Acute Exacerbations of Chronic Bronchitis Etiology, Outcomes and Antibiotics

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Bacterial Etiology of Exacerbations

- Bacteria can be cultured from the distal airways in significant concentrations in >50% of patients
- Acquisition of strains of bacteria new to the patient is associated with a greater than 2 fold increase in the risk of exacerbation
- Specific immune responses develop to infecting bacterial strains following exacerbation
- Neutrophils in sputum are associated with presence of pathogenic bacteria during exacerbation

Monso E, et al. *AJRCCM.* 1995;152:1316-20; Sethi S, et al. *NEJM.* 2002; 347;465-71. Sethi S, et al. *AJRCCM.* 2004;168:448-53; Sethi S, et al. *Chest.* 2000;118:1557-65.

Outcome of Exacerbations

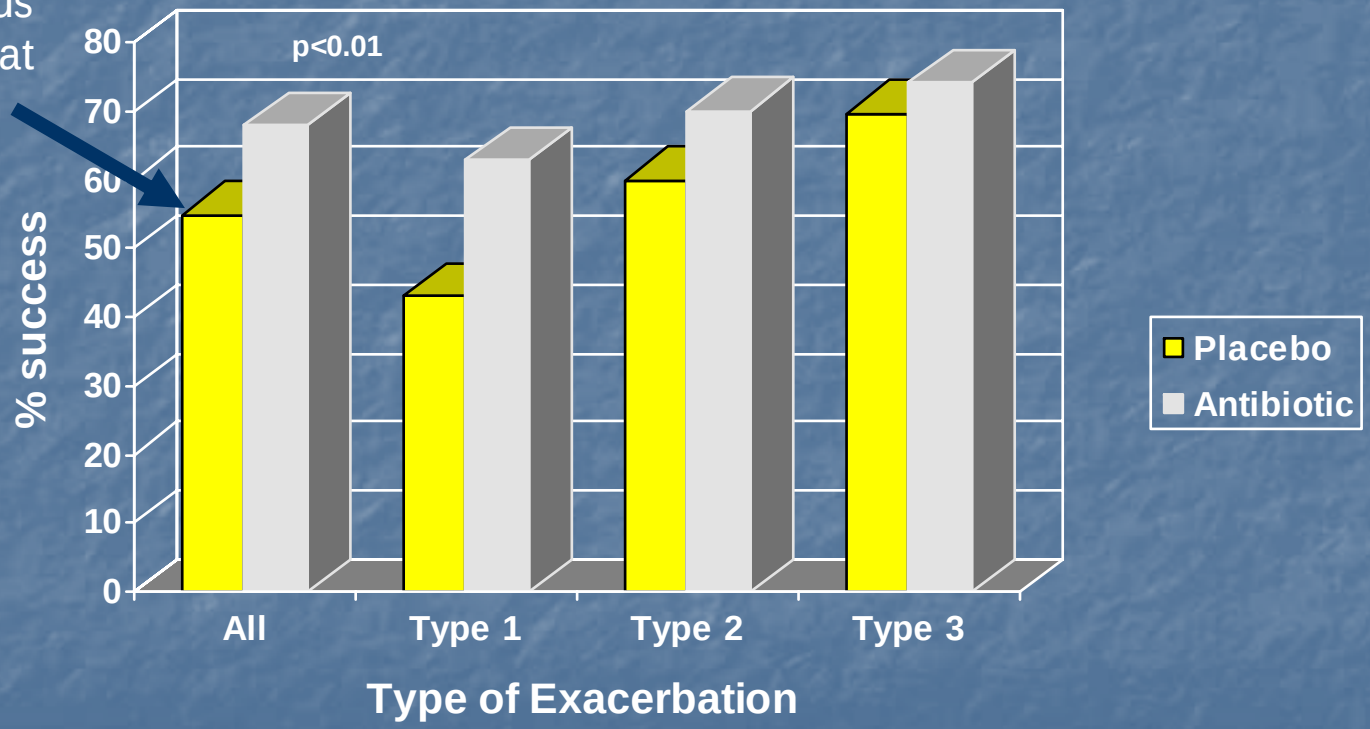
- In ICU patients
  - In-Hospital mortality 11-24 %
- In hospitalized patients
  - Hospital mortality 6 - 8%
- In ER patients
  - Relapse (repeat ER visit) 19 - 32%
- In outpatients
  - Treatment failure rate 13 - 32%
  - Hospitalization rate in treatment failures 16-52%

Connors AJRCCM 1996, Seneff JAMA 1995, Esteban JAMA 2002, Groenewegen Chest 2003, Martin Chest 1992, Murata Ann Emerg Med 1991, Aaron NEJM 2003, Adams Chest 2000, Miravittles ERJ 2001, Ball QJM 1995, Dewan Chest 2000

Antibiotics use in AECB

Correlates with Improved Clinical Resolution

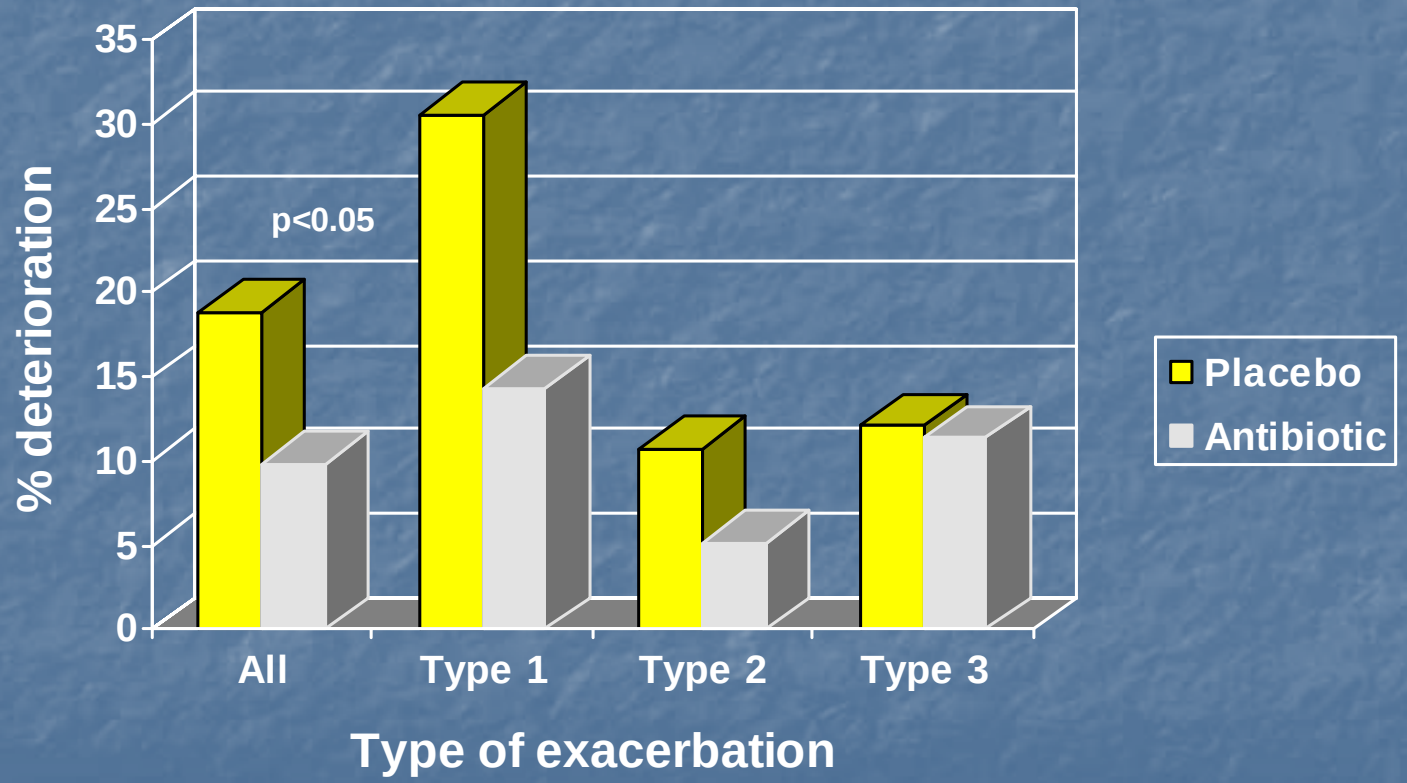
Spontaneous Resolution at 3 weeks



N= 361 in both treatment groups

Anthonisen et al, Ann Intern Med. 1987:106:196-204

Antibiotics use in AECB
Clinical Deterioration at 3 Weeks



Anthonisen et al, Ann Intern Med. 1987:106:196-204

Efficacy of Antibiotics and Steroids in AECB: Systematic Analyses

	Antibiotics (n=11)			Steroids (n=10)		
Outcome	RR	n	NNT or NNH	RR	n	NNT or NNH
Mortality	0.23 (0.10-0.52)	4	8	0.85 (0.45-1.59)	9	
Treatment Failure	0.75 (0.63-0.90)	6	3	0.48 (0.34-0.68)	9	9
Adverse Effects*	2.91 (1.48-5.72)	2	7	2.28 (1.56-3.34)	7	6

- Antibiotics
  - + Sputum purulence resolution
  - -- PEFR and gas exchange
- Steroids
  - + PEFR, FEV_1 and gas exchange

Ram FSF et al, Cochrane Lib Vol 2, 2006

Wood-Baker RR et al Cochrane Lib Vol 2, 2006

AECOPD Antibiotic Treatment GOLD 2005 update

Figure 5-4-11: Stratification of patients with COPD exacerbated for antibiotic treatment and potential microorganisms involved in each group

Group[a]	Definition[b]	Microorganisms
Group A: Patients not requiring hospitalization (***Stage I: Mild COPD***)	Mild exacerbation	*H. influenzae* *S. pneumoniae* *M. catarrhalis* *Chlamydia pneumoniae*[c] Viruses
Group B: Patients admitted to hospital (***Stages II-IV: Moderate to Very Severe COPD***)	Moderate-severe exacerbation without risk factors for *P. aeruginosa* infection	Group A plus: Enterobacteriaceae (*K.pneumoniae, E. coli, Proteus, Enterobacter*, etc)
Group C: Patients admitted to hospital (***Stages II-IV: Moderate to Very Severe COPD***)	Moderate-severe exacerbation with risk factors for *P. aeruginosa* infection	Group B plus: *P. aeruginosa*

a. In some settings, patients with moderate to severe exacerbations may be treated as outpatients. In this case, patients may best be stratified into two groups: an uncomplicated group without any risk factors and a complicated group that has one or more 'risk factors' (co-morbidity, severe COPD, frequent exacerbations, antimicrobial use within last 3 months). The uncomplicated group: use Group A recommendations Figure 5-4-12. Complicated group: use Group B or C recommendations (oral therapy) Figure 5-4-12[217-19].

Figure 5-4-12: Antibiotic treatment in exacerbations of COPD[a,b]

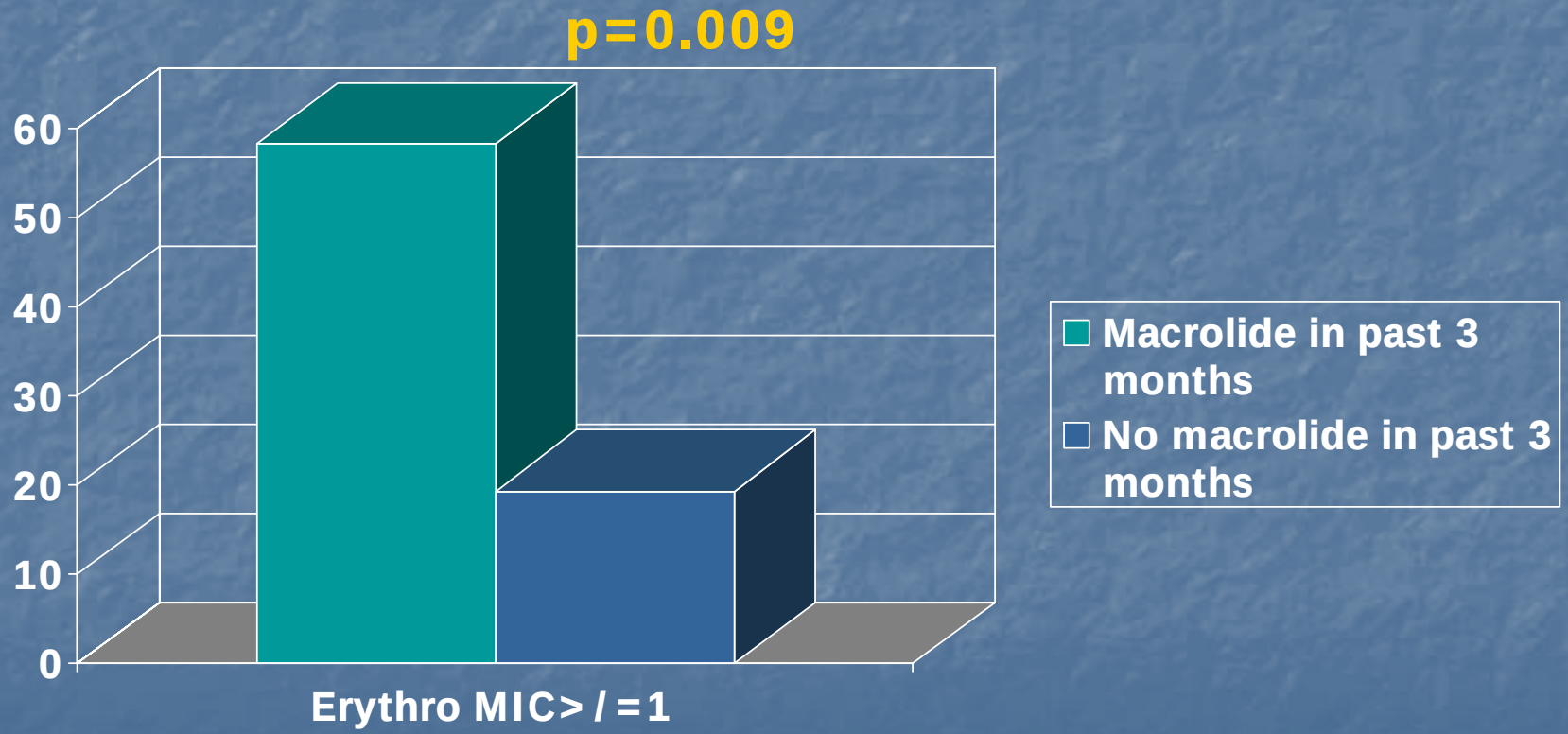
	Oral Treatment *(No particular order)*	Alternative *(No particular order)*	Parental Treatment *(No particular order)*
Group A	***Patients with only one cardinal symptom should not receive antibiotics*** If indication then: • ß-lactam (Ampicillin/Amoxicillin[c]) • Tetracycline • Trimethoprim/Sulfamethoxazole	• ß-lactam/ß-lactamase inhibitor (Co-amoxiclav) • Macrolides (Azithromycin, Clarithromycin, Roxithromycin[d]) • Cephalosporins - 2nd or 3rd generation • Ketolides (Telithromycin)	
Group B	• ß-lactam/b-lactamase inhibitor (Co-amoxiclav)	• Fluoroquinolones[d] (Gatifloxacin, Gemifloxacin, Levofloxacin, Moxifloxacin)	• ß-lactam/b-lactamase inhibitor (Co-amoxiclav, ampicillin/sulbactam) • Cephalosporins - 2nd or 3rd generation • Fluoroquinolones[d] (Gatifloxacin, Levofloxacin, Moxifloxacin)
Group C	• Fluoroquinolones (Ciprofloxacin, Levofloxacin - high dose[e])		• Fluoroquinolones (Ciprofloxacin, Levofloxacin - high dose[e]) or • ß-lactam with *P.aeruginosa* activity

a. All patients with symptoms of a COPD exacerbation should be treated with additional bronchodilators ± glucocorticosteroids.

b. Classes of antibiotics are provided (with specific agents in parentheses). In countries with high incidence of S. pneumoniae resistant to penicillin, high dosages of Amoxicillin or Co-Amoxiclav are recommended. (See Table 1 for definition of Groups A, B, C.)

c. This antibiotic is not appropriate in areas where there is increased prevalence of ß-lactamase producing *H. influenzae* and *M. catarrhalis* and/or of *S. pneumoniae* resistant to penicillin.

Recent Antibiotic Exposure and *S. pneumoniae* resistance in COPD



Sethi et al, Abstract Presented at 46th ICAAC, San Francisco, 2006, Presentation Number: C2-0438

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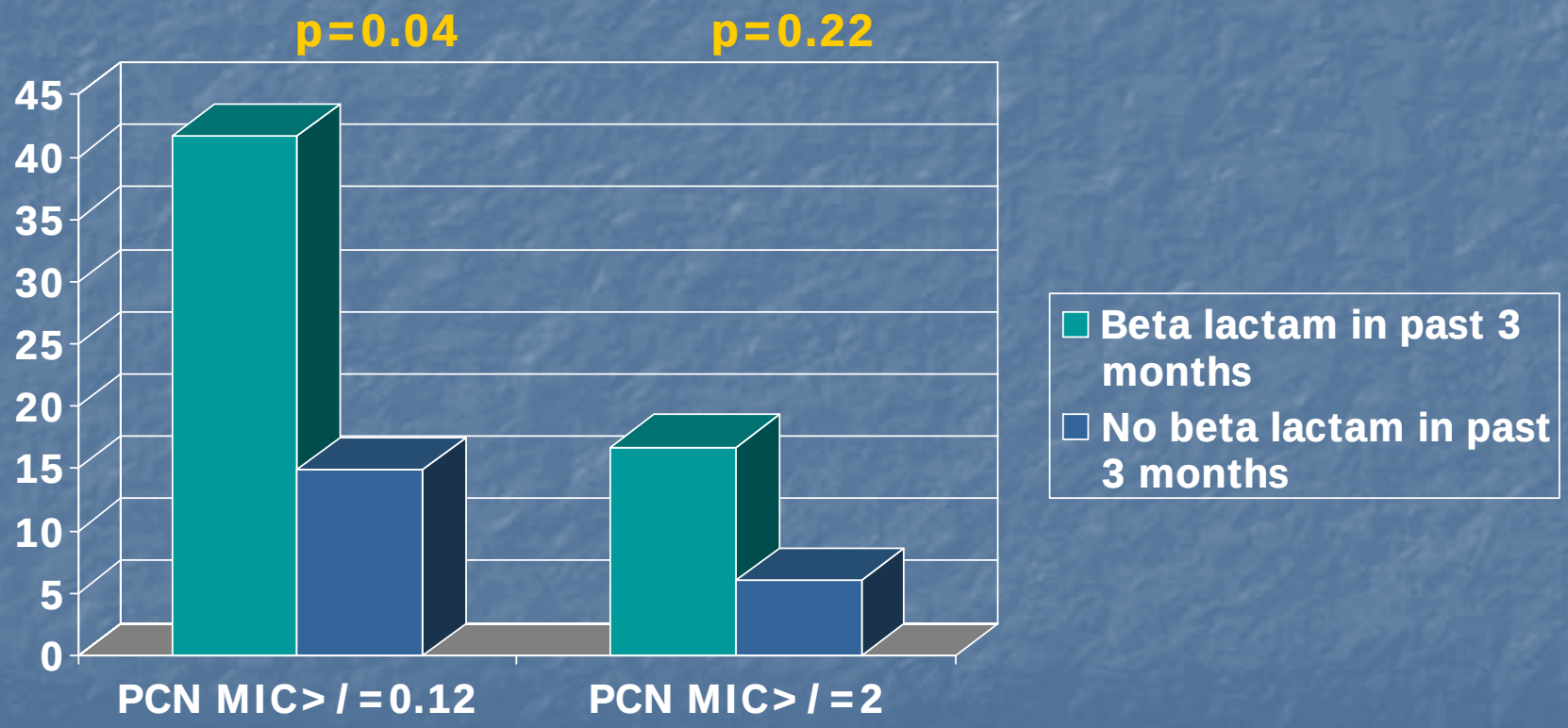

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