V. Brogan, Kavita Parikh, Jason G. Newland, Anne J. Blaschke, Derek J. Williams, Carlos G. Grijalva, Amy Tyler and Samir S. Shah

Pediatrics 2012;130;e823; originally published online October 22, 2012; DOI: 10.1542/peds.2012-1285

But OK for penicillins… in a few hospitals

Neuman MI *et al. Pediatrics*. 2012 Nov;130(5):e823-30.

TABLE 5 Antimicrobial Use Based on CPG Specific Recommendations

Group	Hospitals, *n* (%)	Patients, *n*	% Received	*P*[a]	OR (95% CI)	*P*[b]
Penicillin/Aminopenicillins						
No CPG	28 (68.3)	13 265	23.9	<.0001	Ref	
CPG: recommend as first-line agent	7 (17.1)	3710	46.3		2.7 (1.4–5.5)	.005
CPG: not addressed	6 (14.6)	2735	19.8		0.8 (0.5–1.3)	.37
Macrolide (>5 y old)						
No CPG	28 (68.3)	4013	55.2	<.0001	Ref	
CPG: recommends macrolide use for children ≥5 y	10 (24.4)	1633	58.2		1.1 (0.7–1.9)	.64
CPG: no recommendation for macrolide use	3 (7.3)	286	41.3		0.6 (0.3–0.9)	.026

[a] *P* values comparing differences in proportion of patients receiving antibiotics based on specific mention in the CPG are unadjusted and aggregate (combining across hospitals).

[b] *P* values are adjusted for hospital clustering.

And to finish: an important review…

F1000Prime REPORTS

Published: 01 October 2013
© 2013 Faculty of 1000 Ltd

Major advances in managing community-acquired pneumonia

Waseem Asrar Khan and Mark Woodhead*

Address: Department of Respiratory Medicine, Manchester Royal Infirmary, Manchester

* Corresponding author: Mark Woodhead (mark.woodhead@cmft.nhs.uk)

F1000Prime Reports 2013, **5**:43 (doi:10.12703/P5-43)

Abstract

This article is a non-systematic review of selected recent publications in community-acquired pneumonia, including a comparison of various guidelines. Risk stratification of patients has recently been advanced by the addition of several useful biomarkers. The issue of single versus dual antibiotic treatment remains controversial and awaits a conclusive randomized controlled trial. However, in the meantime, there is a working consensus that more severe patients should receive dual therapy.

Asrar Khan & Woodhead F1000Prime Rep. 2013 Oct 1;5:43.

Other questions
(no time to address them but ask questions …)

- Does the new conjugated vaccine effectively cover important serotypes such as those associated with pleural effusion and non-invasive pneumococcal pneumonia
  - **Yes, but bacteria "adapt" to the new situation…**
- Is the administration of corticosteroids in CAP useful and safe
  - **This remains disputable (and disputed…)**
- Are fluoroquinolones better than macrolides in the empirical treatment of CAP
  - **They probably are but with a low margin…**

CAP: community acquired pneumonia

Back-up slides

Naucler et al. Table 2 with notes

Table 2 Thirty-day mortality risk according to serotype and antibiotic resistance in patients with bacteraemic pneumococcal pneumonia

	No of patients (column %)	No of deaths (row %)	Crude OR (95% CI)	Adjusted OR† (95% CI)
Individual serotype				
9V	191 (12.1)	10 (5.2)	0.62 (0.28 to 1.40)	0.83 (0.36 to 1.93)
7F	177 (11.2)	4 (2.3)	0.26 (0.09 to 0.79)	0.51 (0.16 to 1.59)
4	158 (10.0)	8 (5.1)	0.60 (0.25 to 1.43)	0.88 (0.36 to 2.16)
3	142 (9.0)	17 (12.9)	1.54 (0.76 to 3.12)	1.85 (0.87 to 3.93)
23F	97 (6.1)	11 (11.3)	1.44 (0.65 to 3.21)	1.23 (0.54 to 2.81)
22F	79 (5.0)	7 (8.9)	1.10 (0.44 to 2.76)	1.25 (0.48 to 3.23)
6B	78 (4.9)	15 (19.2)	**2.69 (1.27 to 5.69)**	2.09 (0.96 to 4.57)
6A	76 (4.8)	10 (13.1)	1.71 (0.75 to 3.92)	1.17 (0.49 to 2.75)
19A	55 (3.5)	4 (7.3)	0.89 (0.29 to 2.75)	0.69 (0.21 to 2.22)
14	209 (13.2)	17 (8.3)	1.00 (ref)	1.00 (ref)
Other	318 (20.1)	44 (13.8)	–	–
Serotype category according to CFR‡				
High	509 (32.2)	63 (12.4)	**3.28 (1.89 to 5.70)**	1.63 (0.89 to 2.98)
Medium	484 (30.6)	35 (7.2)	**1.81 (1.00 to 3.28)**	1.27 (0.67 to 2.42)
Low	412 (26.1)	17 (4.1)	1.00 (ref)*	1.00 (ref)**
Serotype category according to invasiveness§				
Low	461 (29.2)	58 (12.6)	**4.21 (1.89 to 9.40)**	1.67 (0.70 to 4.00)
Medium	591 (37.4)	40 (6.8)	2.13 (0.94 to 4.82)	1.19 (0.49 to 2.87)
High	212 (13.4)	7 (3.3)	1.00 (ref)*	1.00 (ref)***
PCV 13 serotypes ¶				
Yes	1277 (80.8)	107 (8.4)	**0.60 (0.41 to 0.89)**	0.78 (0.51 to 1.19)
No	303 (19.2)	40 (13.2)	1.00 (ref)	1.00 (ref)
Penicillin non-susceptible††				
Yes	45 (2.9)	6 (13.3)	1.52 (0.63 to 3.65)	1.07 (0.42 to 2.74)
No	1535 (97.2)	141 (9.2)	1.00 (ref)	1.00 (ref)
Erythromycin non-susceptible††				
Yes	69 (4.4)	5 (7.4)	0.75 (0.30 to 1.90)	0.83 (0.32 to 2.16)
No	1511 (95.6)	141 (9.4)	1.00 (ref)	

Significant results in bold.
p Value trend: *<0.001, **0.09, ***0.11.
†Adjusted ORs: individual serotypes and antibiotic resistance adjusted for age, sex and Charlson Index score; grouped serotypes adjusted for age, sex, smoking, alcohol and comorbidities associated with mortality at a p value of <0.1 in univariate analyses (ie, heart disease, pulmonary disease, liver disease, renal disease and solid tumour).
‡Serotypes classified as associated with low (serotype 1, 4, 5, 7F, 8), medium (serotypes 9V, 12F, 14, 22F) and high (serotypes 3, 6A, 6B, 9N, 19A, 19F, 23F) case fatality rate in a recent meta-analysis.[9] There were 175 patients infected with serotypes not included in this classification.
§Serotypes classified as associated with high (serotype 1, 5 and 7F), medium (serotype 4, 9V, 14 and 18C) and low (serotype 3, 6A, 6B, 8, 19F and 23F) invasiveness.[8 15] There were 316 patients infected with serotypes not included in this classification.
¶Serotypes included in 13-valent pneumococcal conjugate vaccine: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.
††Non-susceptibility for penicillin was defined as minimal inhibitory concentration ≥0.12 mg/l and for erythromycin a zone diameter of ≤21 mm.[22].
CFR, case-fatality rates; PCV, pneumococcal vaccine.

Naucler P *et al.* *Thorax.* 2013;68(6):571-9.

Rodrigo et al. Table 1 with notes

Table 1 Multivariate analyses of the association between antibiotic therapy and clinical outcomes

Outcome measures	Total (n=5240)	β-lactam therapy (n=2001)	β-lactam/ macrolide therapy (n=3239)	Adjusted OR (95% CI)	p Value
30 day IP death rate	1281 (24.4)	536 (26.8)	745 (23.0)	0.72 (0.60 to 0.85)*	<0.001
ICU admission	419 (8)	136 (6.8)	282 (8.7)	0.94 (0.72 to 1.22)†	0.635
Need for MV	151 (2.9)	58 (2.9)	93 (2.9)	0.99 (0.71 to 1.38)†	0.508
Need for INS	130 (2.5)	42 (2.1)	88 (2.7)	0.87 (0.55 to 1.38)†	0.544
30-day IP death rate stratified by pneumonia severity					
Low severity (CURB65=0–1)	201/2247 (8.9)	95/908 (10.5)	106/1339 (7.9)	0.80 (0.56 to 1.16)‡	0.238
Moderate severity (CURB65=2)	370/1480 (25)	171/561 (30.5)	199/919 (21.7)	0.54 (0.41 to 0.72)‡	<0.001
High severity (CURB65≥3)	710/1513 (46.9)	270/532 (50.8)	440/981 (44.9)	0.76 (0.60 to 0.96)‡	0.025

Values given as n (%).
*OR adjusted for age, sex, binary variables within CURB65 excluding age (confusion, urea>7 mmol/l, respiratory rate ≥30/min, systolic blood pressure<90 mmHg or diastolic blood pressure ≤60 mmHg), individual comorbidities, intravenous antibiotic use, nursing home residency and ICU admission.
†OR adjusted for age, sex, binary variables within CURB65 excluding age (confusion, urea>7 mmol/l, respiratory rate ≥30/min, systolic blood pressure<90 mmHg or diastolic blood pressure ≤60 mmHg), individual comorbidities, intravenous antibiotic use and nursing home residency.
‡OR adjusted for sex, individual comorbidities, intravenous antibiotic use, nursing home residency and ICU admission.
ICU, intensive care unit; IP, inpatient; MV, mechanical ventilation; INS, inotropic support.

Rodrigo C *et al. Thorax*. 2013;68(5):493-5.

Ambroggio et al. Table IV with notes

Table IV. LOS according to empiric antibiotic therapy

Antibiotic category	Unadjusted relative risk (95% CI)	Adjusted relative risk (95% CI)*,†,‡
Main analysis		
Monotherapy	Reference	Reference
Combination therapy	0.91 (0.87-0.96)	0.80 (0.75-0.86)
Age category, y		
1-5	N/A	0.96 (0.86-1.06)
6-11	N/A	0.85 (0.79-0.91)
12-18	N/A	0.69 (0.49-0.98)
Monotherapy		
Aminopenicillin	Reference	Reference
Second-generation cephalosporin	1.06 (0.96-1.17)	1.01 (0.91-1.12)
Third-generation cephalosporin	1.16 (1.05-1.28)	1.03 (0.94-1.14)
Combination therapy		
Aminopenicillin + macrolide	Reference	Reference
Second-generation cephalosporin + macrolide	1.03 (0.93-1.15)	1.01 (0.90-1.13)
Third-generation cephalosporin + macrolide	0.88 (0.77-1.01)	0.91 (0.79-1.04)

*Results for main analysis were adjusted for age category, principal payer, prior hospitalization for asthma, receipt of chronic asthma therapy, systemic corticosteroid medication, β-agonist therapy, testing for arterial blood gases, intensive imaging testing, and interaction of therapy and age. The results are also stratified by age as the interaction of therapy and age was statistically significant.

†Results for monotherapy subanalysis were adjusted for age, principal payer, prior hospitalization for asthma, receipt of chronic asthma therapy, systemic corticosteroid medication, β-agonist therapy, testing for arterial blood gases, and intensive imaging testing.

‡Results for combination therapy subanalysis were adjusted for age, principal payer, prior hospitalization for asthma, receipt of chronic asthma therapy, systemic corticosteroid medication, β-agonist therapy, testing for arterial blood gases, and intensive imaging testing.

Ambroggio L *et al. J Pediatr*. 2012;161(6):1097-103.