PNEUMONIA

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Pneumonia

- 8th leading cause of death in United States
- 2-3 million cases/year
- 500,000 admissions/year
- > 60,000 deaths/year
- Mortality

  Outpatient < 1%

  Admit (ward) 10%-14%

  ICU 30%-40%

Pneumonia

- Acute respiratory symptoms associated with lung infiltrate on Chest X ray or CT chest (interstitial infiltrate , lobar consolidation or cavitation)
- Symptoms could be mild SOB and cough to severe with septic shock and acute respiratory failure
- Diagnosis is mainly clinically and Chest image to confirm the diagnosis
- Basic work up includes CBC, KFT, Blood and sputum cultures for severe cases
- CRP and procalcitonin does not help to establish the diagnosis

Definitions

- Community Acquired Pneumonia CAP: refers to an acute infection of the pulmonary parenchyma acquired outside of the hospital.
- Nosocomial Pneumonia refers to an acute infection of the pulmonary parenchyma acquired in hospital settings and encompasses both **hospital-acquired pneumonia** (HAP) and **ventilator-associated pneumonia** (VAP).
  - HAP:Pneumonia diagnosed ≥48 hours after hospital admission.
  - VAP: pneumonia acquired ≥48 hours after endotracheal intubation.
- Heath care associated pneumonia HCAP: retired not used any more

Differential Diagnosis

- acute bronchitis
- hypersensitivity pneumonitis
- COPD Exacerbation
- Acute exacerbation of bronchiectasis
- Pulmonary embolism
- CHF exacerbation
- ILD

Microbiological testing

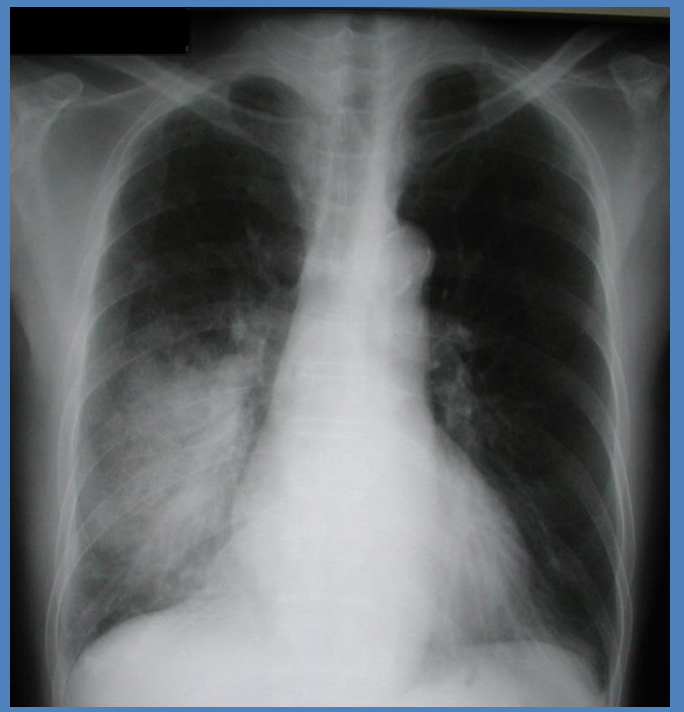
- Blood and sputum cultures (50-70%) depends on timing , antibiotics exposure ,organisms (S. Pneumon & H influ hard to grow vs Staph and GNB grow easily)
- Urine pneumococcal Ag (Sensitivity ~70%)
  - Does not affect with antibiotics use
- Legionella urine Antigen
  - Detect only serotype 1
- Viral PCR (COVID,Influenza)

Condition	Commonly encountered pathogen(s)
Alcoholism	*S. pneumoniae* and anaerobes
COPD and/or smoking	*S. pneumoniae, H. influenzae, M. catarrhalis,* and *Legionella* species
Nursing home residency	*S. pneumoniae,* gram-negative bacilli, *H. influenzae, S. aureus,* anaerobes, and *C. pneumoniae*
Poor dental hygiene	Anaerobes
Epidemic Legionnaires' disease	*Legionella* species
Exposure to bats or soil enriched with bird droppings	*Histoplasma capsulatum*
Exposure to birds	*Chlamydia psittaci*
Exposure to rabbits	*Francisella tularensis*

Bartlett JG, et al. *Clin Infect Dis.* 2000;31:347-82

Question

- 68 YOM patient with Hx of DM,HTN who has 3 day history of cough, fever and sputum production , he went to the ER . On PE his SaO2 is 94 on RA, RR 26, HR 100, BP 120/88. Labs remarkable for WBC 11K,BUN 5 mmol/L,Cr 1.0 , CXR is shown



Choices

- The most appropriate management for this patient

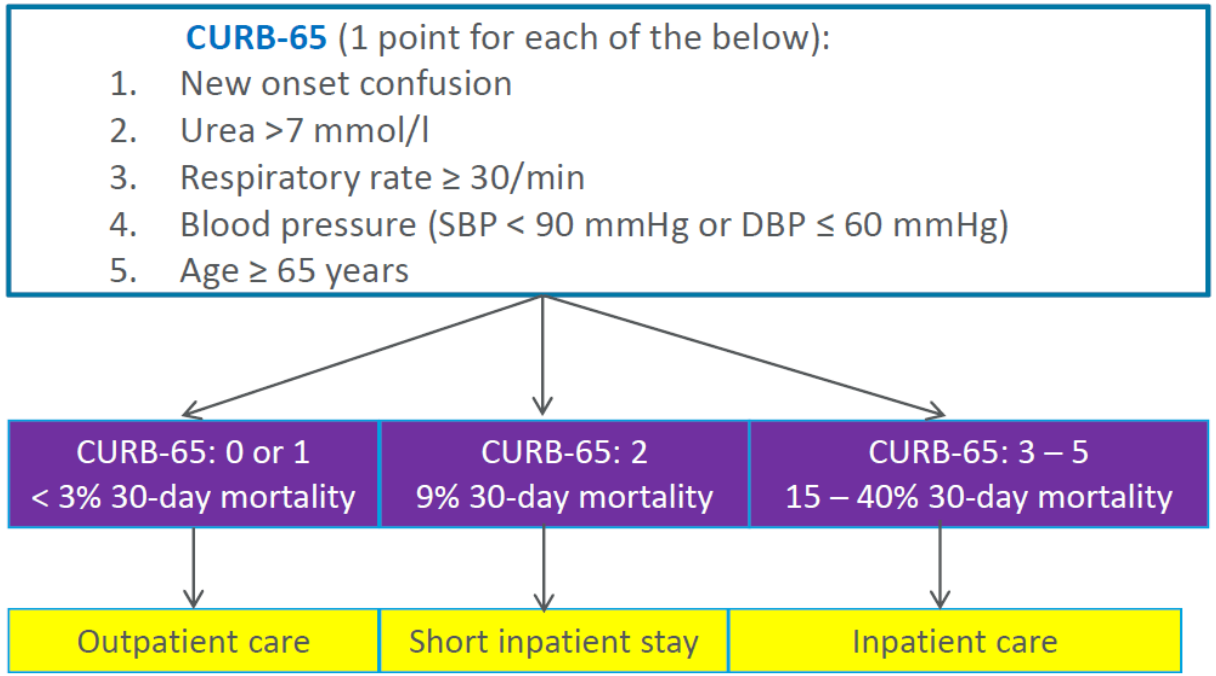
A- Admit the patient to the medical ward and start IV ceftriaxone and Azithromycin

B-Discharge the patient on Moxifloxacin for 5 days

C-Obtain CT chest and admit the patient

D-Consult pulmonary and ID

CURB-65



Lim WS et al. Thorax. 2003; 58:377-82

Severe pneumonia

Validated definition includes either one major criterion or three or more minor criteria

Minor criteria

- Respiratory rate $\geq$ 30 breaths/min
- Pa_{O2}/FI_{O2} ratio $\leq$ 250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (blood urea nitrogen level $\geq$ 20 mg/dl)
- Leukopenia* (white blood cell count $<$ 4,000 cells/μl)
- Thrombocytopenia (platelet count $<$ 100,000/μl)
- Hypothermia (core temperature $<$ 36°C)
- Hypotension requiring aggressive fluid resuscitation

Major criteria

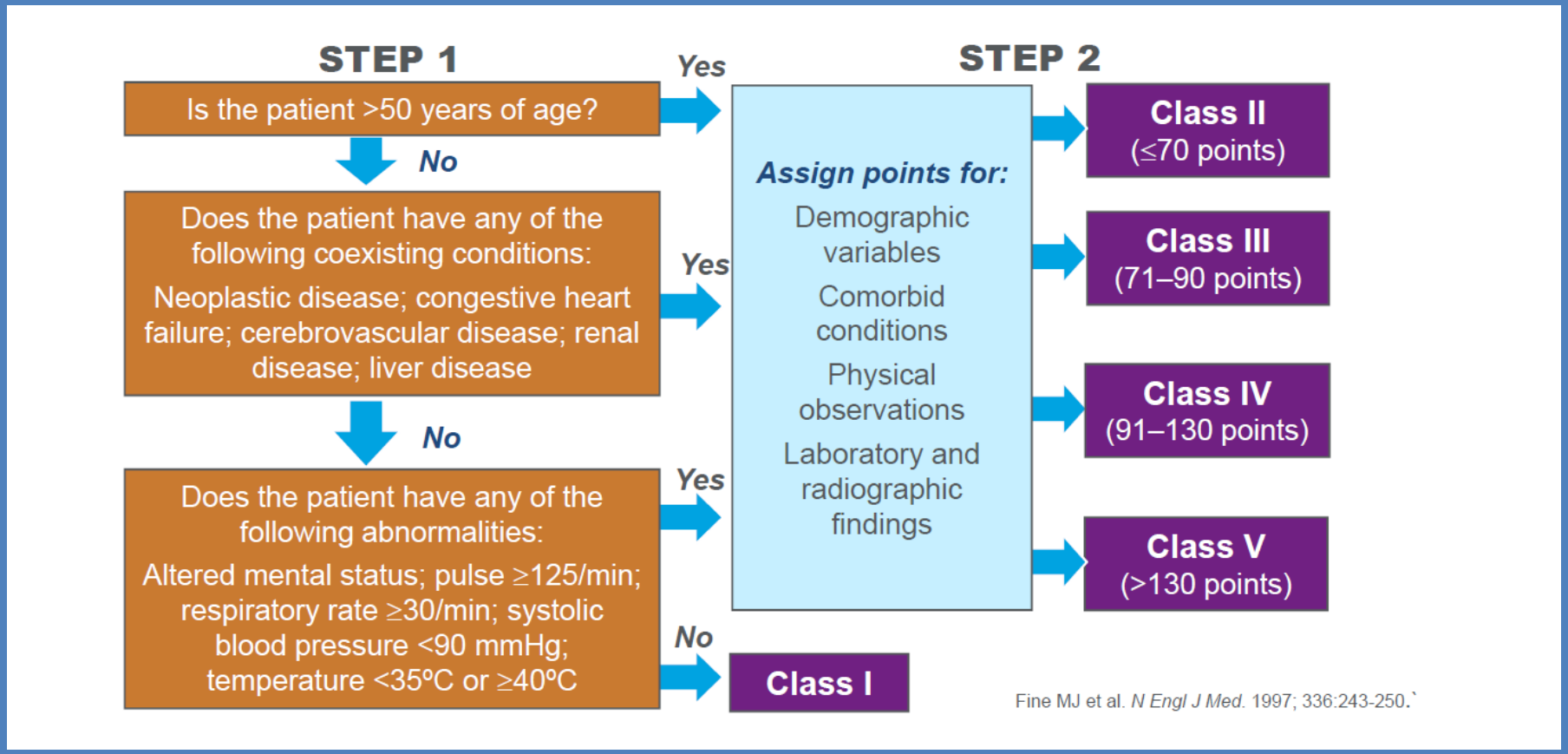
- Septic shock with need for vasopressors
- Respiratory failure requiring mechanical ventilation

Pneumonia Severity Index

Demographics	Co-morbidities	Physical exam / vital signs	Laboratory / imaging
▪ Age (1 point per year) Male Yr Female Yr -10 ▪ Nursing home residency +10	▪ Neoplasia +30 ▪ Liver disease +20 ▪ CHF +10 ▪ Cerebrovascular disease +10 ▪ Renal disease +10	▪ Mental confusion +20 ▪ Respiratory rate +20 ▪ SBP +20 ▪ Temperature +15 ▪ Tachycardia +15	▪ Arterial pH +30 ▪ BUN +20 ▪ Sodium +20 ▪ Glucose +10 ▪ Hematocrit +10 ▪ Pleural effusion +10 ▪ Oxygenation +10

Risk class (Points)	Mortality (%)	Recommended site of care
I (<50)	0.1	Outpatient
II (51–70)	0.6	Outpatient
III (71–90)	2.8	Outpatient or brief inpatient
IV (91–130)	8.2	Inpatient
V (>130)	29.2	Inpatient

Pneumonia Severity Index

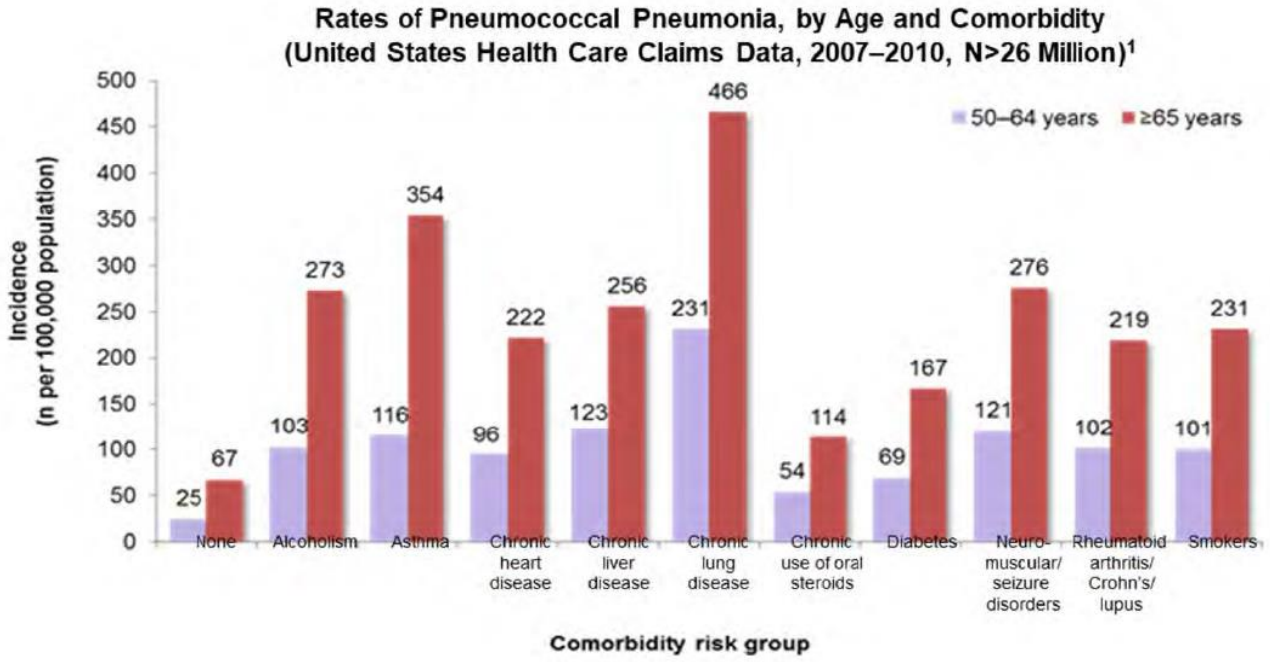


Fine MJ et al. *N Engl J Med.* 1997; 336:243-250.`

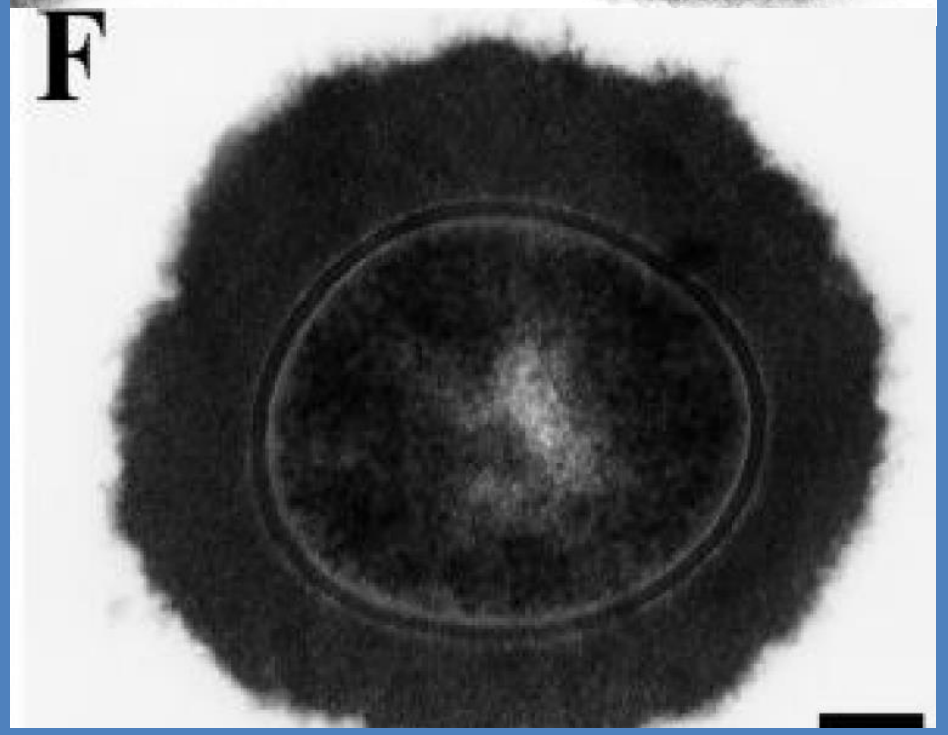
Pneumococcal Pneumonia

- Affect only Human
- Nasopharngeal colonization of young children is the main source of infection in adults
- 50% of daycare children are asymptomatic carrier
- Over 90 serotypes

Comorbidities Increase Pneumococcal Pneumonia Risk in Adults



1. Shea KM, Edelsberg J, Weycker D, et al. *Open Forum Infect Dis* 2014;1(1):ofu024. doi: 10.1093/ofid/ofu024.



Which Pneumococcal pneumonia is associated with severe disease ?

Treatment Guidelines

Table 3. Initial Treatment Strategies for Outpatients with Community-acquired Pneumonia

	Standard Regimen
No comorbidities or risk factors for MRSA or *Pseudomonas aeruginosa*[*]	Amoxicillin or doxycycline or macrolide (if local pneumococcal resistance is <25%)[†]
With comorbidities[‡]	Combination therapy with amoxicillin/clavulanate or cephalosporin AND macrolide or doxycycline[§] OR monotherapy with respiratory fluoroquinolone[‖]

Definition of abbreviations: ER = extended release; MRSA = methicillin-resistant *Staphylococcus aureus*.

Treatment of CAP/Outpatient

- Healthy host, mild

  -Amoxicillin 1gm TID

  -Doxycycline 100mg bid

  - macrolide

- For outpatient adults with comorbidities such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia;

  -amoxicillin/clavulanate and macrolide

  -Respiratory fluoroquinolone

Treatment of CAP/Inpatient

- Non-severe CAP without risk factors for MRSA or *P. aeruginosa*, we recommend the following empiric treatment regimens :

-combination therapy with a beta-lactam (ampicillin+sulbactam 1.5 to 3 g every 6 hours, cefotaxime 1 to 2 g every 8 hours, ceftriaxone 1 to 2 g daily, or ceftaroline 600 mg every 12 hours) and a macrolide (azithromycin 500 mg daily or clarithromycin 500 mg twice daily) or doxycycline

or

-monotherapy with a respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily)

Treatment of CAP/Inpatient

- In inpatient adults with severe CAP without risk factors for MRSA or *P. aeruginosa*, we recommend:

  -a beta-lactam plus a macrolide (strong recommendation, moderate quality of evidence); or

  -a beta-lactam plus a respiratory fluoroquinolone (strong recommendation, low quality of evidence).
- Patient with high risk for MRSA should be treated with Vancomycin , Linozolid or Teicoplanin
- Patient with high risk for pseudomonas should be treated with mereopenem , aztreonam, Piperacilline/tazobactam or Ceftazidiem

MRSA risk factors

- The commonly associated risk factors for MRSA infection are
  - prolonged hospitalization,
  - intensive care admission
  - recent hospitalization
  - recent antibiotic use
  - MRSA colonization
  - invasive procedures
  - HIV infection
  - admission to nursing homes
  - open wounds
  - hemodialysis
  - discharge with long-term central venous access

Psuedomans risk factors

- A compromised immune system (eg, patients with HIV, solid organ or hematopoietic cell transplant recipients, neutropenic hosts, and those on immunosuppressive or immunomodulatory agents such as TNF-alfa inhibitors)
- Recent prior antibiotic use
- Structural lung abnormalities such as cystic fibrosis or bronchiectasis
- Repeated exacerbations of chronic obstructive pulmonary disease requiring frequent glucocorticoid and/or antibiotic use

Early Antibiotics use vs late (within 4 hours)

Table 5. Antibiotic Administration Within 4 Hours of Arrival and Patient Outcomes Stratified by Risk Classes*

Outcome Measures	All Patients, % (95% CI)	Antibiotic Within 4 h, % (95% CI)	Antibiotic After 4 h, % (95% CI)	Unadjusted†		Adjusted‡	
				OR (95% CI)	*P* Value	AOR (95% CI)	*P* Value
All patients							
30-d mortality	12.0 (11.5-12.6)	11.6 (10.9-12.3)	12.7 (11.8-13.6)	0.90 (0.81-1.00)	.045	0.85 (0.76-0.95)	.005
In-hospital mortality	7.0 (6.6-7.5)	6.8 (6.3-7.3)	7.4 (6.7-8.1)	0.91 (0.80-1.04)	.17	0.85 (0.74-0.98)	.03
Length of stay >5 d	43.3 (42.5-44.1)	42.1 (41.0-43.2)	45.1 (43.8-46.5)	0.88 (0.82-0.95)	<.001	0.90 (0.83-0.96)	.003
30-d readmission	13.4 (12.8-14.0)	13.1 (12.4-13.9)	13.9 (12.9-14.9)	0.93 (0.84-1.04)	.20	0.95 (0.85-1.06)	.34
PSI risk classes II and III							
30-d mortality	2.6 (2.1-3.1)	2.1 (1.5-2.7)	3.4 (2.6-4.4)	0.60 (0.40-0.89)	.01	0.62 (0.42-0.93)	.02
In-hospital mortality	1.1 (0.8-1.4)	0.9 (0.6-1.4)	1.2 (0.7-1.9)	0.78 (0.42-1.43)	.42	0.77 (0.42-1.44)	.42
Length of stay >5 d	32.8 (31.3-34.3)	31.2 (29.4-33.1)	35.3 (32.9-37.7)	0.83 (0.73-0.95)	.008	0.86 (0.75-0.99)	.03
30-d readmission	10.0 (9.1-11.0)	9.4 (8.3-10.6)	10.9 (9.4-12.6)	0.85 (0.69-1.05)	.12	0.87 (0.70-1.07)	.19
PSI risk classes IV and V							
30-d mortality	15.9 (15.2-16.6)	15.5 (14.6-16.4)	16.5 (15.4-17.7)	0.92 (0.83-1.03)	.16	0.87 (0.78-0.98)	.03
In-hospital mortality	9.5 (8.9-10.0)	9.2 (8.4-9.9)	9.9 (9.0-10.9)	0.92 (0.80-1.05)	.21	0.86 (0.74-1.00)	.04
Length of stay >5 d	47.6 (46.6-48.6)	46.5 (45.3-47.8)	49.2 (47.6-50.8)	0.90 (0.83-0.98)	.01	0.92 (0.84-1.00)	.04
30-d readmission	14.9 (14.2-15.7)	14.7 (13.8-15.7)	15.2 (14.0-16.5)	0.96 (0.85-1.09)	.53	0.99 (0.88-1.12)	.89

Predictors of mortality and LOS in patients with CAP

TABLE 8 Multiple regression analysis for prediction of length of stay (LOS) of >9 days and mortality

	p-value	OR (95% CI)
Variables associated with increased LOS		
Adherence to ATS guidelines	0.049	0.60 (0.36–0.99)
Pneumonia severity index class V	0.053	1.82 (0.99–3.33)
Respiratory frequency >40 breaths·min^{-1}	0.035	2.51 (1.064–5.92)
Serum sodium <130 mEq·L^{-1}	0.06	1.78 (0.98–3.24)
Acute renal failure	0.06	2.02 (0.97–4.19)
Pleural effusion	<0.001	3.32 (1.97–5.59)
Requirement for mechanical ventilation	0.001	5.55 (2.03–15.16)
Active alcohol intake	0.04	1.95 (1.032–3.69)
Variables associated with increased mortality		
Adherence to ATS guidelines	0.486	0.69 (0.25–1.94)
Obtundation	0.001	7.04 (2.22–22.35)
Arterial oxygen saturation <90%	0.056	2.86 (0.97–8.50)
Acute renal failure	0.075	3.28 (0.89–12.18)
Shock	0.011	5.89 (1.51–23.02)
Aspiration	0.046	2.69 (1.02–15.09)

Macrolide vs None Macrolide

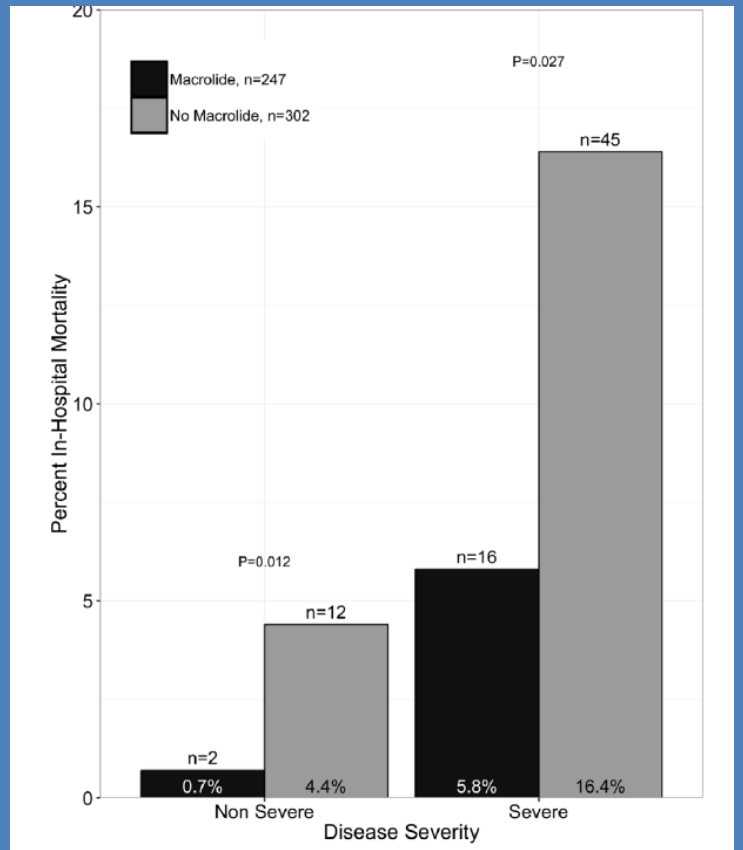
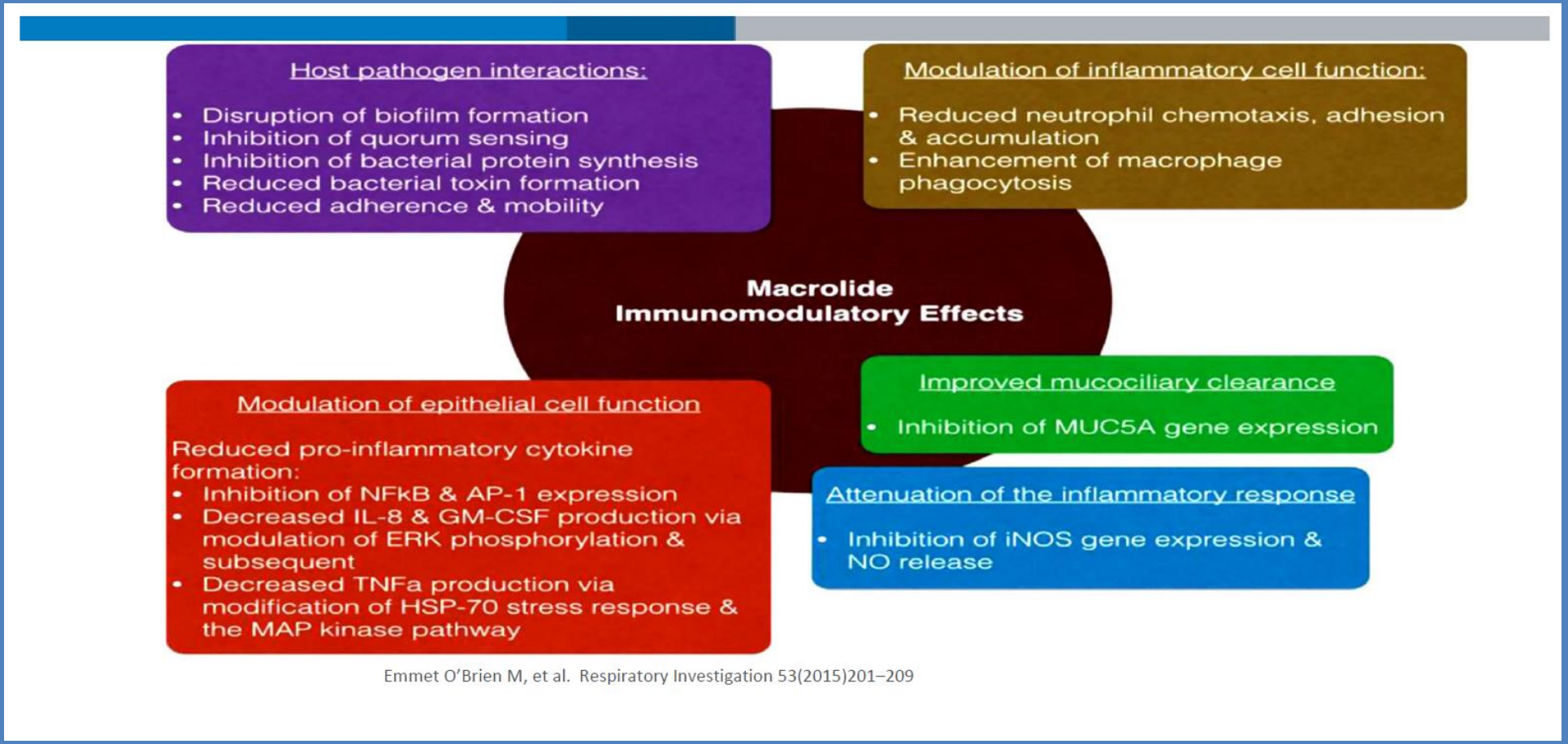


Fig. 1. In hospital mortality for severe and non-severe community-acquired pneumonia patients treated with and without a macrolide.

Macrolide Immunomodulatory Effect



Emmet O'Brien M, et al. Respiratory Investigation 53(2015)201–209

Clarithromycin vs Azithromycin

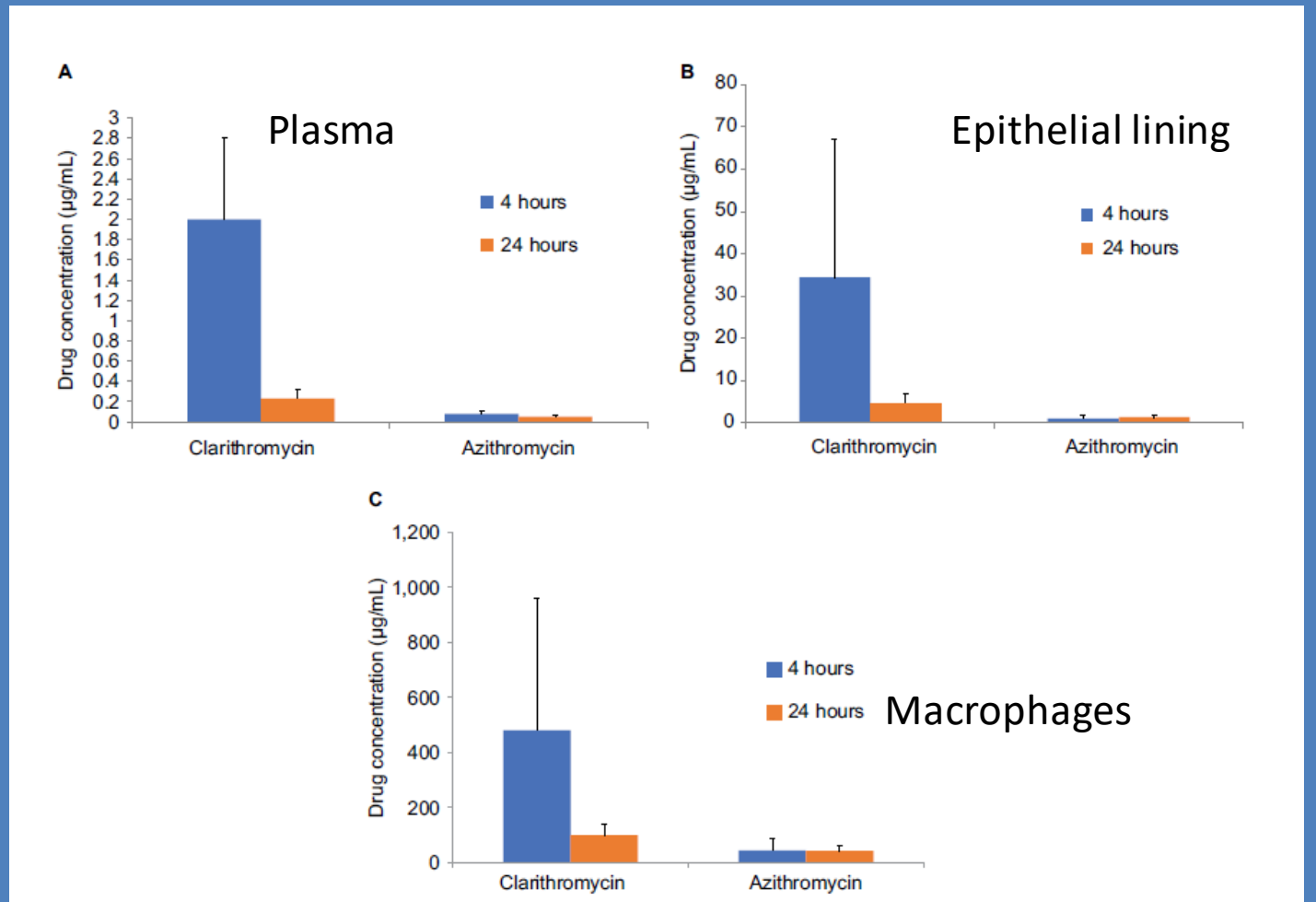


Figure 2 Comparison of achieved concentrations of azithromycin (500 mg on day 1 then 250 mg/day for 4 days) and clarithromycin (500 mg twice daily for 9 days) in (**A**) plasma, (**B**) epithelial lining fluid (ELF), and (**C**) alveolar macrophages of healthy adult volunteers at 4 and 24 hours after last drug administration.
Notes: All comparisons $P<0.05$ vs azithromycin except ELF at 24 hours. The mean ratio of clarithromycin to 14-HC in plasma was 4.7:1 at 4 hours and decreased to 1.2:1 at 24 hours (data not shown). (Derived from data published in reference.[77])

Clinical relevance of Drug-resistance S.pneumonia in CAP

β-lactams

- MIC of ≥4
- 2nd-generation cephalosporins

Macrolides

- Number of cases continues to grow
- Low-level (*mef)* and high-level (*erm*) resistance are relevant

Fluoroquinolones

- Small number of cases
- Judicious use

Yu VL, et al. *Clin Infect Dis.* 2003;37:230-237;
Feikin DR, et al. *Am J Public Health.*

Question?
Procalcitonin

A-High procalcitonin level indicates worse prognosis in patients with CAP

B-Procalcitonin level less than 0.5 indicates low risk for bacterial pneumonia

C-The decision to start antibiotics in a patient with high pretest probability for CAP showed be based on clinical judgment

D-Antibiotics should be stopped after five days regardless of procalicitonin level

Procalcitonin

- Prohormone in normal state it is synthesed solely from thyroid neuroendocrine cells. Undetectable in serum
- Bacterial toxins, IL1,IL6,TNF induce procalcitonin synthesis and release to the serum and thus elevated levels are detected in bacterial infection
- Levels start to rise in 2-4 hrs, peak in 24-48hrs, levels correlate with severity. Levels drops quickly once infection is under control.
- Procalcitonin's greatest utility may be for guiding early antibiotic discontinuation in patients with community-acquired pneumonia (CAP).

Interpretation of procalcitonin levels in respiratory tract infections

Level (ng/mL)	Likelihood of bacterial infection*
<0.10	Very unlikely
0.10 to 0.25	Unlikely
0.25 to 0.50	Likely
>0.50	Very likely

* This interpretation assumes a clinically compatible syndrome and the absence of other causes of procalcitonin elevation.

The effect of microbiologic and clinical factors on procalcitonin levels*

	Rise >0.25 ng/mL	No rise or rise <0.25 ng/mL
Infections¶		
Bacterial		
Typical respiratory bacteria	▪ Most reported thus far	
Atypical respiratory bacteria	▪ *Legionella* spp	▪ *Chlamydia pneumoniae* ▪ *Mycoplasma pneumoniae*
Mycobacteria	▪ Mycobacteria spp$^{\Delta}$	▪ Mycobacteria spp$^{\Delta}$
Other bacteria	▪ *Orientia tsutsugamushi* (scrub typhus)	▪ European *Borrelia* spp (Lyme borreliosis)
Viral		
	▪ None reported thus far	▪ All reported thus far
Fungal		
	▪ *Candida* spp	▪ Aspergillosis ▪ Coccidioidomycosis ▪ Mucormycosis
Parasitic		
	▪ *Plasmodium* spp (malaria)	
Toxin-mediated illnesses	▪ Severe *Clostridioides difficile*-associated disease$^{\diamond}$ ▪ Mushroom poisoning	▪ *C. difficile* colonization
Severe physiologic stress	▪ Burns ▪ Trauma ▪ Surgery ▪ Bowel ischemia ▪ Pancreatitis ▪ Intracerebral hemorrhage ▪ Ischemic stroke ▪ Shock of any kind (septic, anaphylactic, hemorrhagic, or cardiogenic)	
Immune disorders and rheumatologic conditions	▪ Kawasaki disease	▪ Gout and pseudogout ▪ Inflammatory bowel disease ▪ Systemic lupus erythematosus ▪ Rheumatoid arthritis ▪ Granulomatosis with polyangiitis ▪ Still's disease ▪ Temporal arteritis ▪ Behçet syndrome ▪ Polyarteritis nodosa
Malignancies	▪ Medullary thyroid cancer ▪ Lung cancers with neuroendocrine components	▪ Lymphoma ▪ Sarcoma ▪ Pancreatic cancer ▪ Renal cell carcinoma
Other comorbidities	▪ Renal insufficiency	
Drugs	▪ Alemtuzumab (CD52 antibody) ▪ Granulocyte transfusions ▪ Interleukin 2 ▪ Rituximab (anti-CD20 antibody) ▪ T-cell antibodies	▪ Glucocorticoids

* Conditions listed in this table are derived from case series and reports in the medical literature.
¶ Contained infections such as abscesses or empyema may not cause procalcitonin to rise.
Δ Both rise and lack of rise of procalcitonin have been reported with mycobacterial infections.
◇ Effect of *C. difficile* infection on procalcitonin levels not fully defined.

Data from:

1. *Gilbert DN. Procalcitonin as a biomarker in respiratory tract infection. Clin Infect Dis 2011; 52 Suppl 4:S346.*
2. *Scheinpflug K, Schalk E, Grabert E, Achenbach HJ. Procalcitonin is not useful to discriminate between infectious and noninfectious CRP elevation in patients with non-small cell lung cancer. Infect Control Hosp Epidemiol 2015; 36:1117.*
3. *Rao K, Walk ST, Micic D, et al. Procalcitonin levels associate with severity of Clostridium difficile infection. PLoS One 2013; 8:e58265.*
4. *Li G, Zhu C, Li J, et al. Increased level of procalcitonin is associated with total MRI burden of cerebral small vessel disease in patients with ischemic stroke. Neurosci Lett 2018; 662:242.*
5. *He D, Zhang Y, Zhang B, et al. Serum procalcitonin levels are associated with clinical outcome in intracerebral hemorrhage. Cell Mol Neurobiol 2017.*
6. *Reinink AR, Limsrivilai J, Reutemann BA, et al. Differentiating Clostridium difficile colitis from Clostridium difficile colonization in ulcerative colitis: A role for procalcitonin. Digestion 2017; 96:207.*
7. *Grace E, Turner RM. Use of procalcitonin in patients with various degrees of chronic kidney disease including renal replacement therapy. Clin Infect Dis 2014; 59:1761.*

Procalcitonin

- Initiation of antibiotics should be based on clinical judgment
- Serial procalctonin level can be use to monitor response to therapy . Levels are rising or plateauing should alert to other etiologies that cause elevated levels. Change antibiotics if clinically is not improving
- Use procalcitonin in CAP patients decreases antibiotics use without increase adverse events
- In ICU patients, Use 0.5 ng/ml level to stop antibiotics was used without adverse outcome
- Procalcitonin level is elevated in patient with CKD , slow to fall down in case of bacterial infection. In ESRD patients , levels drop by 30-80% after HD

Corticosteroids and CAP

Corticosteroids is recommended in which of the following cases:

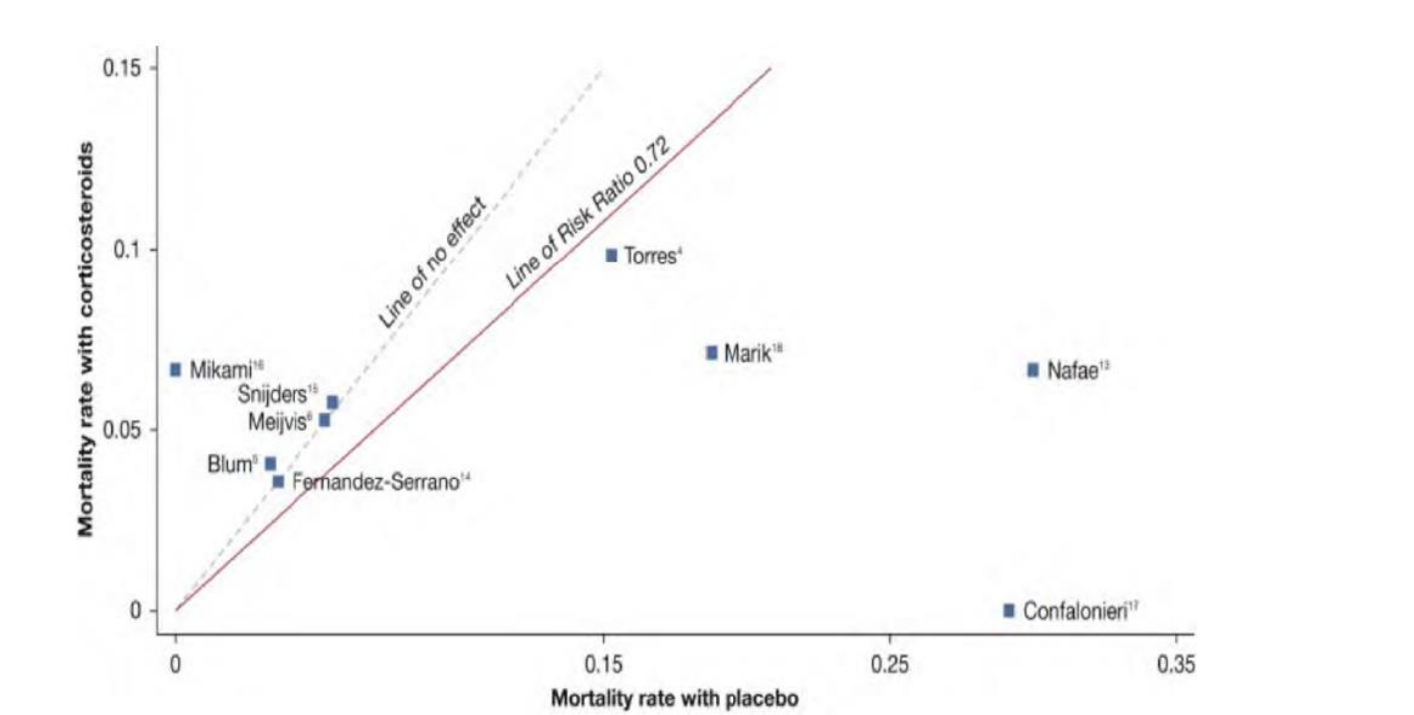
A- 35 yr patient with CAP in regular medical floor

B-66 yr old patient with CAP and large pleural effusion

C- 74 yr patient with severe CAP in the ICU on Norepinephrine and Vasopressin infusion

D- 74 yr patient with pneumonia and right lower lobe cavity

Glucocorticoids in CAP

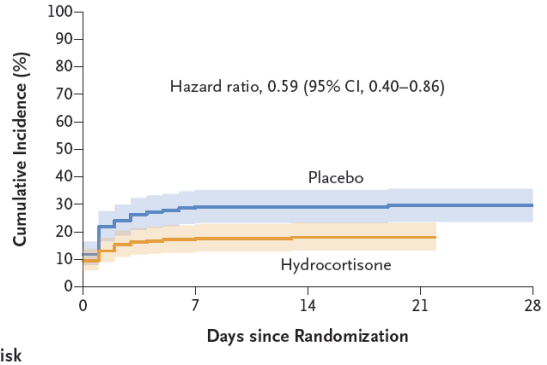


Wan Y-D, et al. Chest. 2016;149(1):209-219

Glucocorticoids in CAP

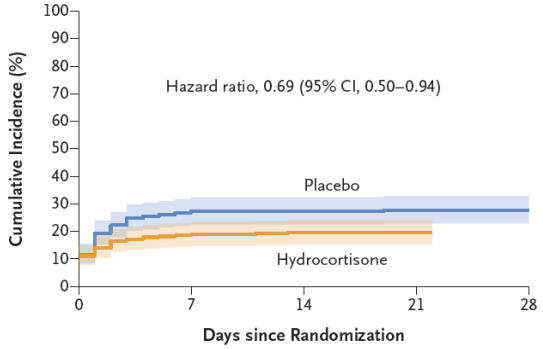
- Conflicting results , small studies
- Net effect is zero
- Side effects(hyperglycemia, risk of infection)
- No recommendation to use steroids in patients with CAP

A Intubation in Patients Who Did Not Receive Any Mechanical Ventilation at Baseline



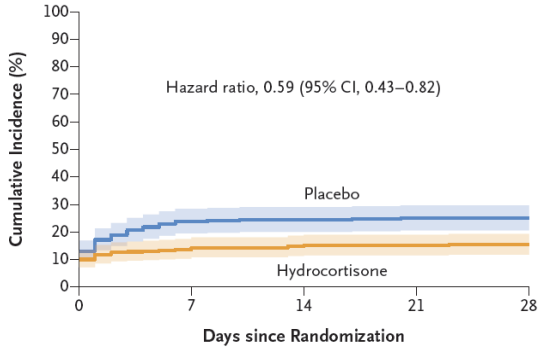
No. at Risk					
Placebo	220	45	8	2	1
Hydrocortisone	222	49	6	1	0

B Intubation in Patients Who Were Not Intubated at Baseline



No. at Risk					
Placebo	310	66	11	3	1
Hydrocortisone	308	60	9	1	0

C Secondary Use of Vasopressors



No. at Risk					
Placebo	344	102	30	13	6
Hydrocortisone	359	95	26	8	3

Table 2. Differences between the 2019 and 2007 American Thoracic Society/Infectious Diseases Society of America Community-acquired Pneumonia Guidelines

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Sputum culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *Pseudomonas aeruginosa*
Blood culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *P. aeruginosa*
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance levels
Use of procalcitonin	Not covered	Not recommended to determine need for initial antibacterial therapy
Use of corticosteroids	Not covered	Recommended not to use. May be considered in patients with refractory septic shock
Use of healthcare-associated pneumonia category	Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines	Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or *P. aeruginosa* coverage. Increased emphasis on deescalation of treatment if cultures are negative
Standard empiric therapy for severe CAP	β-Lactam/macrolide and β-lactam/fluoroquinolone combinations given equal weighting	Both accepted but stronger evidence in favor of β-lactam/macrolide combination
Routine use of follow-up chest imaging	Not addressed	Recommended not to obtain. Patients may be eligible for lung cancer screening, which should be performed as clinically indicated

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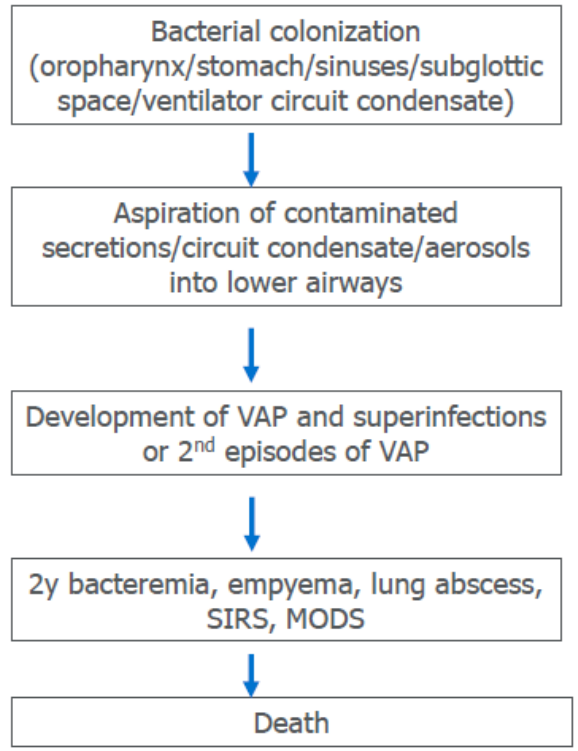
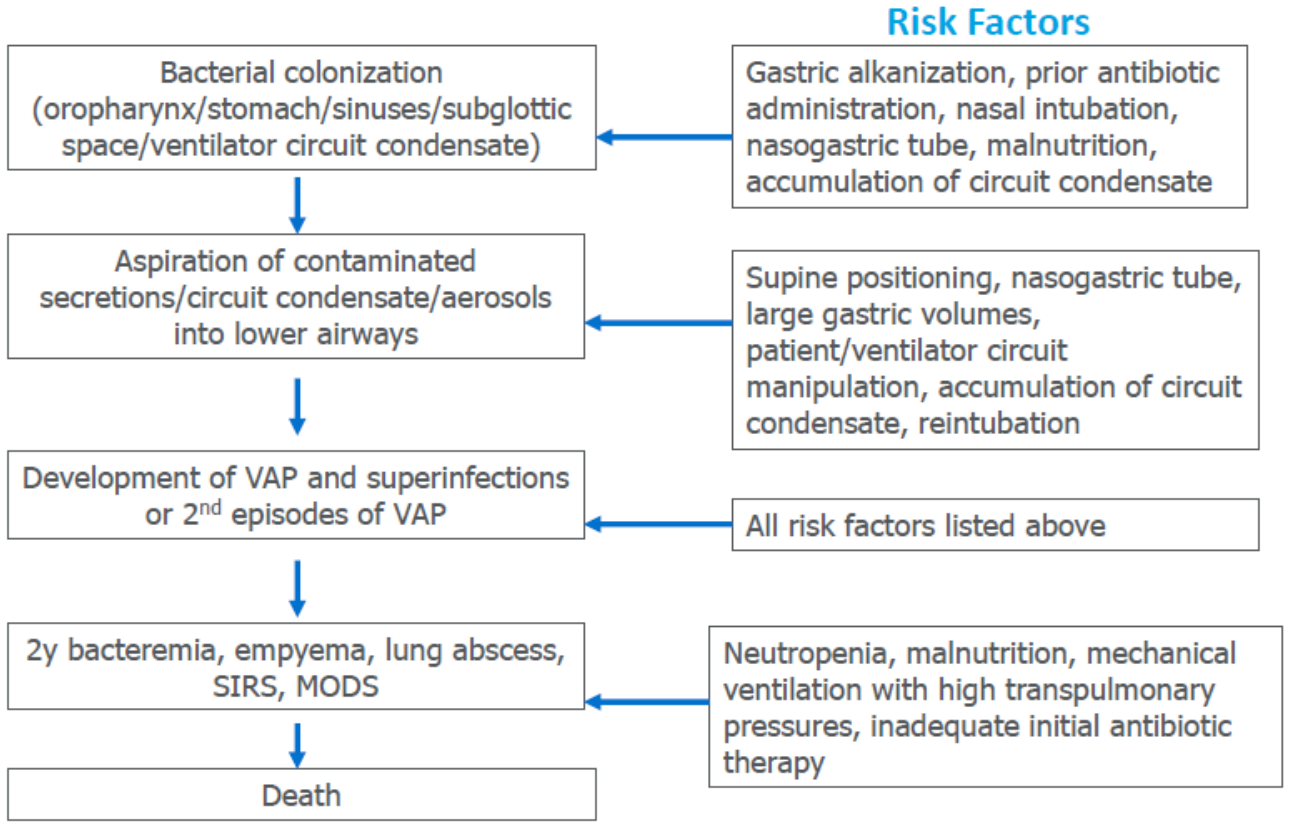
  - HAP:Pneumonia diagnosed ≥48 hours after hospital admission.
  - VAP: pneumonia acquired ≥48 hours after endotracheal intubation.
- Heath care associated pneumonia HCAP: retired not used any more

Hospital acquired infection (including VAP)

Pathogenesis



Pathogenesis



ATS-IDSA Guidelines

- **Use noninvasive sampling with semiquantitative cultures** to diagnose VAP, rather than invasive sampling with quantitative cultures and rather than noninvasive sampling with quantitative cultures
- **Use clinical criteria alone, rather than using serum PCT + clinical criteria**, to decide whether or not to initiate antibiotic therapy
- **Use clinical criteria alone rather than using CRP + clinical criteria**, to decide whether or not to initiate antibiotic therapy
- **Use clinical criteria alone, rather than using CPIS + clinical criteria**, to decide whether or not to initiate antibiotic therapy

Clinical Pulmonary Infection Score

CPIS points	0	1	2
1. Tracheal secretions	Rare	Abundant	Abundant + Purulent
2. Chest X-ray infiltrates	No infiltrate	Diffused	Localized
3. Temperature, °C	≥ 36.5 and ≤ 38.4	≥ 38.5 and ≤ 38.9	≥ 39 or ≤ 36
4. Leukocytes count, per mm3	≥ 4,000 and ≤ 11,000	< 4,000 or > 11,000	< 4,000 or > 11,000 + band forms ≥ 500
5. PaO_2/FiO_2, mmHg	> 240 or ARDS		≤ 240 and no evidence of ARDS
6. Microbiology	Negative		Positive

Footnote to Table 2. The modified CPIS at baseline was calculated from the first five variables

Score of 6 or more considered VAP

AntiPsuedomonal coverage

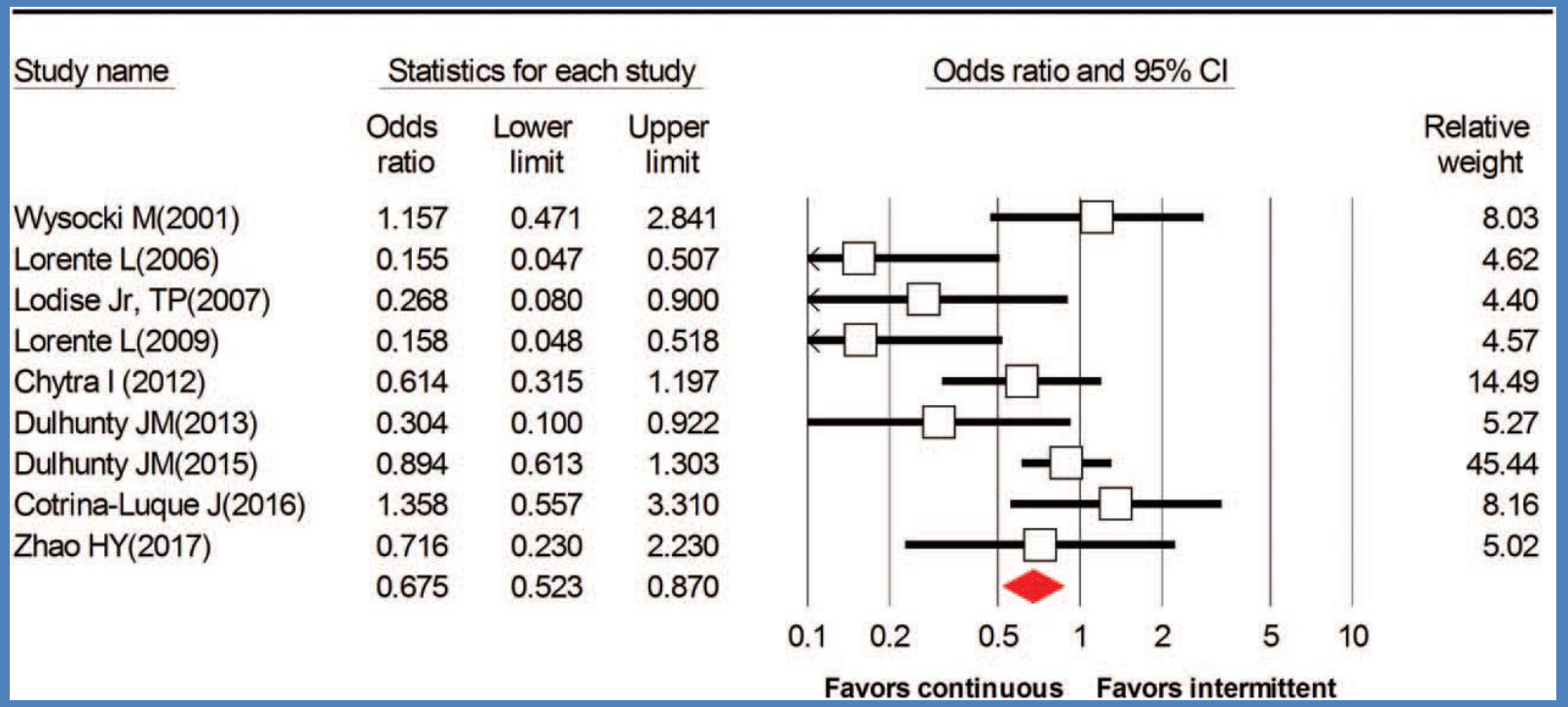
ATS-IDSA Guidelines

- **Use 2 antipseudomonal antibiotics** from different classes for the empiric treatment of suspected VAP only in patients with any of the following:
  - a risk factor for antimicrobial resistance
  - pts in an ICU where >10% of Gm -ve isolates are resistant to an agent being considered for monotherapy
  - pts in an ICU where local antimicrobial susceptibility rates are not available
  - high risk of mortality
- All other pts with HAP who are being treated empirically may be prescribed **a single antibiotic** with activity against *P. aeruginosa*

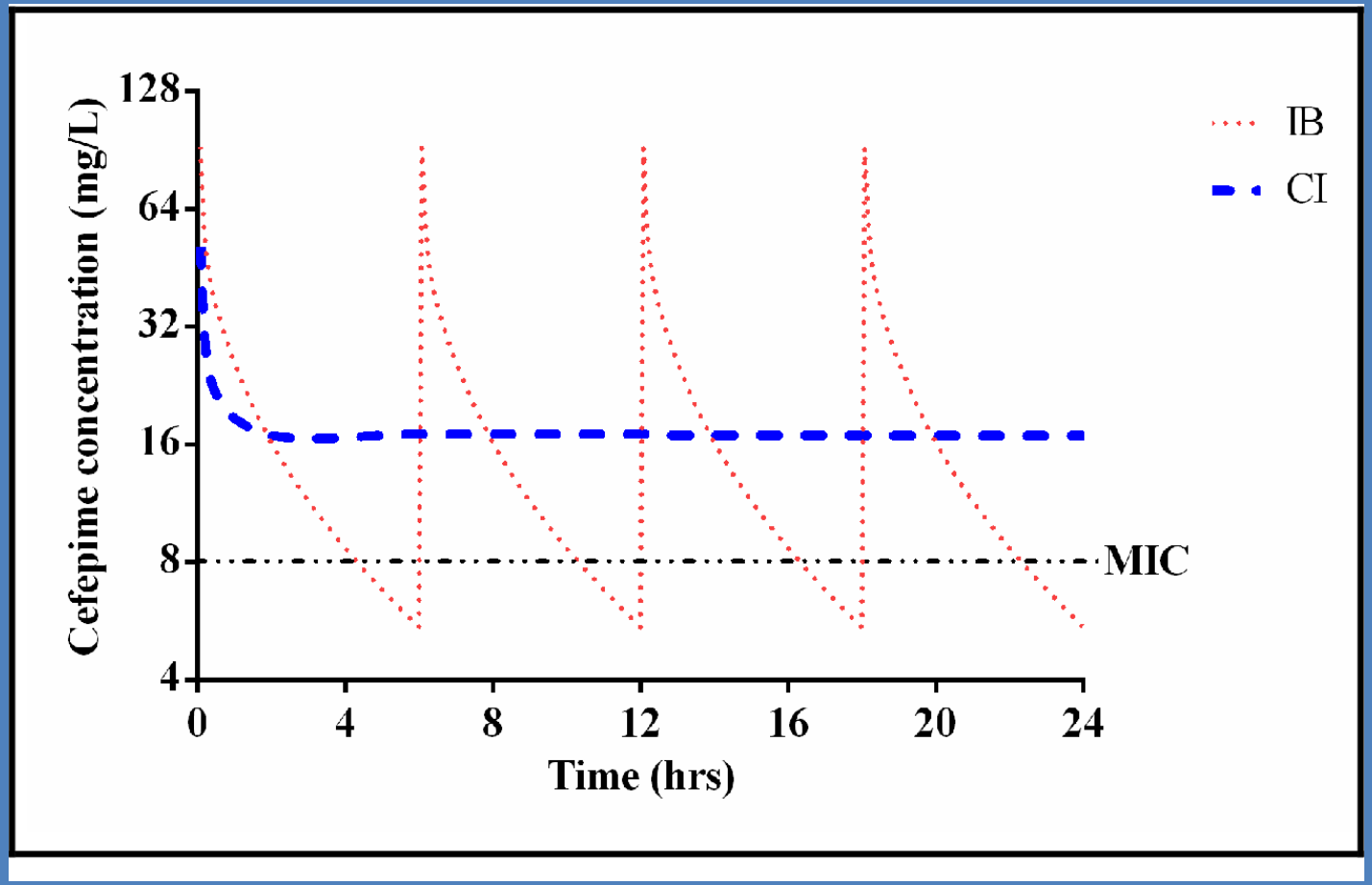
Risk factors for MDR pathogens

- **Risk factors for MDR VAP**
  - Prior IV antibiotic use within 90 days
  - Septic shock at time of VAP
  - ARDS preceding VAP
  - Five or more days of hospitalization prior to the occurrence of VAP
  - Acute renal replacement therapy prior to VAP onset

Continues vs intermittent infusion of antibiotics in treating HAP



Continues vs intermittent infusion of antibiotics in treating HAP



ATS-IDSA Guideline

- **7-8 days** of antimicrobial therapy is recommended
- No differences in mortality, clinical cure, and recurrent pneumonia compared to longer courses
- Should decrease antibiotic exposure with decreased costs and undesirable side effects
- Applies to all organisms including non-glucose-fermenting gram-negative bacilli

New antibiotics

Table 1. New antibiotics for multidrug-resistant Gram-negative bacteria.

Drug	Class	Development stage	Activity	FDA indication
Aztreonam/avibactam	Monobactam/β-lactamase inhibitor	Phase II	ESBL, KPC, class C β-lactamase, MBL	Not applicable
Cefiderocol	Siderophore cephalosporin	Phase III	ESBL, CRE (class A, B, and D enzymes), carbapenem-resistant *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, and *Acinetobacter baumannii*	Not applicable
Ceftazidime/avibactam	Cephalosporin/β-lactamase inhibitor	FDA-approved	ESBL, KPC, AmpC, some class D serine β-lactamases	HABP/VABP, cIAI, cUTI
Ceftolozane/tazobactam	Cephalosporin/β-lactamase inhibitor	FDA-approved	ESBL, MDR *P. aeruginosa*	cUTI, cIAI
Delafloxacin	Fluoroquinolone	FDA-approved	*Klebsiella pneumoniae*, including AmpC and class A ESBL-producers, ciprofloxacin-resistant *Escherichia coli* and *A. baumannii*	ABSSSI
Eravacycline	Fluorocycline tetracycline	FDA-approved	ESBL, CRE, MDR *A. baumannii*	cIAI
Imipenem+cilastatin/relebactam	Carbapenem/β-lactamase inhibitor	Phase III	KPC, MDR *P. aeruginosa*	Not applicable
Meropenem/vaborbactam	Carbapenem/boronic acid inhibitor	FDA-approved	CRE (class A and C enzymes)	cUTI
Murepavadin	Cyclic peptide that targets outer membrane	Phase III	MDR *P. aeruginosa*	Not applicable
Omadacycline	Aminomethylcycline	FDA-approved	ESBL, *A. baumannii*	ABSSSI, CABP
Plazomicin	Aminoglycoside	FDA-approved	ESBL, CRE excluding NDM producers, *A. baumannii*, *P. aeruginosa*	cUTI

ABSSSI, acute bacterial skin and skin structure infection; CABP, community-acquired bacterial pneumonia; cIAI, complicated intra-abdominal infection;

Question

- A 65 years old female patient who is a known case of DM, HTN and scleroderma. She was admitted to the medical ward for right lower pneumonia. Lab tests significant for leukocytosis and sputum culture is negative. She was started on IV Piperacillin/Tazobactam. Today is her 5th day of hospitalization, she improved and her labs normalized
- For this case, which statement is correct?
- A-Continue IV Piperacillin/Tazobactam for 10 days
- B-Stop Piperacillin/Tazobactam
- C-Repeat sputum cultures
- D-Stop antibiotics if CRP is normal
- E-Collect procalcitonin to determine if you can stop antibiotics

Question

- A 65 years old female patient who is a known case of asthma, HTN,DM and atrial fibrillation. She is on the following medications: Budesonide inhaler, Amiodarone, Metoprolol, Aspirin, Metformin and Atorvastatin.
- Which of her medications increase risk of pneumonia ?

  a- Budesonide inhaler

  b-Amiodarone

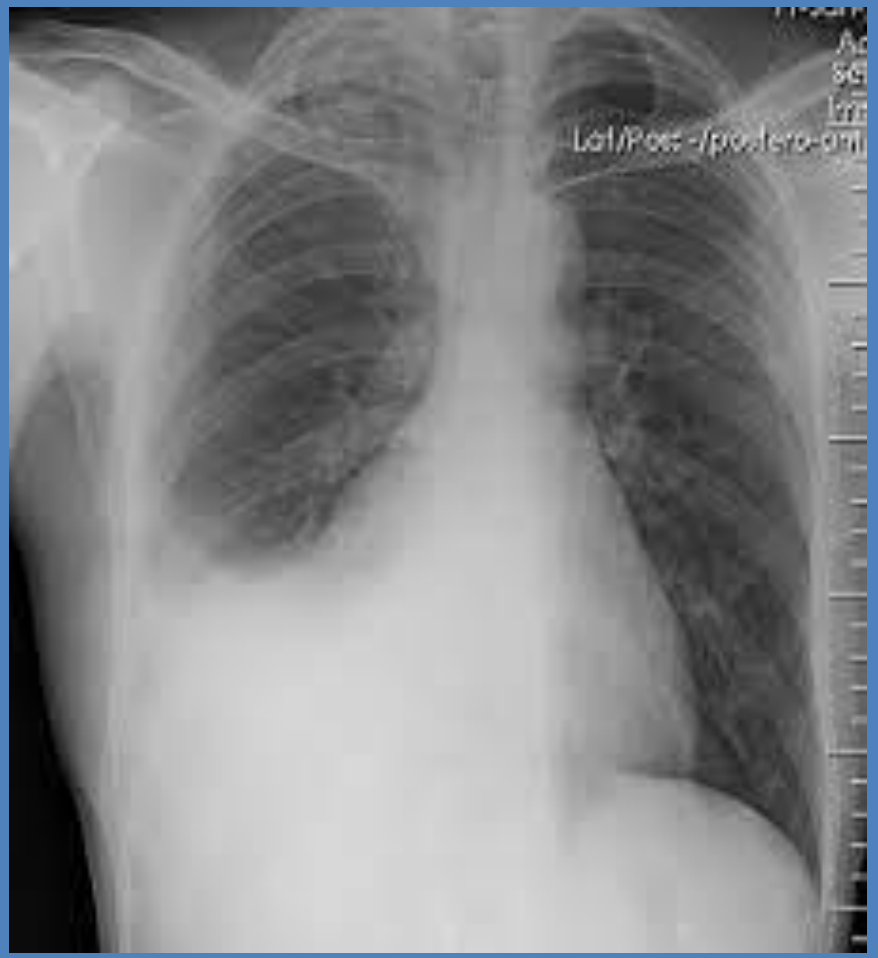
  c-Metoprolol

  d-Aspirin

  e-Metformin

Question

- A 45 year old male patient presented to your clinic for 2- week history of shortness of breath, cough and pleurisy. One week ago he visited the ER and was prescribed a course of antibiotics. Since then he felt better .Physical exam showed normal vital signs , but decreased breath sounds posteriorly on the right side .Chest x ray is shown below. Basic lab work was unremarkable including WBC.


Lat/Post -/pos

- The best course of action for this patient is :

A-Admit the patient for IV antibiotics

B – Send the patient home with oral antibiotics

C- Admit the patient for insertion of chest drain

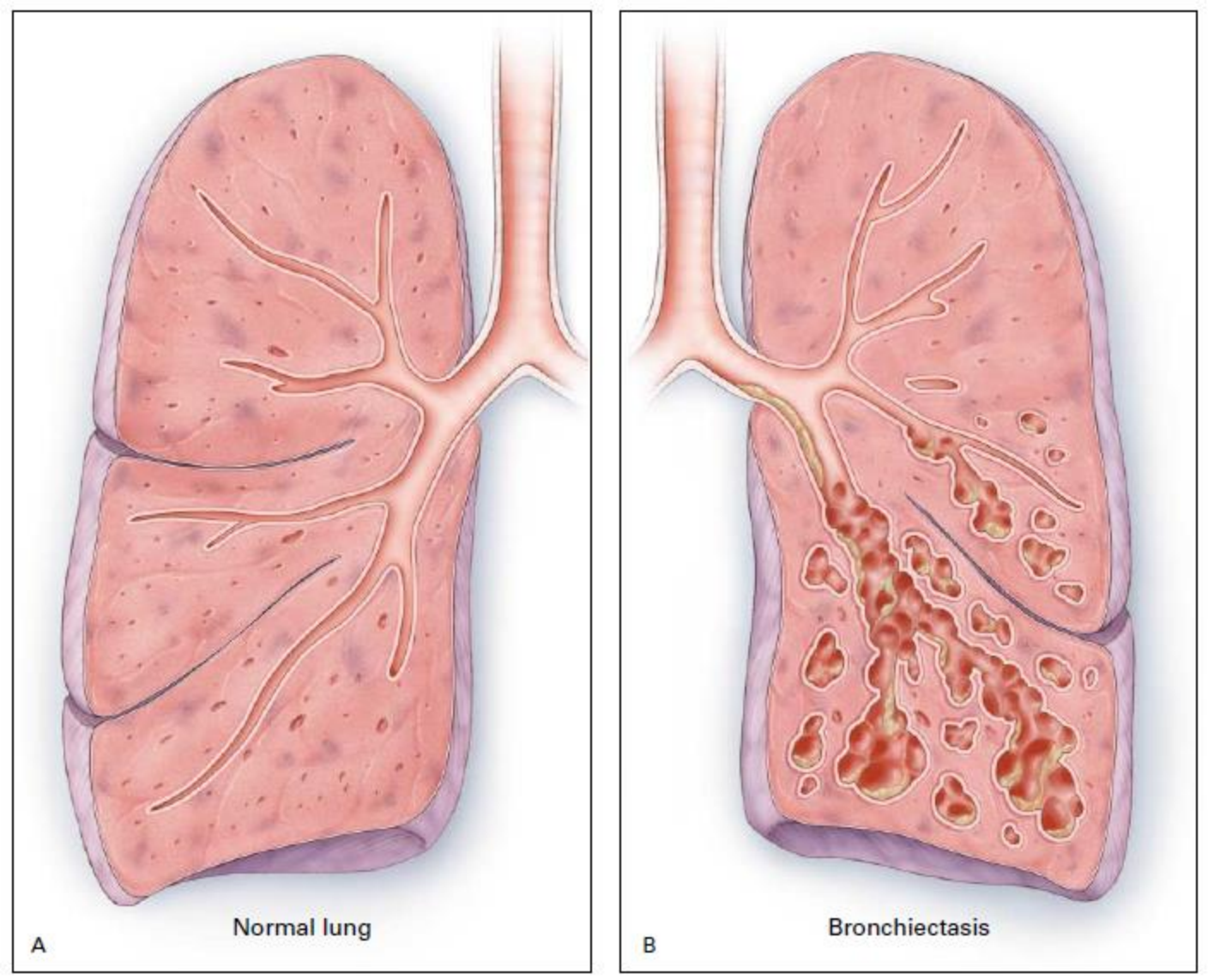
D-Send the patient home with no antibiotics and follow up in 2 weeks with chest-X ray.

E- Admit the patient to medical ward and start intravenous Lasix

Bronchiectasis

Bronchiectasis

- Definition - Abnormal dilatation of bronchi
  - Common forms are cylindrical, saccular, and varicose
- Incidence
  - Difficult to define as may be asymptomatic or symptoms may be those of chronic bronchitis
  - Incidence declining since preantibiotic era


A
Normal lung
B
Bronchiectasis

Etiology

- Post necrotizing infection such as pneumonia, especially in childhood
  - Measles, pertussis, influenza
- Immune deficiency - IgG, IgA, complement deficiency
- Ciliary disorders (immotile cilia syndrome)
- Granulomatous infection - TB, fungi
- Cystic fibrosis

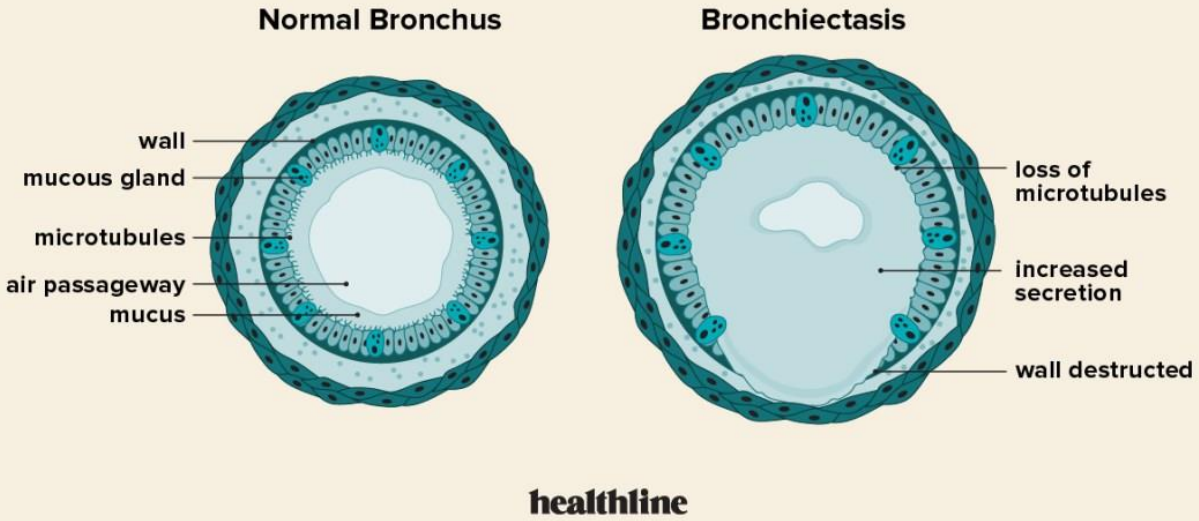
ETIOLOGY

- Connective tissue disease
  - Rheumatoid arthritis, Sjögrens, mixed connective tissue disease
- HIV
- Inflammatory bowel syndrome
- Alpha-1-antitrypsin deficiency
  - Classic presentation emphysema but may present with recurrent pulmonary infections
- Reflux: recurrent aspiration
- Allergic bronchopulmonary aspergillosis
- Bronchial obstruction – tumor, foreign body

Pathophysiology

- **Bronchiectasis** occurs as a result of a vicious circle consisting of an impaired mucociliary transport system, inflammation, infection and repair of the airways with peribronchial fibrosis
- Damage to the mucociliary system prevents secretion elimination and facilitates bacterial growth and bronchial inflammation.

Bronchiectasis



healthline

Pathophysiology

- Expectorated sputum has increased concentrations of elastase and the chemoattractants ,interleukin-8, tumor necrosis factor (TNF*a)* ,prostanoids.
- Localized vs. diffuse

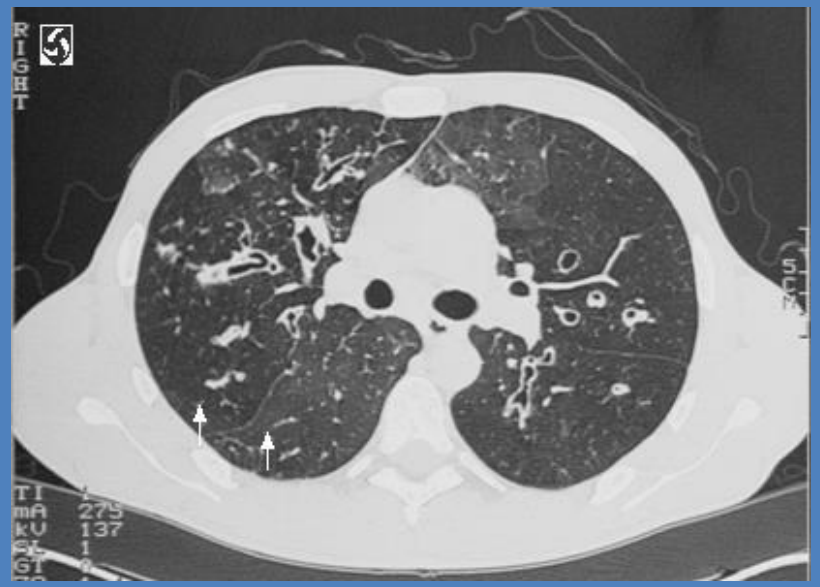
Signs & Symptoms

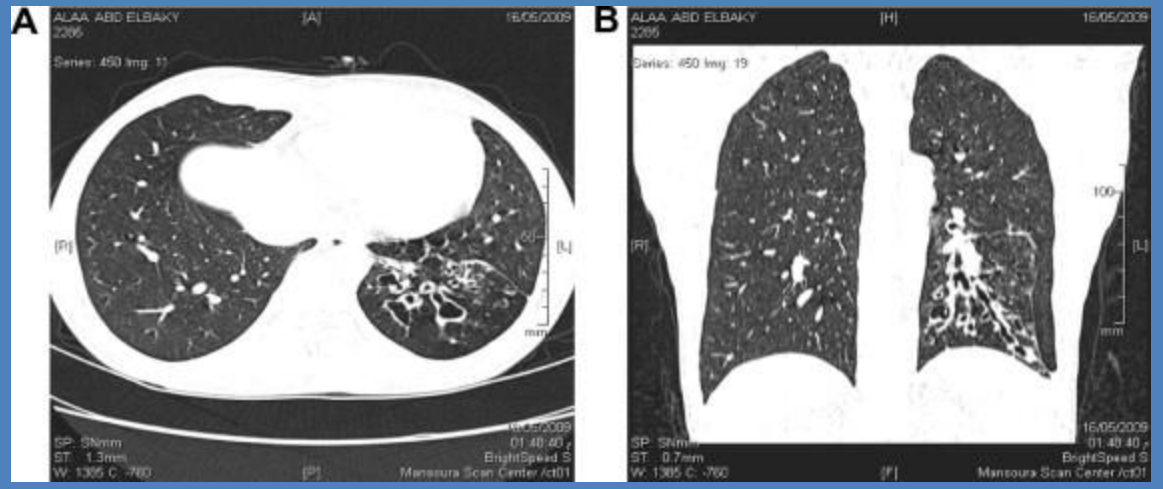
- Symptoms
  - Chronic cough
  - dyspnea
  - Sputum production
  - Hemoptysis

Signs

  - Wheezes and crackles
  - Bronchial breathing
  - Clubbing

Diagnosis


RIGHT
TI
mA 275
kV 137


A
ALAA ABD ELBAKY
2286
[A]
16/05/2009
Series: 450 Img: 11
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W: 1305 C: 760
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Mansoura Scan Center /ct01
B
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Series: 450 Img: 19
100
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mm
SP: 5Nmm
ST: 0.7mm
W: 1305 C: 760
[F]
Mansoura Scan Center /ct01

Diagnostic Testing

TABLE 3. DIAGNOSTIC TESTING FOR BRONCHIECTASIS.*

LEVEL OF TESTING	APPROPRIATE TESTS		
	BLOOD	IMAGING	OTHER
Primary	Complete and differential blood count, IgG, IgA, IgM	High-resolution CT	Spirometry or bronchodilator test
Secondary	Rheumatoid factor; IgE, aspergillus precipitins (ABPA); IgG subclasses; $alpha_1$-antitrypsin level	Sinus CT	Sputum bacterial, mycobacterial, fungal culture and sensitivity; bronchoscopy with mucosal biopsy, cultures (for focal obstruction, infection, primary ciliary dyskinesia); sweat chloride test analysis (for cystic fibrosis)

Treatment

- Antibiotics for exacerbations
  - Bacterial colonization increases risk of exacerbation
  - Inhaled vs oral vs parenteral
- Bronchodilators for reversible airflow limitation.
- Surgery in cases of medical failure and localized disease (rare)
- Treatment of hemoptysis

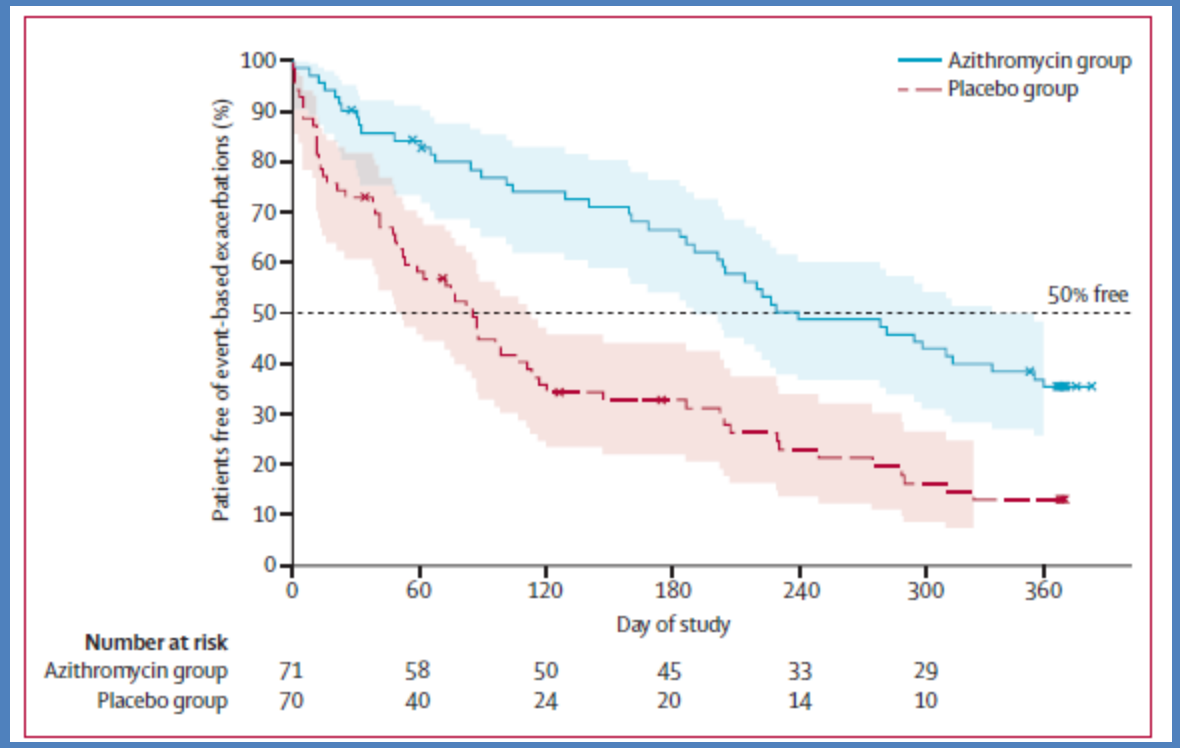
Treatment

- Bronchopulmonary hygiene
  - Physical measures to promote sputum clearance
  - DNAase
  - NAC

- Treatment of underlying cause

Nebulized Hypertonic saline

- Improvement of mucociliary clearance
- Decreases mucus viscosity
- Stimulates cough
- Enhances the effectiveness of respiratory physiotherapy
- Inhibits epithelial sodium channels (ENaC)



- azithromycin treatment for 6 months in patients with non-cystic fibrosis bronchiectasis significantly decreases the rate of event-base exacerbations and increases the time to the first event based exacerbation compared with placebo

Questions