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Update on Community Acquired Pneumonia

Thunder Bay Medical Society ~ Fall School

November 6th, 2015

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Faculty/Presenter Disclosure

- **Faculty:** Dr. Vanessa Luks
- **Relationships with commercial interests:**
  - **Speakers Bureau/Honoraria:**
    - Astra Zenica, Novartis, Grifols

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Disclosure of Commercial Support

- **This program has not received any financial support**
- **Potential for conflict(s) of interest:**
  - none

Objectives

- To describe the most common pathogens causing CAP
- To be able to assign a severity to cases of CAP and a risk assessment for more virulent or drug-resistance organisms
- To be aware of the utility of novel and standard diagnostic tests in CAP
- To be aware of recent evidence in management of CAP

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Pneumonia

- **CAP:**
  - Suspected/Outpatient: symptoms of LRTI, at least 1 systemic feature, new focal chest signs, no other explanation
  - Definite/Hospital: as above AND new radographic "shadowing"
- **HCAP:** Pneumonia in those patients with any one of the following:
  - hospitalized within 90 days of the infection, resided in a nursing home or long-term care facility, or received parenteral antimicrobial therapy, chemotherapy, or wound care within 30 days of pneumonia, or attended hemodialysis or a hospital
- **HAP:** pneumonia occuring ≥ 48 h after hospital admission, not brewing prior to admission
- **VAP:** pneumonia occurring ≥ 48 h after intubation in ICU (early and late)

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Epidemiology of CAP

- *S. pneumoniae* caused 95% of cases of pneumonia pre-antibiotics (Heffron, R. Harvard U Press 1939)
- 2008 – 2013: *S. pneumo* detected in 10 to 15% of cases only
  - Inpatients, may not represent outpatient population
  - Pneumococcal vaccinations
  - Decreased incidence of smoking
  - Higher in Europe

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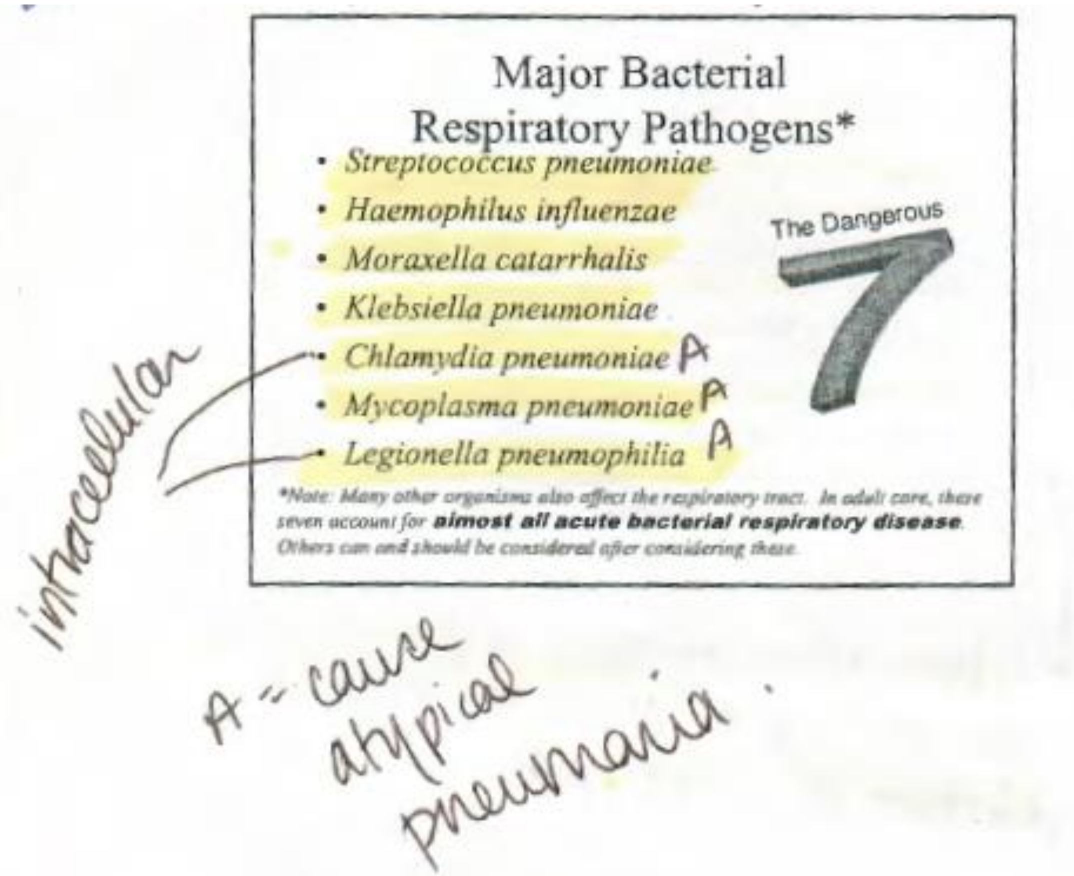
Medical School 1st year Jan 2004


Major Bacterial Respiratory Pathogens*

- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Moraxella catarrhalis*
- *Klebsiella pneumoniae*
- *Chlamydia pneumoniae*
- *Mycoplasma pneumoniae*
- *Legionella pneumophilia*

*Note: Many other organisms also affect the respiratory tract. In adult care, these seven account for **almost all acute bacterial respiratory disease**. Others can and should be considered after considering these.

Dr. Michael Noble, Vancouver General Hospital

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Features associated with specific causes

Table 2. Clinical Features Associated with Specific Causes of CAP.

Favoring typical bacterial or legionella pneumonia
Hyperacute presentation
Presentation with septic shock
Absence of upper respiratory symptoms
Initial upper respiratory illness followed by acute deterioration (suggesting viral infection with bacterial superinfection)
White-cell count, >15,000 or ≤6000 cells per cubic millimeter with increased band forms
Dense segmental or lobar consolidation
Procalcitonin level, ≥0.25 μg per liter
Favoring atypical bacterial (mycoplasma or chlamydophila) pneumonia
Absence of factors that favor typical bacterial pneumonia
Family cluster
Cough persisting >5 days without acute deterioration
Absence of sputum production
Normal or minimally elevated white-cell count
Procalcitonin level, ≤0.1 μg per liter
Favoring nonbacterial (viral) pneumonia
Absence of factors that favor bacterial pneumonia
Exposure to sick contacts
Upper respiratory symptoms at time of presentation
Patchy pulmonary infiltrates
Normal or minimally elevated white-cell count
Procalcitonin level, ≤0.1 μg per liter
Favoring influenza pneumonia
Absence of factors that favor typical bacterial pneumonia
Influenza active in the community
Sudden onset of flulike syndrome
Positive diagnostic test for influenza virus

N ENGL J MED 371;17

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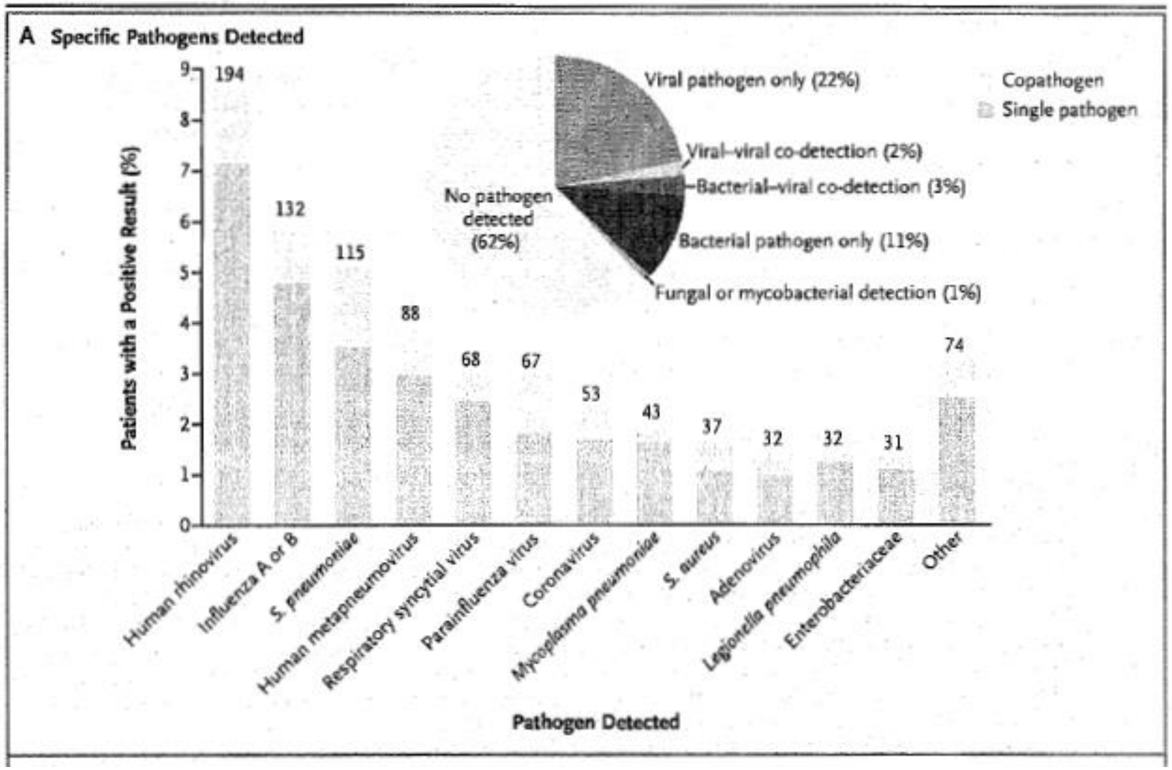
Etiology of Pneumonia in the Community (EPIC)

- Jain, et al. NEJM July 2015
- Population based surveillance for hospitalized CAP Jan 2010 to 2012
- Extensive investigations
- Excluded recently hospitalized, IC'ed
- Only 68% of eligible patients were enrolled
  - Non-enrolled were older, died more frequently, and more required IMV; specimens not obtained

Results



Mean age 57 y
Median LOS 3 days (IQR 2 to 6)
21% required ICU, 6% IMV, 2% died

Most common pathogens overall
Human rhinovirus (9%)
Influenza (6%)
S. pneumo (5%)

ICU vs non-ICU (*S. pneumo*, *S. aureus*, and enterobacteriacea more common)16% versus 6%

Atypicals detected in 4%

Overall incidence: 24.8 cases/10,000 adults
Increased incidence with age

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Viral Causes of CAP

- Influenza
  - Avian influenza A (H7N9)
- Parainfluenza
- RSV
- Human metapneumovirus
- Adenovirus
- Coronavirus
- Rhinovirus
- Middle East respiratory syndrome corona virus

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Secondary Bacterial infection

- Viruses denude the epithelium → ↑ risk of bacterial infection, especially S. aureus
- Virus facilitates increase nasal colonization, and ability of bacteria to adhere and invade
- S. pneumo (48%), S. aureus (19%)
  - CA- MRSA – estimates of 25% of severe bacterial CAP in influenza outbreaks, high mortality

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Why no pathogens found

- Only 41% had sputum & only high quality specimens tested (↑ Sp, ↓ Sn)
- < 12% of specimens (other than blood cultures) obtained pre-abx
- 13% of blood cultures obtained post-antibiotics
- Blood Cx in 91%, serology in 37%, Ur Ag in 85%
- Did not test for coxiella
- Diagnostic tests insensitive
- Range of detection in other epidemiologic studies (20 to 76%) but much lower than pediatric EPIC (81%)

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CAP Severity Scores

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CURB-65

CURB65	
Symptom	**Points**
Confusion	1
Urea>7mmol/l	1
Respiratory rate>30	1
S**B**P<90mmHg, D**B**P<60mmHg	1
Age>=**65**	1

CRB-65	Mortality
0	1.2%
1	5.3%
2	12.2%
3-4	33%

CURB-65	Predicted Mortality	Action
0 to 1	< 3%	Outpatient
2	9%	Admit, short stay
≥ 3	15 to 57%	Admit, consider ICU for scores ≥ 4

Pneumonia Severity Index (PSI)

Risk factor	Points
Demographics	
Men	Age (years): ___
Women	Age (years) - 10: ___
Nursing home resident	+10
Comorbidities	
Neoplasm	+30
Liver disease	+20
Heart failure	+10
Stroke	+10
Renal failure	+10
Physical examination findings	
Altered mental status	+20
Respiratory rate ≥ 30 breaths per minute	+20
Systolic blood pressure < 90 mm Hg	+20
Temperature < 95°F (35°C) or ≥ 104°F (40°C)	+15
Pulse rate ≥ 125 beats per minute	+10
Laboratory and radiographic findings	
Arterial pH < 7.35	+30
Blood urea nitrogen > 30 mg per dL	+20
Sodium < 130 mmol per L	+20
Glucose ≥ 250 mg per dL	+10
Hematocrit < 30 percent	+10
Partial pressure of arterial oxygen < 60 mm Hg	+10
Pleural effusion	+10
Total points:	

Point total	Risk class	Deaths/total (%)		Recommendation†
		Adults with CAP*	Nursing home patients with CAP[1]	
< 51	I	3/1,472 (0.2)	None	Outpatient therapy should be considered, especially for patients in classes I and II
51 to 70	II	7/1,374 (0.5)	None	
71 to 90	III	41/1,603 (2.6)	1/21 (4.8)	
91 to 130	IV	149/1,605 (9.3)	6/50 (12.0)	Patient should be hospitalized
> 130	V	109/438 (24.9)	28/85 (32.9)	

*—Data for community-acquired pneumonia (CAP) are weighted averages from validation studies.[2,4]
†—Recommendations are consistent with clinical guidelines.[3,5] Clinical judgment may overrule the guideline recommendation.

- Fine et al. NEJM 1997;336:243-250.
- Much more sensitive for determining need for ICU
- Very age-dependent therefore if score is high in a young person, be alarmed!
- ≥ 91 → Admit
- ≤ 90 → Discharge home

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For determining need for intensive respiratory or pressor support

S
- Systolic blood pressure < 90mmHg (1 point)

M
- Multilobar CXR involvement(1 point)

A
- Albumin < 3.5 g/dL (1 point)

R
- Respiratory rate ≥ 30/min or (≥ 25/min if pt. ≤ 50 yrs. old) (1 point)

T
- Tachycardia (≥ 125 bpm) (1 point)

C
- Confusion (new onset) (1 point)

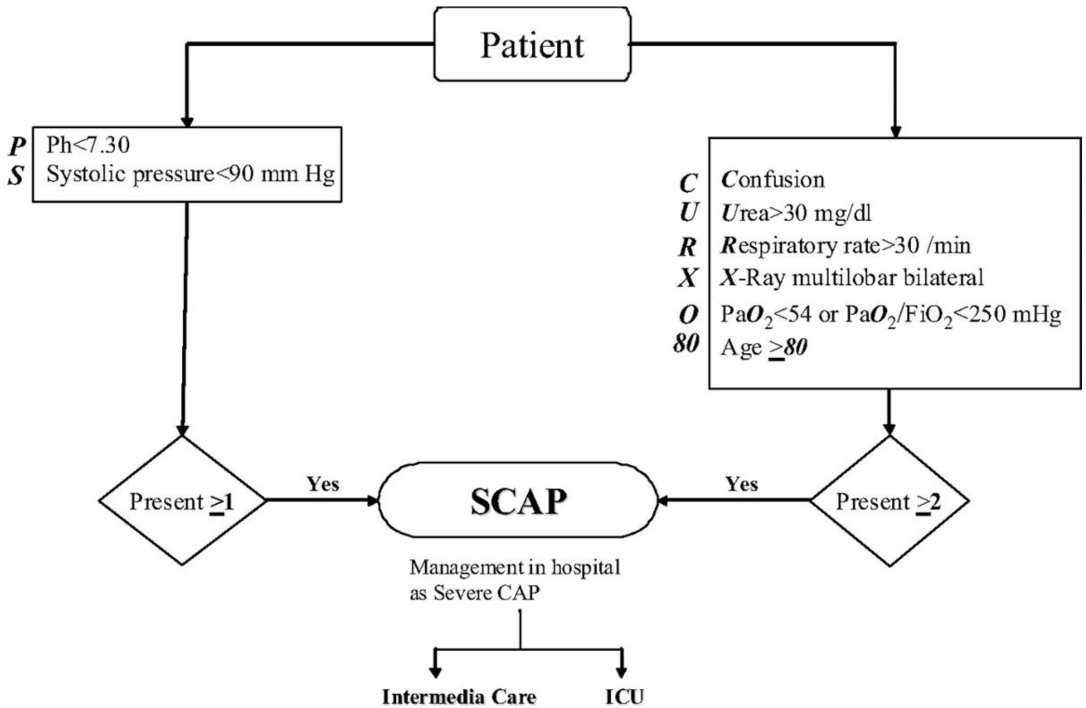
O
- Oxygen saturation < 90% (or ≤ 93% mmHg if pt. ≤ 50 yrs. old) OR PaO_2 ≤ 60 mmHg (or ≤ 70 mmHg if pt. ≤ 50 yrs. old) OR PaO_2 / FiO_2 < 250 (or < 333 if pt. ≤ 50 yrs. old) (2 points)

P
- pH < 7.35 (2 points)

0-2 Points	3-4 Points	5-6 Points	7+ Points
• Low risk of needing IRVS	• Moderate risk of needing IRVS	• High risk of needing IRVS	• Very high risk of needing IRVS

Severe CAP is classified at score of 5 or more.

Mnemonic: "SMART COP"



SCAP = severe community-acquired pneumonia score Points assigned to each variable of SCAP score[12]: P = arterial pH (13 points); S = systolic pressure (11 points); C = confusion (5 points); U = BUN (5 points); R = respiratory rate (9 points); X = x-ray (5 points); O = Pao2 (6 points); 80 = Age ≥ 80 years (5 points). The 8 variables of the score were grouped in major and minor criteria on relation to points assigned to each. Classifying a patient as SCAP is based on the presence of one major criterion or two minor criteria.

Comparison between scores

- Sensitivity
  - PSI > CURB-65 > SCAP
- Specificity
  - CURB-65 > PSI
- For determining need for ICU
  - SCAP, SMART-COP, IDSA/ATS > PSI, CURB-65, and Smrt-CO

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Risk for MDR organisms

- Nursing home
- Dialysis
- Hospital admit/contact within 90 days
- Any ICU admission
- IV home antibiotics
- MDR colonized
- MDR contact
- Pneumonia developing > 5 days into hospitalization
- Immunocompromised state

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Changing how to look at pneumonia classifications

- Decision for antibiotics should be based on severity and risk for MDR organisms

- PES score
  - Prina et al. ERJ 2012 Sept
  - **P**seudomonas, **E**SBL, MR**S**A
  - Risk factors: age, aspiration, recent antibiotics, chronic respiratory or neurologic disease
  - NOT nursing home residence

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Diagnostic testing in CAP

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Why test at all?

- Diagnostic testing is expensive
- Inconclusive in 2/3 of patients, therapy change in 10%
- Prompt empiric antimicrobial therapy based on guidelines results in good outcomes
  - 90% cure in inpatients with resp FQ or β lactam/macrolide in mild to moderate CAP

- Test → pathogen-directed therapy → reduced duration of antibiotics, narrower spectrum → decreased superinfection, population-resistance, C. difficile, complications of under/mis-treated CAP (abscess, empyema, hypoxic/hypercarbic respiratory failure)

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Routine Panel

- Community
  - None per BTS unless failure to respond, outbreak situations
- Chest radiograph*
- CBC, renal and liver function, oxygen assessment
- Sputum Gram stain and culture/sensitivity
  - Neither sensitive nor specific
- Blood cultures
- Urinary antigens for legionella and pneumococcus
- Multiplex PCR assays for M. pneumonia, C. pneumonia, virsuses
- More specific tests based on exposures or risk factors
- ? Procalcitonin ? CRP
  - BTS recommends baseline CRP and repeat at day 3 if not improving

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Sputum cultures

- S. pneumonia sputum cultures positive in 80% of cases if
  - Good quality
  - Obtained prior to, or within 12 h of initiation of antibiotics
- Nebulization with hypertonic saline (induced) can be helpful

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Blood cultures

- 20 to 25% of inpatients with pneumococcus will have + blood cultures
- *S. aureus*
  - Hematogenous pneumonia ~100%
  - Aspiration ~25%

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NPS

- PCR much more sensitive than ELISA
- Commercial available PCR assays can detect most important resp viruses as well as atypical bacterial causes
- How to interpret a positive result…
  - Asymptomatic controls can have + viral PCR
  - 20% of patients with proven bacterial pneumonia are co-infected with a virus
  - PCR detection of a bacteria
    - Colonization versus infection ?
    - Infection stems from colonization

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Urine antigen testing (ELISA)

- Legionella urine antigen
  - Sn 74% in those with *serotype 1*, Sp 100%
  - Improved Sn in more severe disease
  - May be negative initially
- Pneumococcal antigen
  - Sn 77 to 88% (bacteremic pneumonia), 64% (non-bacteremic)
  - False + (nasal colonization in children, CAP within 3 months in adults)
  - No sensitivities

Procalcitonin

- Ubiquitous release during infection
- Persistently high levels~ poor prognosis
- Decreasing levels ~ good prognosis
- Roles
  - Diagnosing infection
    - Sn 80s, NPV 80s
    - Adjunct only?
  - Guiding antibiotic duration in infection
  - Distinguishing
    - Viral versus bacterial
    - Acute exacerbation asthma/COPD from CAP
- European counterpart: CRP

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Procalcitonin guidance of antibiotics therapy in CAP

- Christ-Crain, M. AJRCCM 2006
- Inpatient CAP, Switzerland 2003 to 2005; defn (new infiltrate + signs/symptoms); all severities
- Intervention: usual care for CAP vs PCT-guided therapy (to start and stop abx)
  - PCT at days 0, 4, 6, and 8
  - PCT < 0.1 mcg/L: bacterial infection not present
    - Initiation/continuation of abx strongly discouraged
  - PCT 0.1 to 0.25 mcg/L : bacterial infection unlikely
    - Initiation/continuation of abx discouraged
  - PCT 0.25 to 0.5 mcg/L: bacterial infection likely
    - Initiation/continuation of abx encouraged
  - PCT > 5 mcg/L: bacterial infection very likely
    - Initiation/continuation of abx strongly encouraged
  - PCT decreased to < 10% of initial value at day 0
    - Strongly suggest discontinue abx

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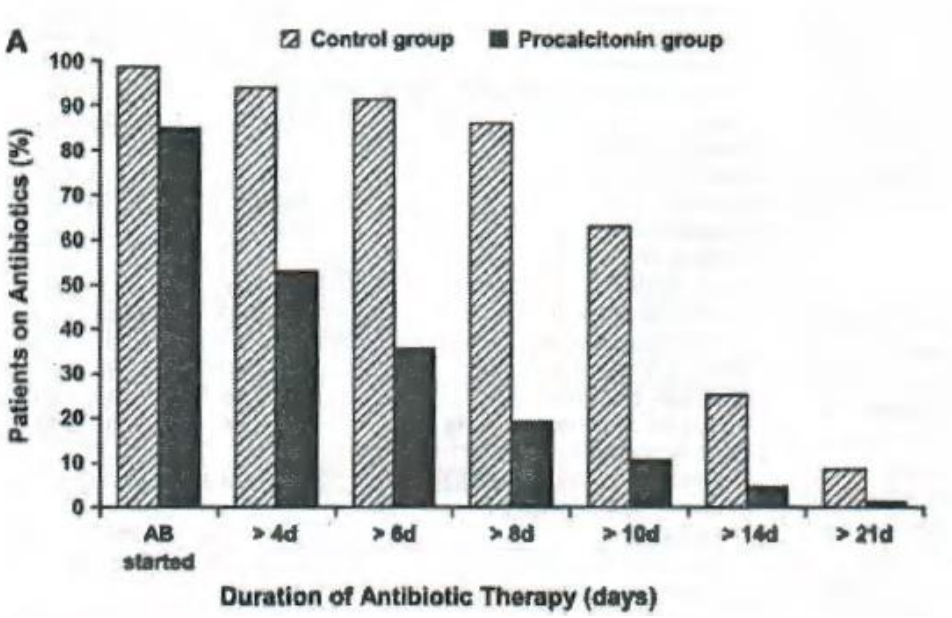
- PCT strategy
  - Reduced antibiotic Rx on admission
  - Reduced antibiotic exposure
  - Earlier discontinuation (5 d vs 12 d)
  - Same cure rate



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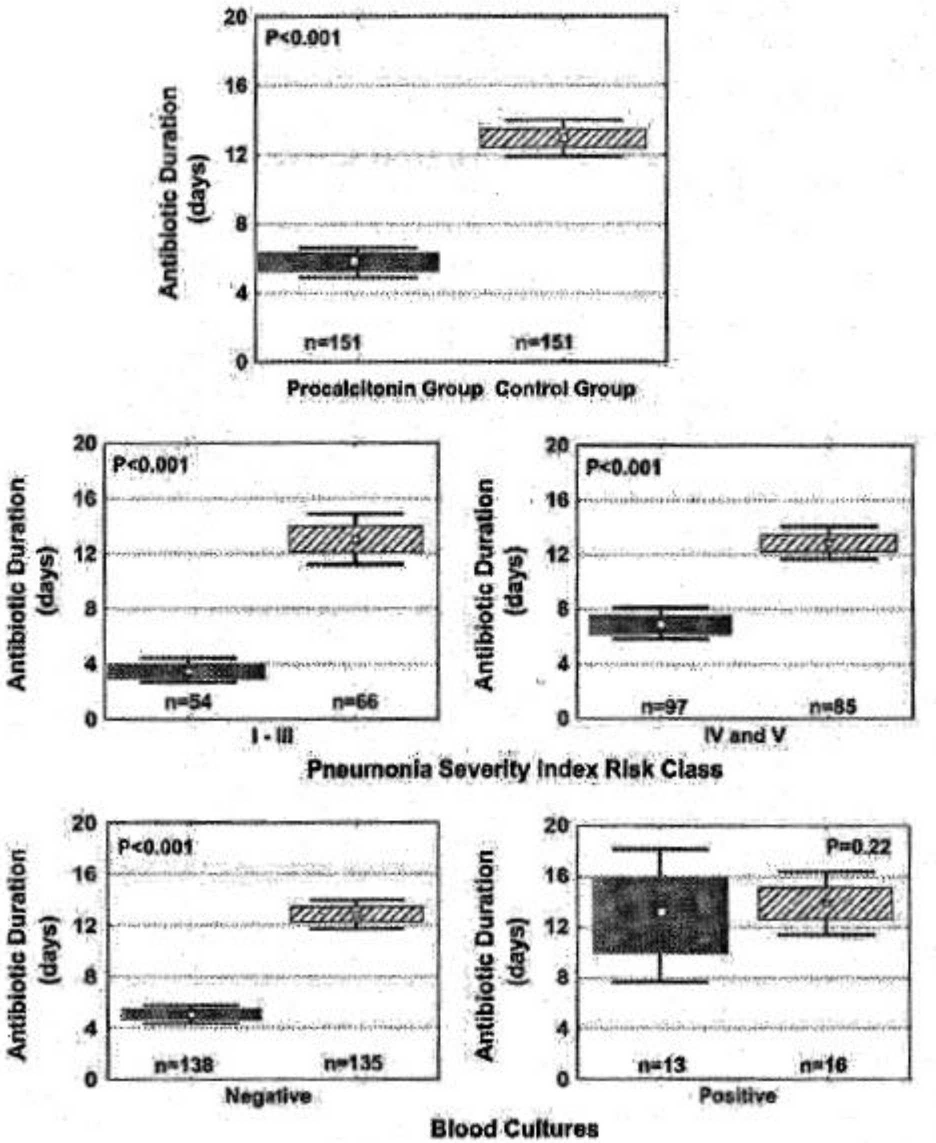

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Repeat imaging

- No need to repeat if improving while in hospital
- BTS recommends follow-up imaging at 6 weeks only in those with risk factors for malignancy (age > 50 or smoking history) or those with persistent symptoms

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Thoracentesis

- Parapneumonic effusions in 1/3 of patients
- 1/3 of infected pleural fluid have no discernable adjacent pneumonia
- Microbiology different, 40% obscure
- Sample anything > 1 cm
  - pH > 7.2, LDH low, glucose not low → abx alone
  - Large, free-flowing, pH > 7.2, LDH low, glucose not low → therapeutic drainage
  - pH < 7.2, or high LDH or low glucose or positive gram stain or culture or pus or loculated → tube drainage
  - Small tube (<14Fr) vs Large tube OR failure 0.86 (15% vs 17%)
- Data for ↓surgical referrals, ↓ LOS by 50%, ↓ size on CXR with upfront intrapleural TPA & Dnase
  - Also data for rescue (93% success rate)
- 15% of patients fail chest tube & antibiotics
- Surgery: failure to drain, entrapped lung
  - Debridement, decortication
  - No mortality benefit to VATs first approach
- BTS guidelines 2010 Management of pleural infection in adults

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Antibiotic Choices

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Most recent guidelines

- CTS/CIDS
  - Can Respir J 2000; 7(5): 371 – 382.
- IDSA/ATS guidelines
  - CID 2007;44
- British Thoracic Society
  - Thorax 2009;64 (Suppl III)
- European Society of clinical microbiology and infectious diseases
  - CMI 2011; 17 (supp 6):

	CTS	IDSA/ATS	BTS
Healthy outpatient*	macrolide doxycycline	macrolide* doxycycline	amoxicillin doxy or clarithro
Co-morbidities Recent abx	levofloxacin β lactam + macrolide	Resp FQ OR β lactam + macrolide	amoxicillin doxy or clarithro
Macro-aspiration	clavulin +/- macrolide OR 4th G FQ		
Nursing Home (outpatient)	FQ or clavulin +/- macrolide 2nd G ceph + macrolide		
Hospitalized	levofloxacin 2nd/3rd/4th G ceph + macrolide	Resp FQ OR β lactam + macrolide	amoxil + clarithro doxy or levo or moxi
Requiring ICU	3G ceph/clav + IV FQ 3G ceph/clav + IV macrolide	β lactam (3Gceph or ampsulb) + (FQ > macrolide)	clavulin + clari PCN + levo/cipro 2/3G ceph + clari
Requiring ICU & ? PA	APFQ + (APsβL or AG) APsβL + AG + macrolide	APsAP β lactam + cipro/levo OR APsAP β lactam + AG + macrolide OR APsAP βlac+AG +FQ	

β Lactam as first line?

- S. pneumo much more susceptible to βL than to macrolides or tetracycline classes
- 15 to 30% resistance to macrolides
- 1/3 of *H. influenzae*, and most M. catarrhalis produce beta-lactamases → clavulin preferrable, esp if chronic lung disease
- 2001 TRUST 18.4% of *S. pneumo* resistant to PCN
  – TBRHSC 2014/2015 antibiogram 7% PRSP

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βL vs β L + macrolide vs FQ

- Postma et al. NEJM 2015; 372(14):1312 – 1323
- Cluster-randomized crossover trial, 4 month periods in the Netherlands 2011 to 2013
  - CAP admitted to non-ICU wards
    - βL (amoxil, clavulin, 3G cephalosporin)
    - β L – macrolide (as above but included penicillin, and any macrolide)
    - FQ (moxifloxacin or levofloxacin)

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- Outcome: 90 day morality
  - βL strategy non-inferior to FQ and β L-macrolide
    - Intention-to-treat, strategy-adherent, antibiotic-adherent, radiographically proven
- Caveats
  - Average PSI score was 84 +/- 29 , CURB 65 was 1
  - 24.8% of cases had antibiotic deviation (200/565 for non-medical reasons)
  - Mycoplasma detected in only 2% of cases
  - Legionella detected in only 1% of cases
  - 15% of cases due to *S. pneumo*
  - Vaccine rate PPSV 23 and PCV 13 were 2.7% and 1% respectively
  - The resistance of *S. pneumo* to PCN is only 4% in the Netherlands
    - Highest resistance was during β-lactam therapy and this did not lead to worse outcomes*

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For combination therapy

- Rodrigo et al. Chest 2013
  - Wales, prospective, non-randomized study of inpatient CAP, βL (including any PCN or cephalosporin) versus βL-macrolide

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 combination 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

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Another study for combination therapy

- Brown, R. et al. Ch
- Retrospective hos of inpatient CAP

1) Monotherapy best for death, LOS, charges
2) Of all monotherapies, Ceftriaxone + macrolide best for LOS & charges

Table 3—*Outcomes of Overall Patients, Monotherapy vs Dual Therapies*

Variables	Monotherapy	Macrolide Combination	p Value
Ceftriaxone			
Subjects, No.	8,554	9,605	
LOS*	4.99 (4.19)	4.98 (3.51)	< 0.0001
Died†	561 (6.31)	265 (2.76)	< 0.0001
Total charges,* $	7,270.20 (6,109.48)	7,940.92 (6,043.76)	< 0.0001
Other cephalosporins			
Subjects, No.	8,729	7,175	
LOS*	5.82 (4.80)	5.60 (3.80)	0.9891
Died†	446 (5.11)	155 (2.16)	< 0.0001
Total charges,* $	9,395.68 (7,940.24)	9,694.29 (7,565.26)	< 0.0001
Penicillins			
Subjects, No.	3,130	1,420	
LOS*	6.09 (4.26)	6.08 (3.82)	0.0867
Died†	255 (8.15)	35 (2.46)	< 0.0001
Total charges,* $	10,430.31 (8,201.14)	10,688.89 (8,330.95)	0.0549
Quinolones			
Subjects, No.	1,335	618	
LOS*	6.71 (5.78)	6.47 (4.76)	0.5543
Died†	66 (4.94)	18 (2.91)	0.0396
Total charges*, $	10,943.03 (10,781.48)	11,291.74 (10,683.63)	0.2230

*Values given as mean (SD).
†Values given as No. (%).

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Why combination therapy, no montherapy in ICU

- Leroy et al. Chest 2005; 128(1):172-183.
- Severe CAP requiring ICU
- Levofloxacin vs Ceftriaxone and ofloxacin

41% of cases due to pneumococcus and ofloxacin has low activity against *S. pneumo*

Table 6–28-Day and Overall Mortality Rates*

	L Group	C + O Group	p Value
	30/194 (15.5)	37/201 (18.4)	0.44
	149 (12.1)	20/159 (12.6)	0.89
	76 (22.4)	18/82 (22.0)	0.95
	15/139 (10.8)	18/132 (13.6)	0.47
	15/73 (20.6)	16/71 (22.5)	0.77
	34/194 (17.5)	45/201 (22.4)	0.23
mITT popu	20/149 (13.4)	24/159 (15.1)	0.68
Mechanically ventilated patients	17/76 (22.4)	20/82 (24.4)	0.76
PP population	17/139 (12.2)	22/132 (16.7)	0.3
Mechanically ventilated patients	15/73 (20.6)	18/71 (25.4)	0.49

*Data are presented as No. of patients in the subgroup/total No. of patients in the group (%).

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Combination vs Monotherapy in intubated CAP patients

- Loeches-Martin,I et al. Combination therapy with macrolides improves survival in intubated patients with community acquired pneumonia. Intensive Care Medicine. 2010; 36(4): 612-620.

- Prospective, observational cohort, multicentre study
- Intubated patients ICU
- Mortality HR 0.48 (CI 0.23 to 0.98)

- No FQ monotherapy in intubated CAP patients

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Covering for influenza

- Suggested with CAP when influenza is active in the community
- D/C if PCR negative (if likelihood high, continue even if rapid test negative b/c of insensitivity)
- Gram stain negative & no suspicion bacterial superinfection → no abx
  - Otherwise, ceftriaxone + (vanco/linezolid)???

Any role for inhaled antibiotics ?

- BAY41-6551
  - Niederman, M. ICM 2012
  - Inhaled amikacin in gram negative VAP in addition to systemic antibiotics
  - Premise: back to concentration dependent killing
    - Able to safely achieve much higher levels in the epithelial lining and secretions using inhaled antibiotics
    - The higher the concentration, the better the cidal activity

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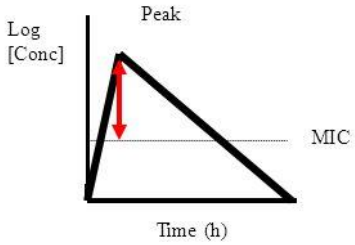
Pharmacodynamics

Relationship between Abx Concentration & Effect

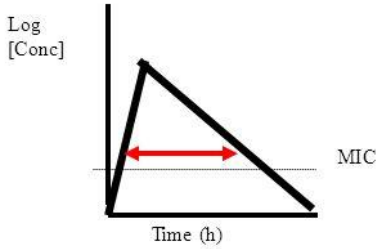
Concentration Dependent Killing

- Higher the peak, better the kill
- i.e. Ratio of peak drug concentration and M.I.C. determines rate of kill.
- Eg. FQs, AGs



Time Dependent Killing

- Time over MIC matters
- i.e. Independent of peak concentration. Determined by length of time over MIC
- Eg. B-lactams (Pen, Ceph etc)



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Results

- Bronchial concentrations 4000 x **higher** than peak serum obtained with IV amikacin
- **Lower rate of failure** with the addition of inhaled amikacin to usual care by CPIS criteria
- Overall "**less** systemic antibiotics" at the end of the trial
- Proprietary devices, monitoring issues

Duration of therapy

- Increasing resistance is a problem
- We are not developing new antibiotics
- Solutions?
  - Use the antibiotics we have but use them better
    - Restricting use of antibiotics to BACTERIAL infections
    - Reduce duration of therapy to minimum required
    - Optimize antibiotic Rx by using pharmacodynamic principles

Guideline recommendations on severity

- BTS:
  - Low to moderate risk, uncomplicated: 7 days
  - Severe: 7 to 10 days, may be extended to 14 to 21 days in cases SA or GNB

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Levofloxacin short vs long course

- Dunbar et al. CID 2003;37:752-761
- Concentration-dependent killing
- Double blind placebo RCT
  - Levofloxacin 750 mg IV/PO x 5 days, placebo x 5 days
  - Levofloxacin 500 mg IV/PO x 10 days
- CAP mild to severe (PSI), in and out-patients
  - Excluded PSI > 130, and CrCl< 30 mL/min
- No difference in clinical & microbiological cure rates 38 days out
- More rapid symptom and fever resolution in high dose group (67.4% vs 54.6%, p = 0.006)
- Patients in the short-course arm received 25% less drug
- All specimens S to levofloxacin, relatively high case rate of Mycoplasma pneumoniae

8 vs 15 days of antibiotics for VAP

- Chastre, J. JAMA 2003;290(19):2588-2598.
- RCT
- No difference in morality (60 day), LOS, organ-failure-free days, MV-free days
- VAP due to non-fermenting GNB receiving 8 days had a higher pulmonary infection recurrence rate (40.6% vs 25.4%)
  - But in those who developed recurrent infections, if you received 8 days, you had less multiresistant pathogens (42.1% vs 62%)
- Unblinded, excluded severe, and immunocompromised

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Time to antibiotics

- Houch et al. Arch. Int Med 2004

Time to antibiotics	< 4 hours	> 4 hours	P value
Risk-adjusted mortality	6.8	7.4	0.03

- BTS: within 4 h of presentation to hospital but after confirmation with CXR
  - Life-threatening: treat immediately

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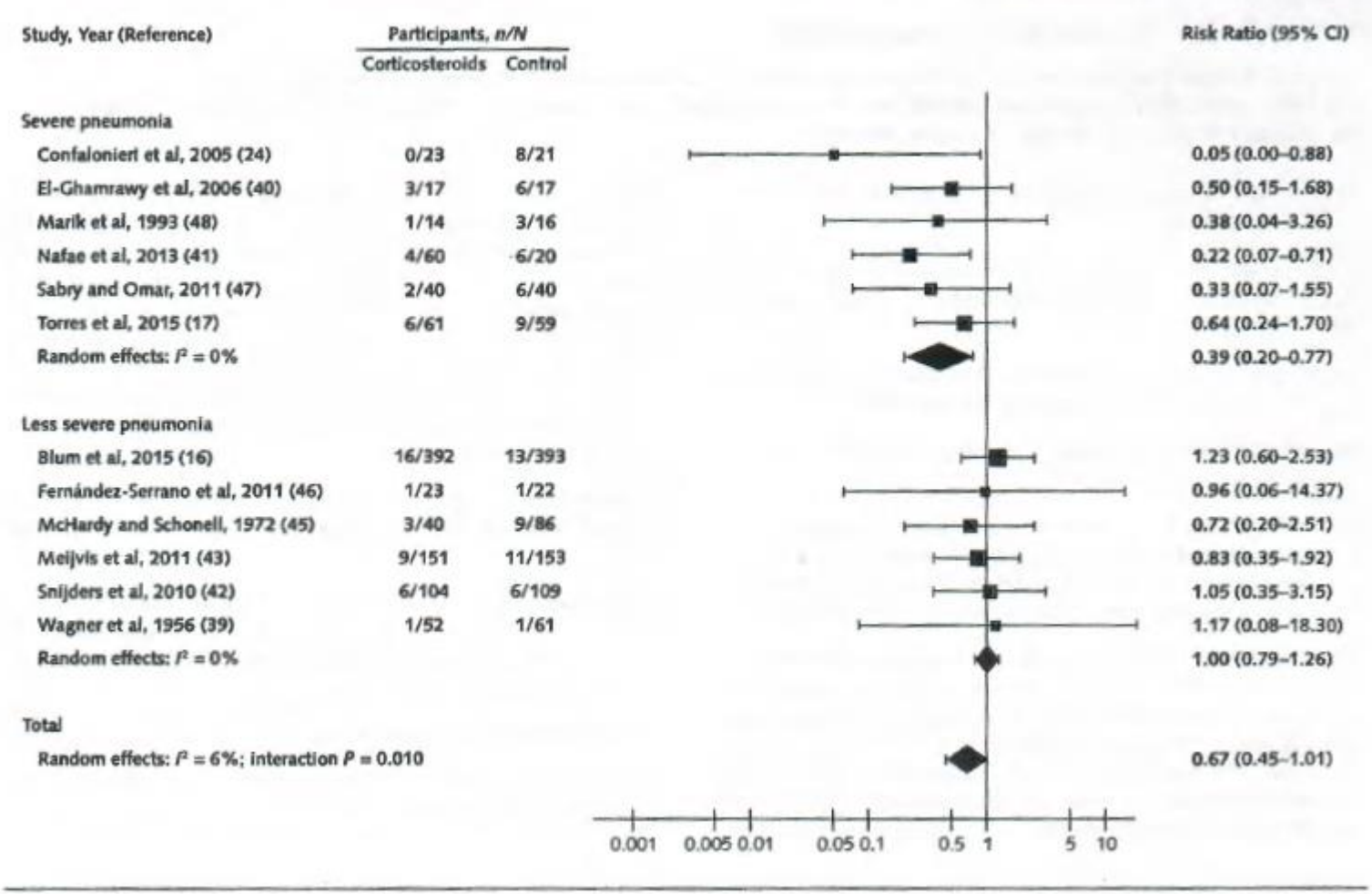
What about steroids?

- Inflammation – moderation is a good thing
  - Immunoparalysis → failure to clear pathogens
  - Dysregulation immune system → ARDS
- 13 RCTs published
- Siemieuiuk, R. SR and MA of steroids in CAP, Annals of Int Med 2015

Figure 1. Effect of corticosteroids on all-cause mortality in patients hospitalized with community-acquired pneumonia, by severity of pneumonia.



Mortality

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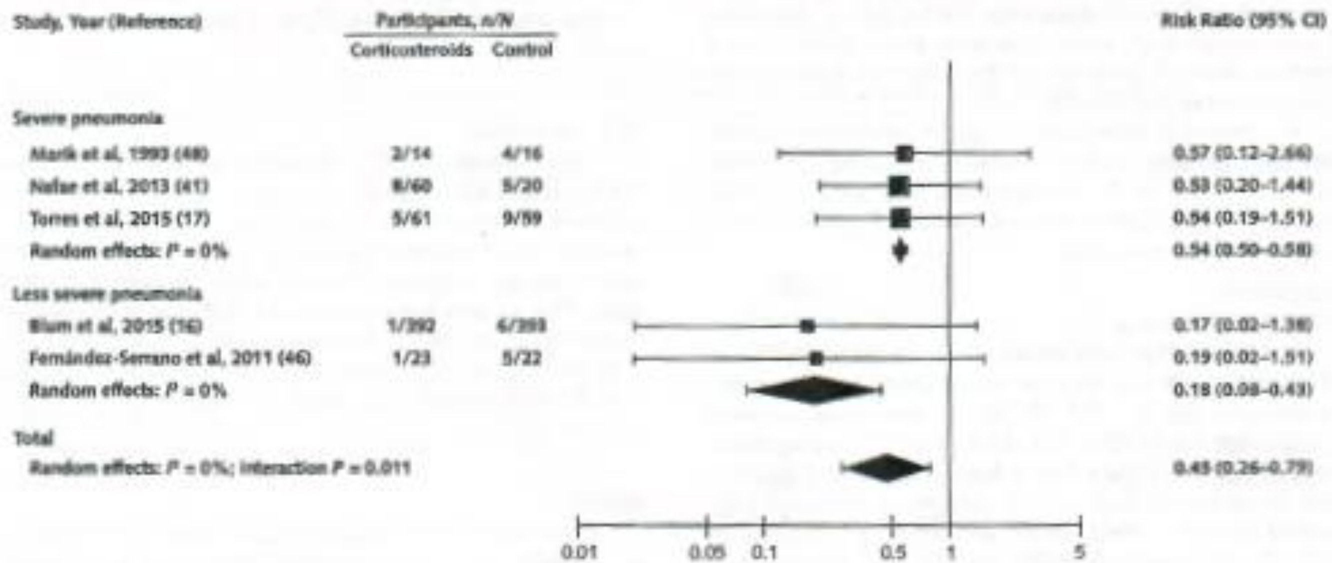
Need for IMV

Figure 2. Effect of corticosteroids on need for mechanical ventilation in patients hospitalized with community-acquired pneumonia, by severity of pneumonia.



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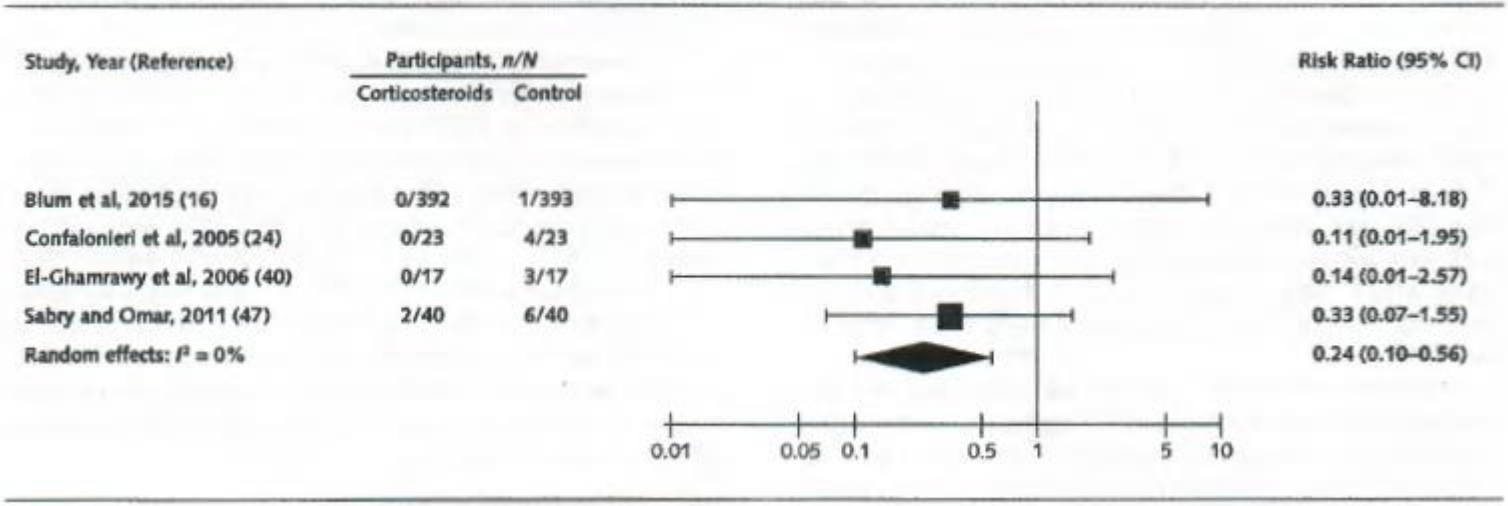
Development of ARDS

Figure 3. Effect of corticosteroids on development of the acute respiratory distress syndrome in patients hospitalized with community-acquired pneumonia.



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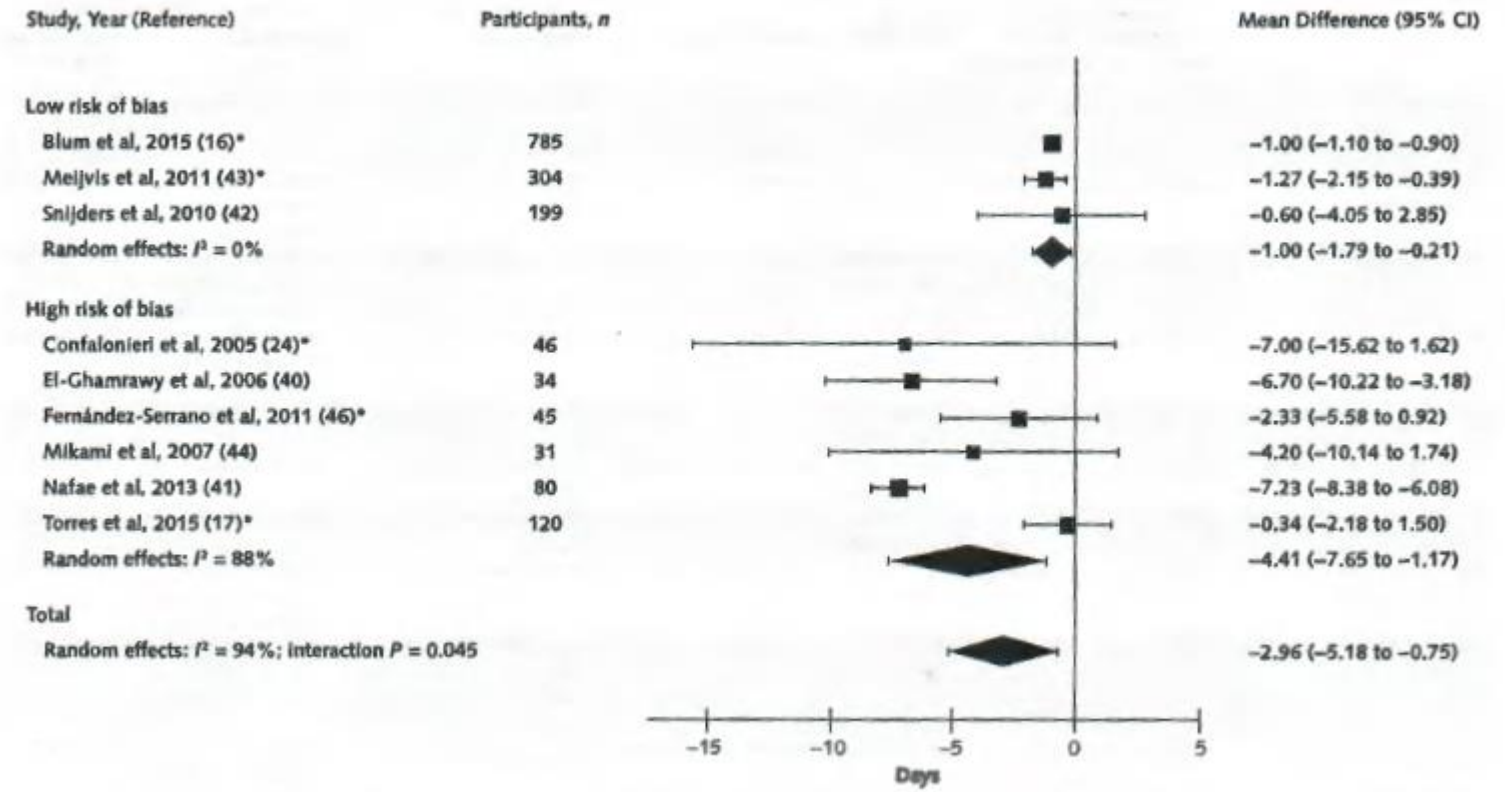
Effect on Length of Stay

Figure 4. Effect of corticosteroids on duration of hospitalization in patients with community-acquired pneumonia, by study risk of bias.



* Mean length of stay is estimated from the median.

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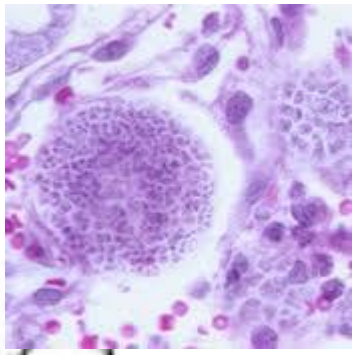
- Adverse Events
  - Hyperglycemia
  - No difference in GI bleed, rehospitaliztion, neuropsychiatric
- Summary
  - Reduction in IMV by 5%, NNT 20
  - Reduces time to clinical stability and LOS by 1 day
  - Mortality and ARDs benefits may be spurious



Areas Endemic for Coccidioidomycosis

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Pneumonia in Snowbirds

- Hyper-/hypo-/transient endemic areas
- Mostly late fall and winter, 25% of cases
- Persistent CAP, rash, eosinophils, travel history
- Almost universal protection from re-infection
- Most sub-clinical, most resolve spontaneously
- Dx: culture, serology (-ve early)
- Who to treat?
  - Depends on which state you live in
  - IC'ed, diabetic, heart disease, pregnancy, Phillipino or African American, severe pulmonary disease
- Rx: fluconazole, itraconazole better for skeletal disease, echinocandins have no activity

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Special notes for chronic lung disease patients

- Repeating antibiotics
- Cipro in pirfenidone

Non-infectious complications

- Inpatients hospitalized with CAP
  - 7% risk of MI
  - 10% risk of atrial fibrillation
  - 20% have worsening CHF

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Lack of response to treatment

Table 4. Reasons for a Lack of Response to Treatment of CAP.

Correct organism but inappropriate antibiotic choice or dose
Resistance of organism to selected antibiotic
Wrong dose (e.g., in a patient who is morbidly obese or has fluid overload)
Antibiotics not administered
Correct organism and correct antibiotic but infection is loculated (e.g., most commonly empyema)
Obstruction (e.g., lung cancer, foreign body)
Incorrect identification of causative organism
No identification of causative organism and empirical therapy directed toward wrong organism
Noninfectious cause
Drug-induced fever
Presence of an unrecognized, concurrent infection

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Helpful websites

- www.cdc.gov
- www.hopkins-abxguide.org/main.cfm
- www.dobugsneeddrugs.org/healthcare/index.html
- www.idsociety.org/IDSA_Practice guidelines
- www.antimicrobialstewardship.com

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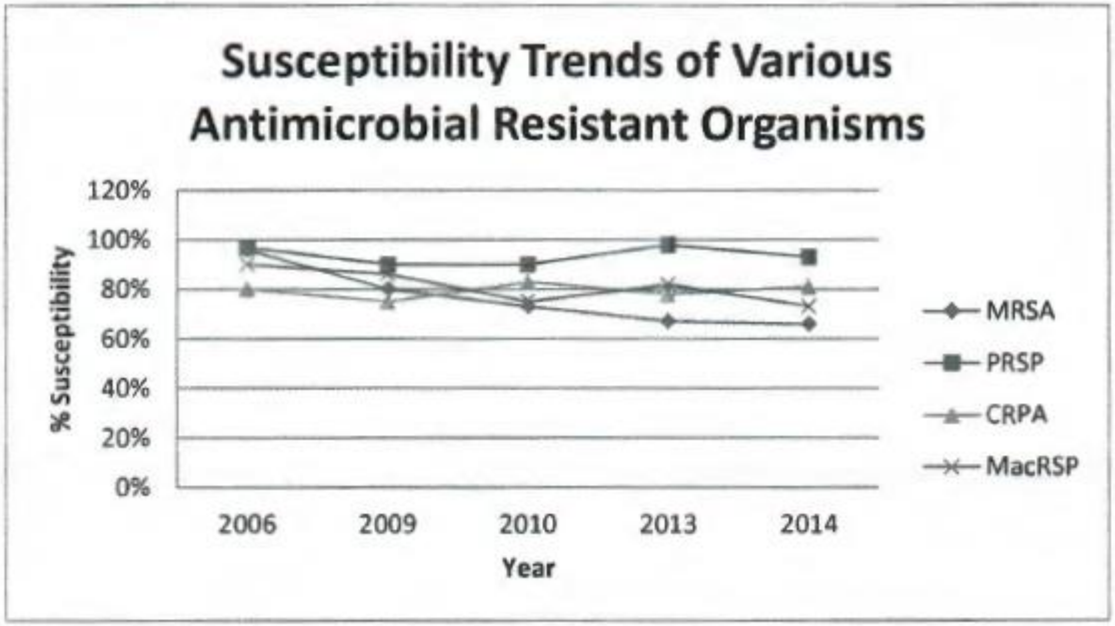
Thunder Bay Antibiogram 2014/15



Antibiogram:	2006	2009	2010	2012/13	2013/14
MRSA:	96%	80%	73%	67%	66%
PRSP[1]:	97%	90%	90%	98%	93%
CRPA:	80%	75%	83%	78%	81%
MacRSP[2]:	90%	86%	75%	82%	73%

1. Implied (as per Antibiogram ampicillin/amoxicillin susceptibilities)
2. Implied from Antibiogram erythromycin susceptibilities

MRSA = Methicillin resistant *Staphylococcus aureus*
PRSP = Penicillin resistant *Streptococcus pneumoniae*
CRPA = Ciprofloxacin resistant *Pseudomonas aeruginosa*
MacRSP= Macrolide resistant *Streptococcus pneumoniae*

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THANK YOU

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Influenza

- Influenza A&B, winter months
- Transmitted via large droplets
- Incubation ~ 2 days (1 to 4 days)
- Shedding: 24 to 48 h pre-symptoms, on average 4.8 days post symptoms (up to 10 days)
- Non-respiratory: myocarditis, pericarditis, encephalitis, GBS, aseptic meningitis, transverse myelitis, myositis, rhabomyolysis, toxic shock syndrome