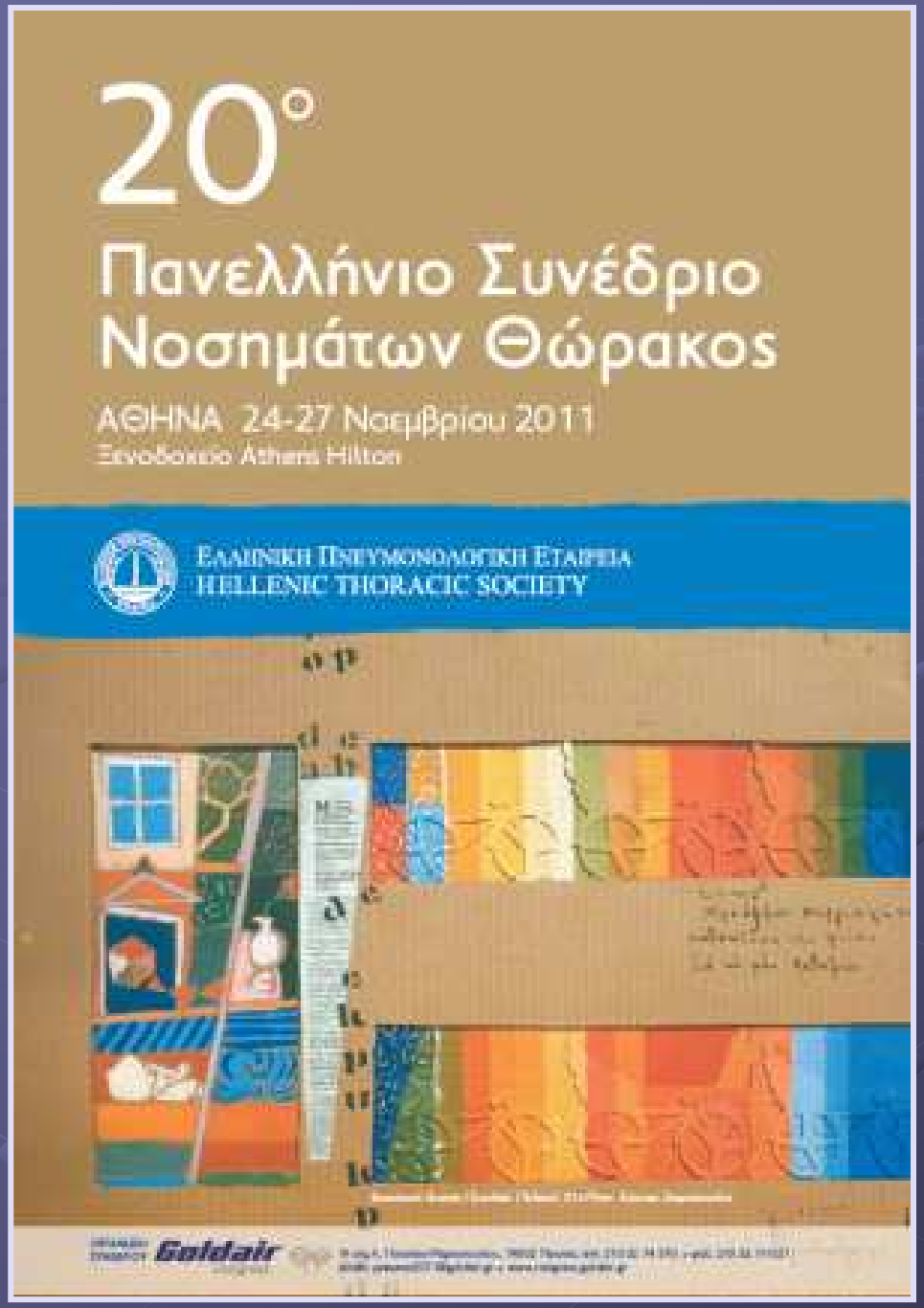


Στρογγυλό τραπέζι

Νοσοκομειακή πνευμονία: νεότερες εξελίξεις και αμφιλεγόμενα θέματα

Μικροβιολογική διάγνωση της Πνευμονίας του αναπνευστήρα: Έχει σημασία η τεχνική λήψης καλλιεργειών;

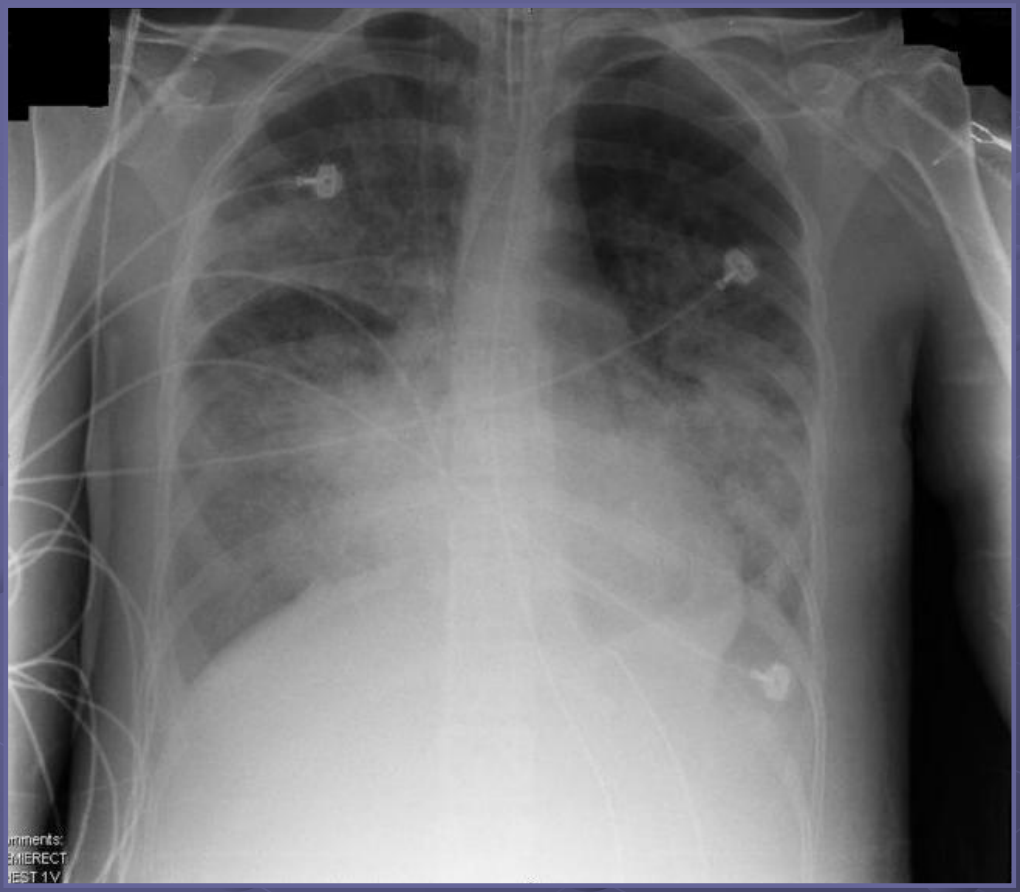
Ευφροσύνη Δ. Μάναλη

Α΄ Πανεπιστημιακή Πνευμονολογική Κλινική ΓΝΝΘΑ «Η Σωτηρία» Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών

What Is Ventilator-Associated Pneumonia and Why Is It Important?

Marin H Kollef MD

Respir Care 2005; 50:714-724



VAP refers to pneumonia that arises more than 48-72 hours after endotracheal intubation

Am J Respir Crit Care Med 2005; 171:388-416

Nosocomial Pneumonia in the Intensive Care Unit Acquired by Mechanically Ventilated versus Nonventilated Patients

Mariano Esperatti[1,3], Miquel Ferrer[1,3], Anna Theessen[1], Adamantia Liapikou[1], Mauricio Valencia[1], Lina Maria Saucedo[1], Elisabeth Zavala[2], Tobias Welte[4], and Antoni Torres[1,3]

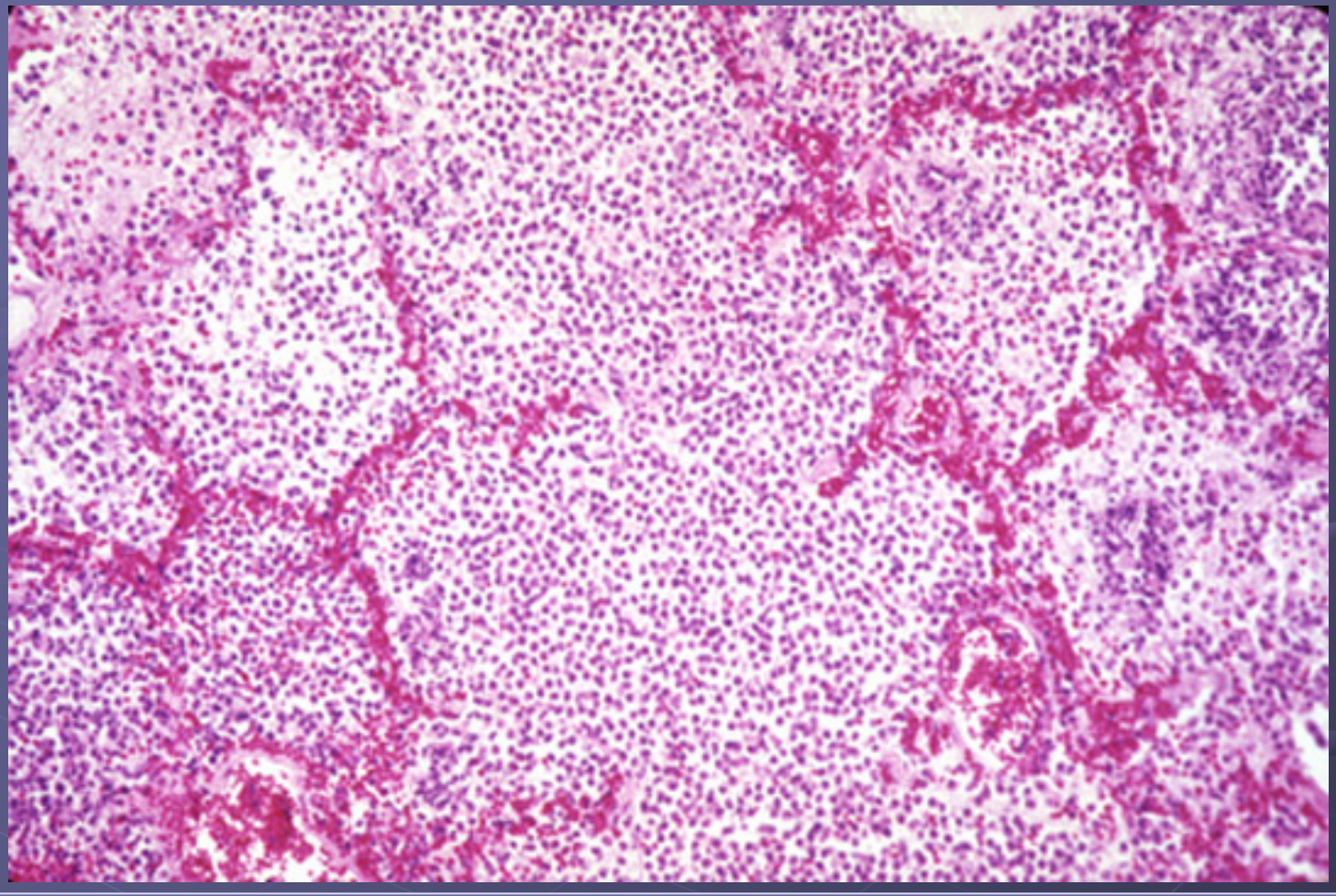
TABLE 6. OUTCOME OF PATIENTS ACCORDING TO THE TYPE OF PNEUMONIA

	VAP (*n* = 164)	NV-ICUAP (*n* = 151)	*P* Value
Appropriate empiric treatment, n (%)*	93 (80)	44 (69)	0.15
Initial nonresponse to treatment, n (%)	71 (43)	67 (44)	0.94
Microbial prediction of the 2005 ATS/IDSA guidelines, n (%)*	102 (90)	51 (81)	0.17
Adherence to the 2005 ATS/IDSA guidelines, n (%)	92 (56)	86 (57)	0.97
Length of ICU stay, d	24 ± 17	18 ± 19	0.008
Length of hospital stay, d	41 ± 34	41 ± 30	0.88
Hospital mortality, n (%)	68 (42)	54 (36)	0.36

Definition of abbreviations: ATS = American Thoracic Society; ICU = intensive care unit; IDSA = Infectious Disease Society of America; NV-ICUAP = nonventilator ICU-acquired pneumonia; VAP = ventilator-associated pneumonia.

* Appropriateness of treatment and microbial prediction could be assessed in patients with etiologic diagnosis only.

Am J Respir Crit Care Med Vol 182. pp 1533–1539, 2010



Definite pneumonia:
pathogenic evidence of pneumonia on histological examination of the lung tissue obtained by open lung biopsy or at postmortem examination. Pneumonia is defined as an area of consolidation with intense PMN accumulation in the bronchioles and alveolar airspaces with or without abscess formation

Marquette CH, et al. ERJ 1994; 7:105-113

Diagnosis of VAP has been a controversial subject:

(1) Differentiation between colonization and infection of the lower respiratory tract

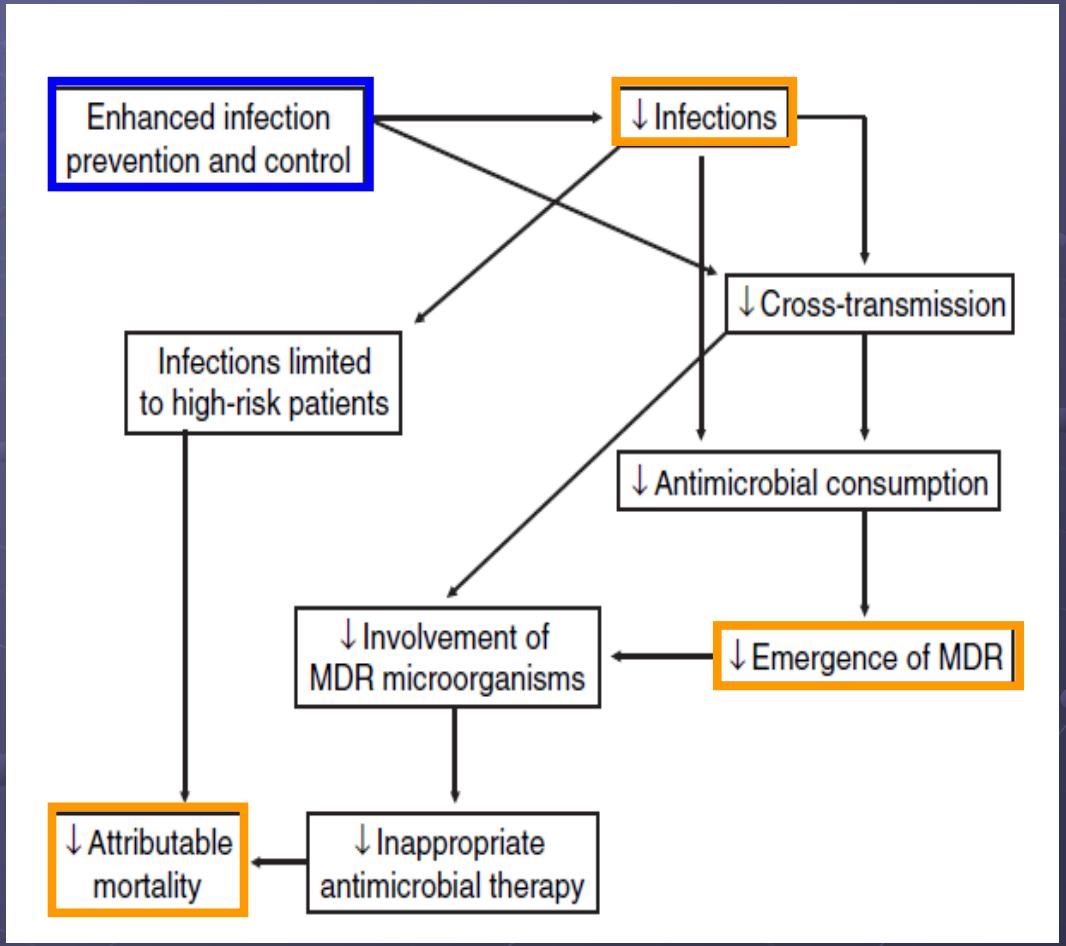
(2) Interpretation of clinical signs and symptoms suggestive of lung infection

(3) Use of antibiotics in the intensive care unit

JY Fagon. Semin Respir Crit Care Med 2006; 27:34-44

Use of antibiotics in the intensive care unit…

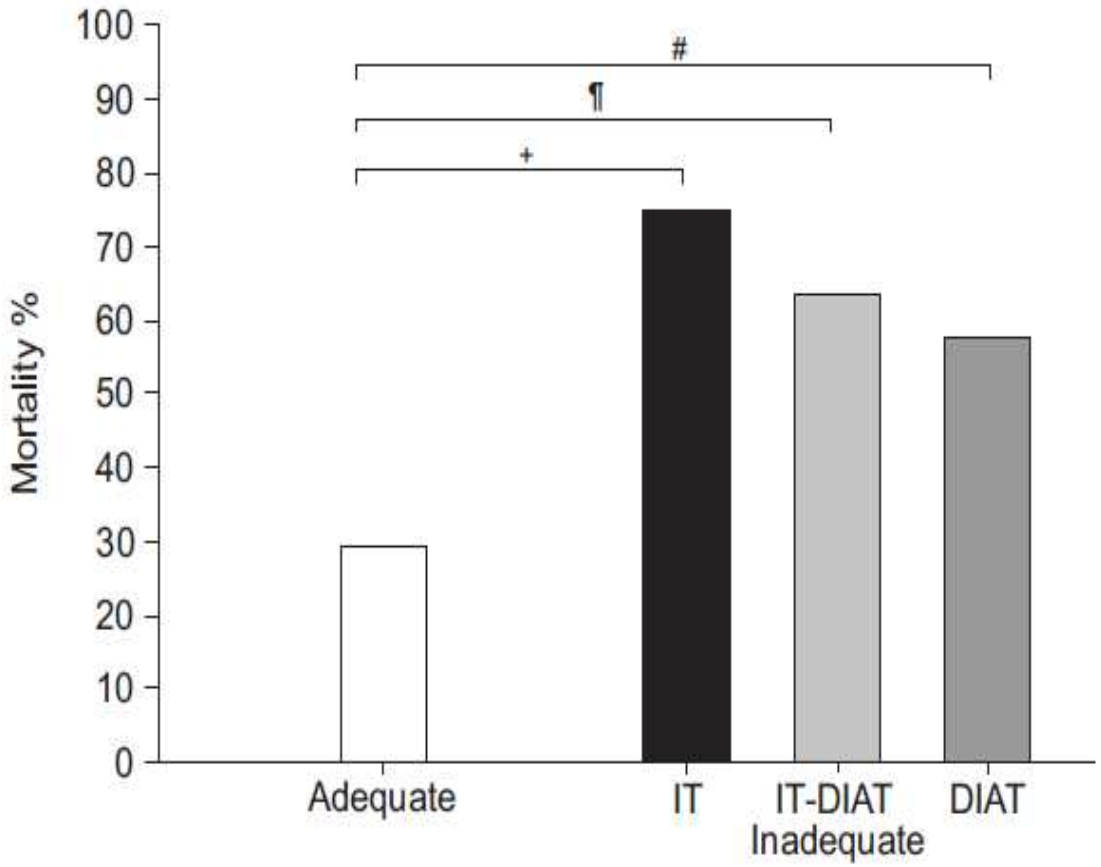
- The excessive use of antibiotics in the ICU determines a higher morbidity and mortality rate in the ICU



Blot S. Clin Microbiol Infect 2008; 14: 5-13

Appropriateness and delay to initiate therapy in ventilator-associated pneumonia

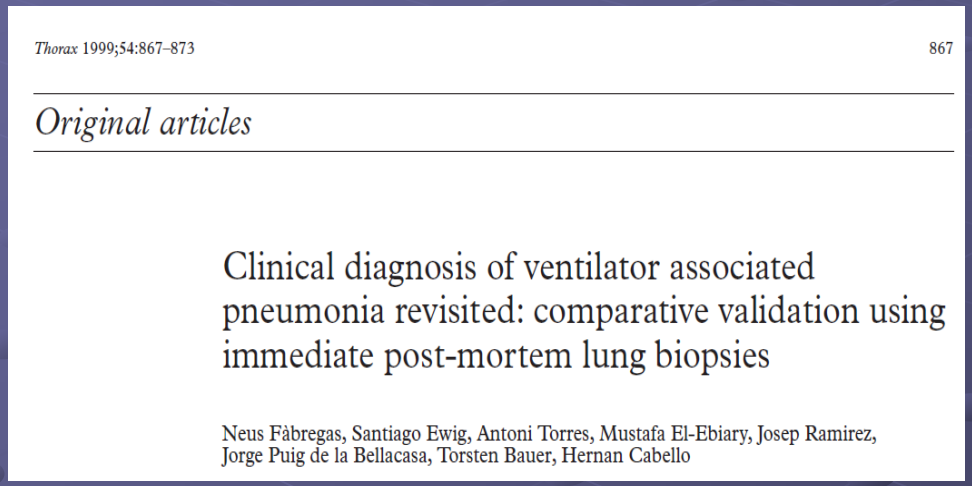
C.M. Luna*, P. Aruj*, M.S. Niederman[#], J. Garzón*, D. Violi*, A. Prignoni*, F. Ríos[¶], S. Baquero* and S. Gando*, for the Grupo Argentino de Estudio de la Neumonía Asociada al Respirador (GANAR) group



[#]: p=0.036; [¶]: p=0.007; [+]: p=0.009.

ERJ 2006; 27:158-164

Interpretation of clinical signs and symptoms suggestive of lung infection…



Thorax 1999;54:867–873 867

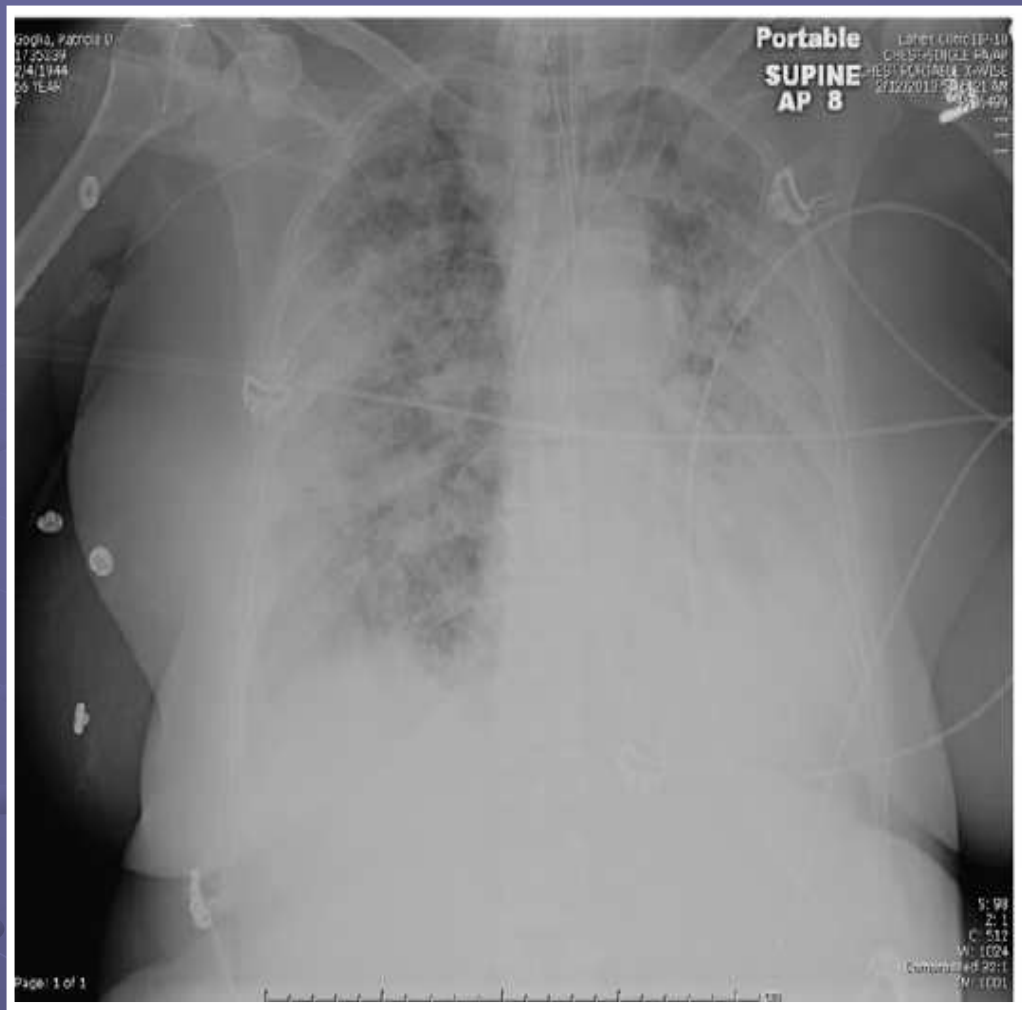
Original articles

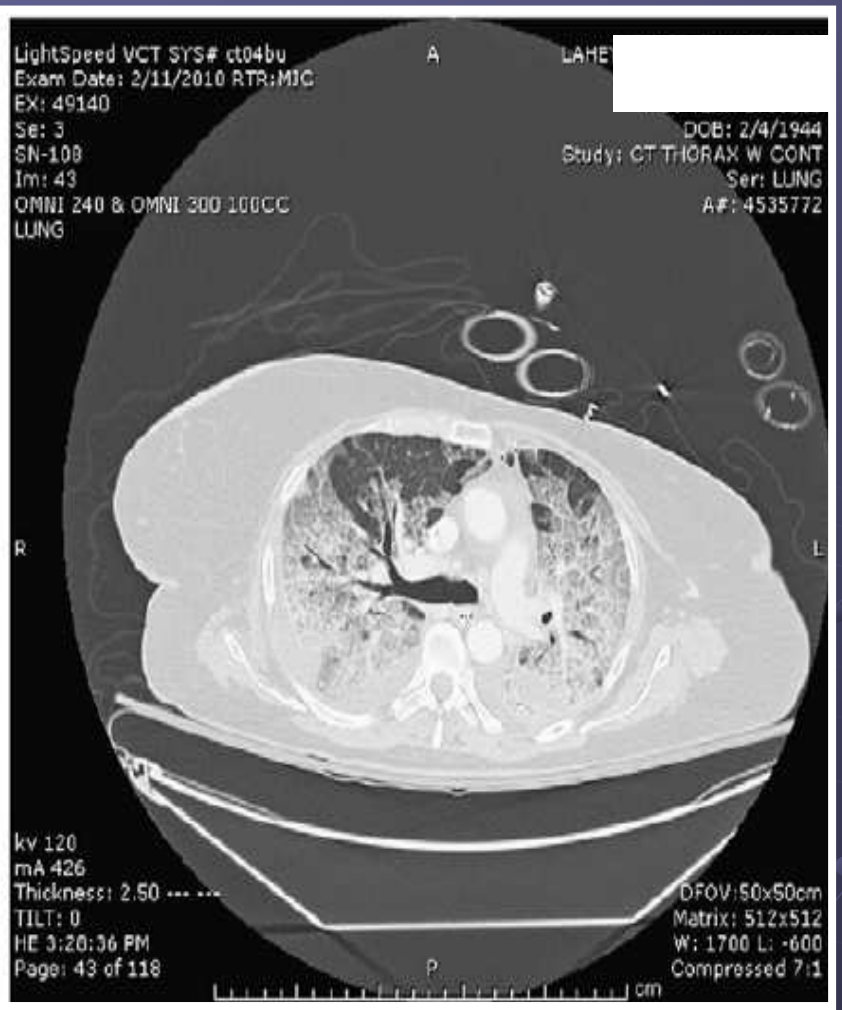
Clinical diagnosis of ventilator associated pneumonia revisited: comparative validation using immediate post-mortem lung biopsies

Neus Fàbregas, Santiago Ewig, Antoni Torres, Mustafa El-Ebiary, Josep Ramirez, Jorge Puig de la Bellacasa, Torsten Bauer, Hernan Cabello

No pathognomonic test for VAP

New or progressing lung infiltrates
Plus
Clinical evidence of infection:
Two or more
Fever >38oC or hypothermia
Leukocytosis or leukopenia
Purulent secretions
Reduced oxygenation





Basing the diagnosis of VAP exclusively on clinical and radiological findings: 30-35% false negatives, 20-25% false positives

ERM 2011; 53:11-23

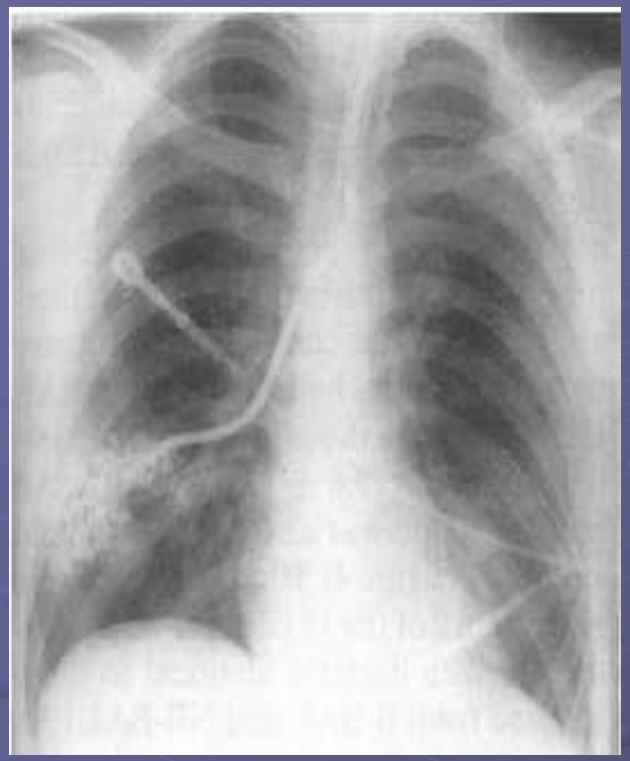
TABLE 1

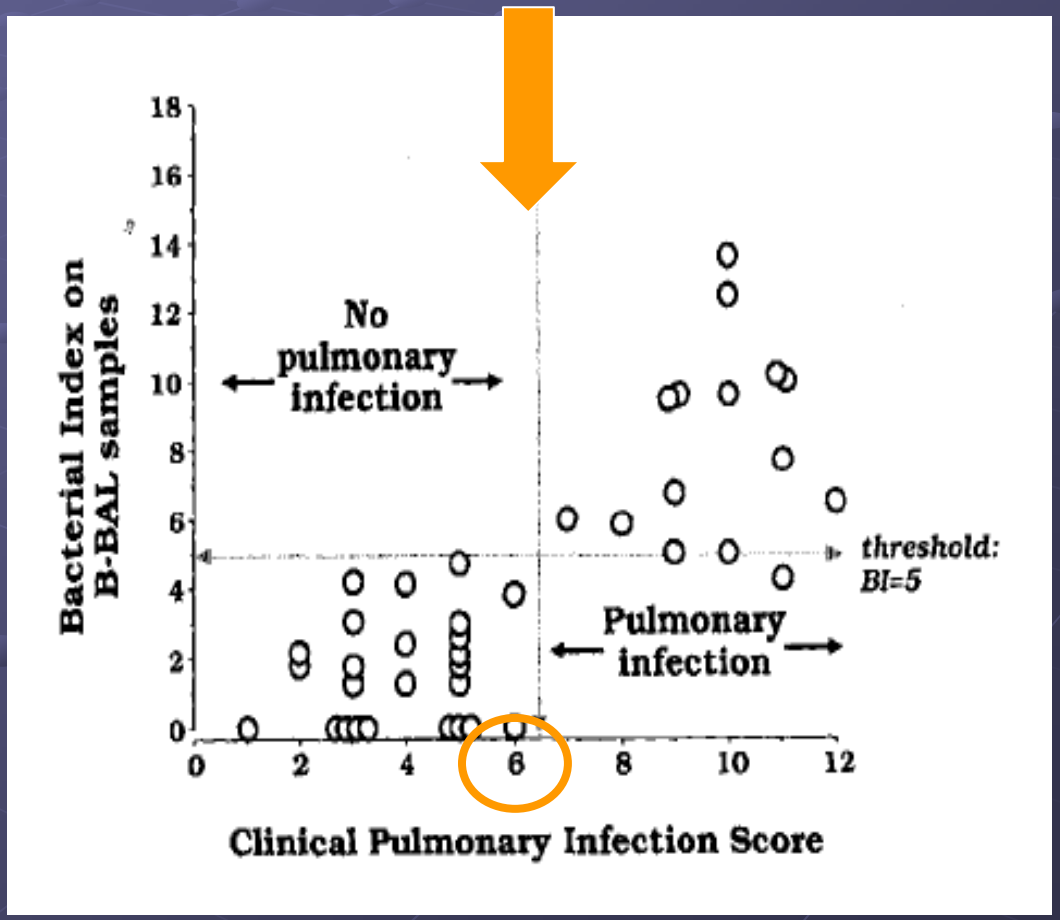
CPIS USED FOR THE DIAGNOSIS OF VA PNEUMONIA*

1. Temperature °C
   - ⩾ 36.5 and ⩽ 38.4 = 0 point
   - ⩾ 38.5 and ⩽ 38.9 = 1 point
   - ⩾ 39 or ⩽ 36.0 = 2 points
2. Blood leukocytes, mm^{-3}
   - ⩾ 4,000 and ⩽ 11,000 = 0 point
   - < 4,000 or > 11,000 = 1 point + band forms ⩾ 500 = +1 point
3. Tracheal secretions
   - < 1+ of tracheal secretions = 0 point
   - ⩾ 1+ of tracheal secretions = 1 point + purulent secretion = +1 point
4. Oxygenation: Pa_{O_2}/FI_{O_2}, mm Hg
   - > 240 or ARDS = 0 point
   - ⩽ 240 and no evidence of ARDS = 2 points
5. Pulmonary radiography
   - No infiltrate = 0 point
   - Diffused (or patchy) infiltrate = 1 point
   - Localized infiltrate = 2 points
6. Culture of tracheal aspirate (semiquantitative: 0-1-2 or 3+)
   - Pathogenic bacteria cultured ⩽ 1+ or no growth = 0 point
   - Pathogenic bacteria cultured > 1+ = 1 point + same pathogenic bacteria seen on the Gram stain > 1+ = +1 point

* Total points = CPIS (varies from 0 to 12 points).

Pugin J, et al. Am Rev Respir Dis 1991; 143:1121-1129




Bacterial Index on B-BAL samples
18
16
14
12
10
8
6
4
2
0
No pulmonary infection
Pulmonary infection
threshold: BI=5
0
2
4
6
8
10
12
Clinical Pulmonary Infection Score

Diagnosing Pneumonia during Mechanical Ventilation

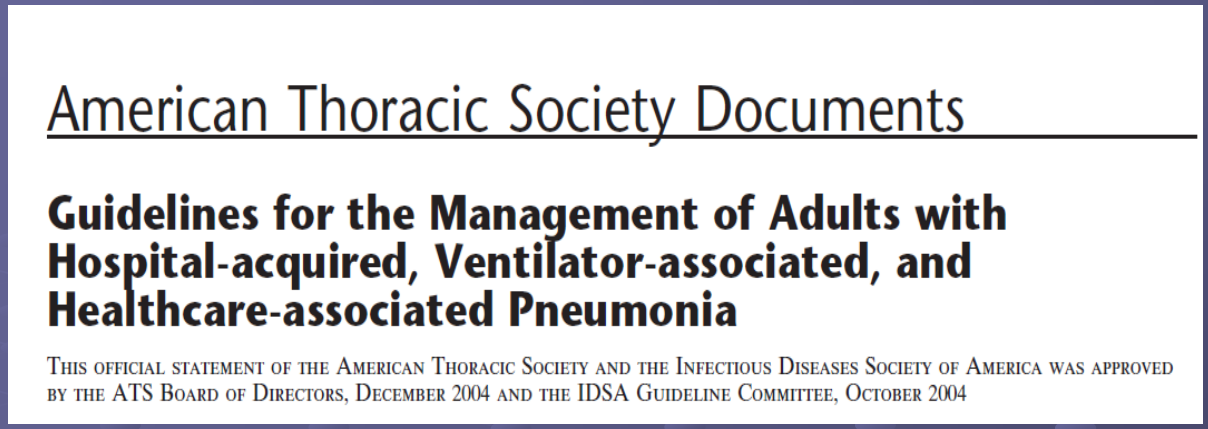
The Clinical Pulmonary Infection Score Revisited

Muriel Fartoukh, Bernard Maître, Stéphanie Honoré, Charles Cerf, Jean-Ralph Zahar, and Christian Brun-Buisson

TABLE 4. ACCURACY OF DIAGNOSIS IN SUSPECTED EPISODES OF VENTILATOR-ASSOCIATED PNEUMONIA OF THE CLINICAL PULMONARY INFECTION SCORE AND THE PHYSICIANS' ESTIMATE OF CLINICAL PROBABILITY OF PNEUMONIA AT BASELINE AND AFTER INCORPORATING THE RESULTS OF RESPIRATORY SPECIMENS GRAM STAINS

	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)	Likelihood Ratio
Pretest clinical probability > 60%	50%	49%	58%	49%	1.19
n	20/40	19/39			
CPIS baseline > 6	60%	59%	60%	59%	1.46
n	24/40	23/39			
CPIS gram BAL > 6	85%	49%	63%	76%	1.67
n	34/40	19/39			
CPIS gram PTC > 6	78%	56%	65%	71%	1.77
n	31/40	22/39			

Am J Respir Crit Care Med 2003; 168:173-179



1. Diagnostic testing is ordered for two purposes:
   - To define whether a patient has pneumonia
   - To determine the etiologic pathogen when pneumonia is present

2. All patients suspected of having VAP
   should undergo LRT sampling,
   with subsequent microscopic analysis and culture of the specimen

3. All samples should be collected before antibiotic changes

AJRCCM 2005; 171:388-416

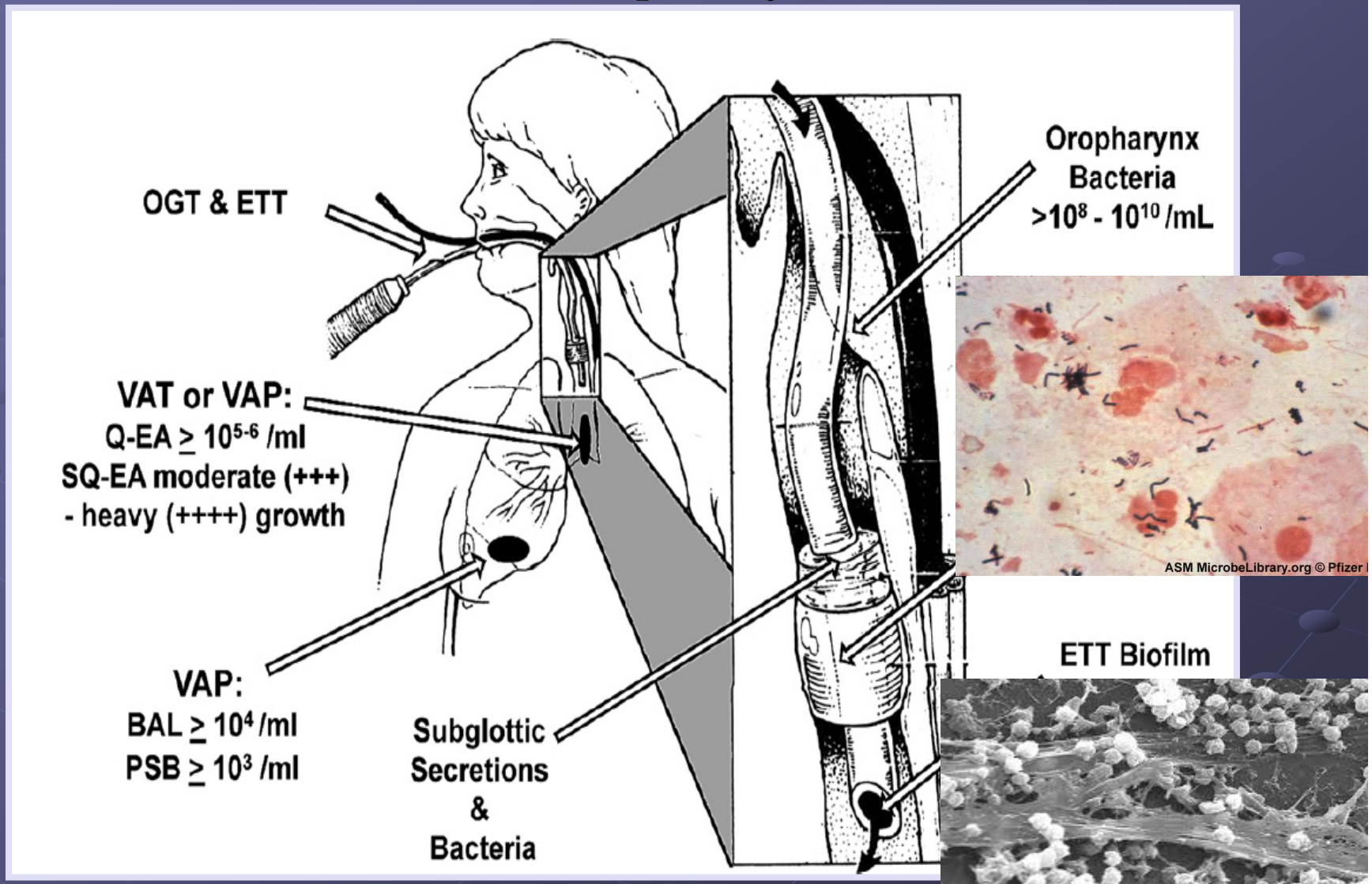
Table I. Common pathogenic organisms in ventilator-associated pneumonia according to presence or absence of risk factors for multidrug-resistant organisms[10]

Risk factors	Commonly isolated organisms
No risk factors	*Streptococcus pneumoniae* *Haemophilus influenzae* Antibacterial-sensitive enteric Gram-negative bacilli *Escherichia coli* *Klebsiella pneumoniae* *Enterobacter* spp. *Proteus* spp. *Serratia marcescens*
Late onset (>5 days) or one of the following risk factors: antimicrobial therapy in preceding 90 days, current hospitalization of ≥5 days, high frequency of antibacterial resistance in the community or in the specific hospital unit, presence of risk factors for HCAP (hospitalization for ≥2 days in the preceding 90 days, residence in a nursing home or extended care facility, home infusion therapy [including antibacterials], chronic dialysis within 30 days, home wound care, family member with multidrug-resistant pathogen), immunosuppressive disease and/or therapy	As above plus: *Pseudomonas aeruginosa* *K. pneumoniae* (ESBL) *Acinetobacter* spp. Methicillin-resistant *Staphylococcus aureus*

ESBL = extended-spectrum β-lactamase; **HCAP** = healthcare-associated pneumonia.

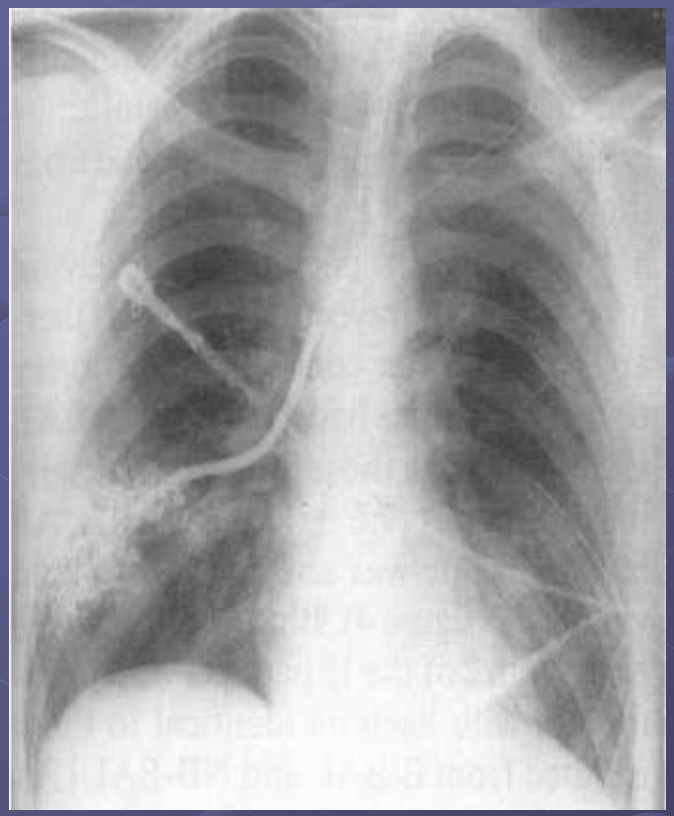
JL Vincent et al. Drugs 2010; 70 (15): 1927-1944

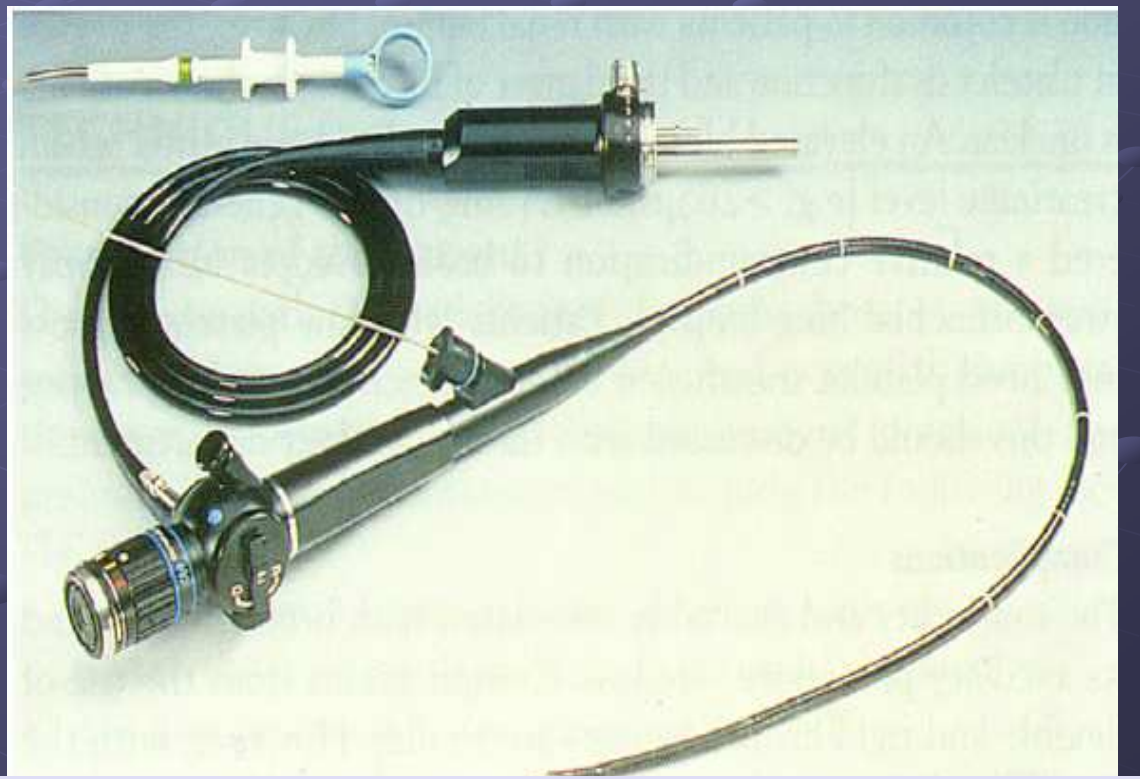
Differentiation between colonization and infection of the lower respiratory tract



Craven DE et al. Clin Chest Med 2011; 32:547-557

Samples can include
1. an endotracheal aspirate,
2. bronchoalveolar lavage sample,
3. or protected specimen brush sample





The sampling area is selected based on location of infiltrate or the segment with the most purulent secretions

Diagnosis and Treatment of Ventilator-Associated Pneumonia: Fiberoptic Bronchoscopy with Bronchoalveolar Lavage Is Essential

Jean-Yves Fagon, M.D.[1]

1. Pathogens causing pneumonia at concentrations > 10^5 to 10^6 CFU/ml
2. Contaminants generally < 10^4 CFU/ml
3. Because PSB collects 0.001-0.01 ml of secretions, the presence of >10^3 bacteria in the originally diluted 1ml sample represents 10^5 to 10^6 CFU/ml
4. 10^4 CFU/ml for BAL, which collects 1ml of secretions in 10-100ml of effluent represents 10^5 to 10^6 CFU/ml for pulmonary secretions

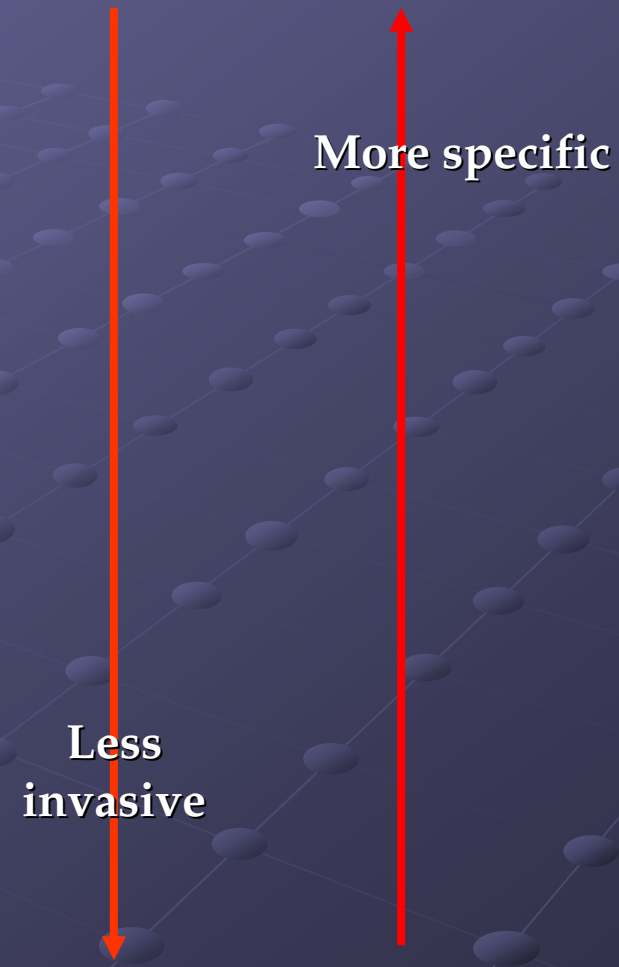
Semin Respir Crit Care Med 2006; 27:34-44

Techniques for Bacterial Sampling

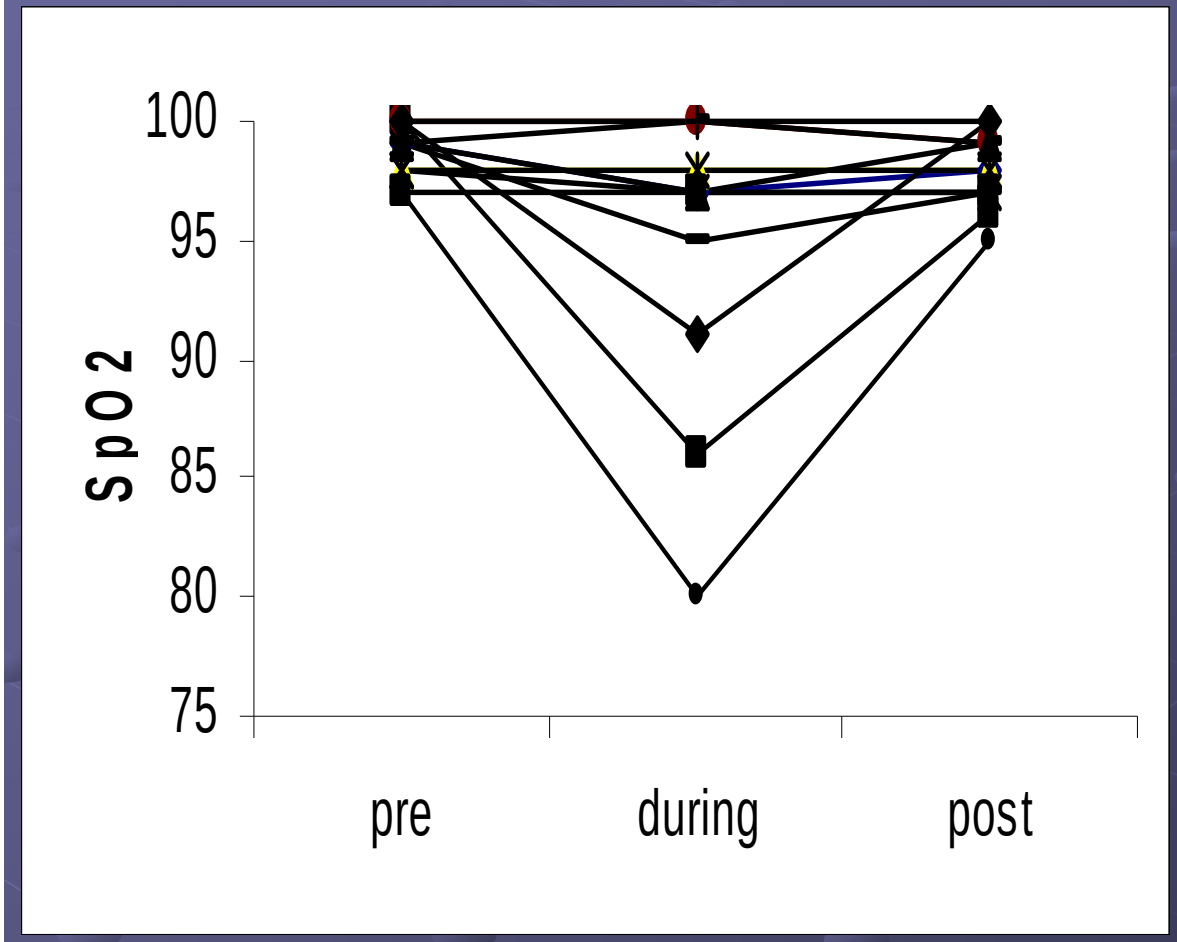
- Bronchoscopic PSB
- Bronchoscopic BAL

- Non-Bronchoscopic BAL
- Blind Bronchial Suctioning

- Endotracheal aspirates



Safety and tolerability of non-bronchoscopic lavage in ARDS



- HR and SBP 23% & 18%
- 3 patients had ST-segment depression
- Reduced minute ventilation by 63 +/- 17.3%
- ++PaCO2

GD. Perkins et al. Chest 2005;127 1358-1363

Table 3

Studies comparing quantitative cultures with pathology

First author	Sample	Dx Tests	Gold standard	Results
Balthazar, 2001, ** [13]	Mixed ICU, 37 pts	BAL (10^4) & Gram & cells from BAL	Pathology + Culture	• BAL: sens = 19%, spec = 94%; fever: sens = 50%, spec = 76%; leucocytosis (>10000): sens = 60%, spec = 76%; Gram stain: sens = 85%, spec = 94%; total cell (>400000): sens = 90%, spec = 94%.
Torres, 2000, ** [26]	Medical ICU, 25 pts	TBA (10^5) & PSB (10^3) & BAL (10^4) & pBAL (10^4)	Pathology + Culture	• TBA: sens = 50%, spec = 67%. • PSB: sens = 67%, spec = 75%. • pBAL: sens = 63%, spec = 83%. • BAL: sens = 83%, spec = 68%.
Fabregas, 1999, ** [11]	Mixed ICU, 25 pts	Johanson & CPIS & TBA (10^5), PSB (10^3), pBAL (10^4) and BAL (10^4)	Pathology + Culture	• Johanson criteria (2): sens = 69%, spec = 75%. • Any Johanson criteria: Chest Rx: sens = 92%, spec = 33%; leukocytosis: sens = 77%, spec = 58%; fever: sens = 46%, spec = 42%; purulent secretions: sens = 69%, spec = 42%. • CPIS: sens = 77%, spec = 42%. • TBA: sens = 69%, spec = 92%. • pBAL: sens = 39%, spec = 100%. • BAL: sens = 77%, spec = 58%. • PSB: sens = 62%, spec = 75%. • QtC increased little to clinical diagnosis accuracy.
Papazian, 1997, # [29]	Mixed ICU, 28 pts	Gram & ICO	Pathology + Culture	• BBS Gram stain: sens = 56%, spec = 73%. • mini-BAL Gram Stain: sens = 44%, spec = 87%. • BAL Gram stain: sens = 56%, spec = 100%. • BBS ICO (>10%): sens = 56%, spec = 40%. • Mini-BAL ICO (>5%): sens = 67%, spec = 53%. • BAL ICO (>4%): sens = 56%, spec = 40%.
Kirtland, 1997, ** [27]	Mixed ICU, 39 pts	TA &PSB & pPSB & BAL & BAL cells	Pathology + Culture	• TA: sens = 87%, spec = 31%. • pPSB: sens = 30%, spec = 81%. • PSB: sens = 44%, spec = 81%. • BAL: sens = 65%, spec = 63%. • >50% neutrophils in BAL: sens = 100%.
Marquette, 1995, ** [28]	Mixed ICU, 28 pts	TA (10^5 & 10^6) & PSB (10^3) & BAL (10^4)	Pathology	• TA (10^5): sens = 63%, spec = 75%. • TA (10^6): sens = 50%, spec = 85%. • PSB (10^3): sens = 57%, spec = 88%. • BAL (10^4): sens = 47%, spec = 100%. • ICO (any%): sens = 36%, spec = 100%.
Torres, 1996 *, ** [25]	Mixed ICU, 25 pts	ICO (≥ 5%), mini-BAL (10^4) & BAL (10^4)	Pathology	• ICO (≥ 5%) compared to mini-BAL: PPV = 75%, NPV = 83%. • ICO (≥ 5%) compared to BAL: PPV = 57%, NPV = 83%. • Mini-BAL: sens = 22%, spec = 100%. • BAL: sens = 45%, spec = 55%.

Rea- Neto A. et al. Crit Care 2008; 12:R56

Deciding on the best type of samples for diagnosing VAP is still a controversial issue

To evaluate a strategy……..

An answer is needed for the two following questions:

(1) Does application of the strategy result in a benefit for the patient

(2) Does application of the strategy result in reducing and controlling overuse of antimicrobial agents

Semin Respir Crit Care Med 2006; 27:34-44

Impact of Invasive and Noninvasive Quantitative Culture Sampling on Outcome of Ventilator-Associated Pneumonia

A Pilot Study

J. M. SANCHEZ-NIETO, A. TORRES, F. GARCIA-CORDOBA, M. EL-EBIARY, A. CARRILLO, J. RUIZ, M. L. NUÑEZ, and M. NIEDERMAN

51 Patients

TABLE 3

ISOLATED MICROORGANISMS FROM THE DIFFERENT TECHNIQUES IN BOTH GROUP A AND GROUP B PATIENTS

	Group A			Group B
	BAL	PSB	QEA	QEA
Pseudomonas aeruginosa	11	9	13	3
Acinetobacter calcoaceticus	5	5	5	8
Legionella spp.	1	1		1
Streptococcus pneumoniae	2	2	2	5
Hemophilus influenzae	2	2	2	5
Proteus mirabilis	67%	58%	67%	1
Corynebacterium spp.				1
Moraxella catarrhalis				2
Staphylococcus aureus				2

74%

Definition of abbreviations: BAL = bronchoalveolar lavage; PSB = protected specimen brush; QEA = endotracheal aspirate. For definition of groups, *see* Table 1.

AJRCCM 1998; 157:371-376

TABLE 4

MORTALITY ACCORDING TO APACHE II SCORE ON ADMISSION

APACHE II	Survivors (*n*)	Nonsurvivors (*n*)	Nonsurvivors (%)	p Value
Group A + B				
< 18	19	6	24	
⩾ 18	14	12	46	NS
Group A				
< 18	6	5	45	
⩾ 18	7	6	46	NS
Group B				
< 18	13	1	7	
⩾ 18	7	6	46	0.032

1. **Absence of difference in mortality and morbidity when comparing invasive versus non invasive diagnostic management**

2. **Quantitative EA isolates agreed with those obtained by PSB and BAL**

Invasive and Noninvasive Strategies for Management of Suspected Ventilator-Associated Pneumonia

A Randomized Trial

Jean-Yves Fagon, MD; Jean Chastre, MD; Michel Wolff, MD; Claude Gervais, MD; Sylvie Parer-Aubas, MD; François Stéphan, MD; Thomas Similowski, MD; Alain Mercat, MD; Jean-Luc Diehl, MD; Jean-Pierre Sollet, MD; and Alain Tenaillon, MD, for the VAP Trial Group*

Design: Multicenter, randomized, uncontrolled trial.

Setting: 31 intensive care units in France.

Patients: 413 patients suspected of having ventilator-associated pneumonia.

Ann Intern Med 2000; 132:621-630

Table 3. Study Outcomes according to the Intention-to-Treat Analysis*

End Point	Patients Who Received Invasive Management (n = 204)	Patients Who Received Clinical Management (n = 209)	Difference (95% CI)	P Value
Primary				
Mortality at 14 days, *n (%)*	33 (16.2)	54 (25.8)	−9.6 (−17.4 to −1.8)†	0.022
Multiple organ dysfunction‡§				
At 3 days				
SOFA score	6.1 ± 4.0	7.0 ± 4.3	−0.9 (−1.7 to −0.1)	0.033
ODIN score	1.7 ± 0.9	1.9 ± 1.1	−0.2 (−0.4 to −0.05)	0.014
At 7 days				
SOFA score	4.9 ± 4.0	5.8 ± 4.4	−0.9 (−1.8 to −0.03)	0.043
ODIN score	1.4 ± 1.0	1.6 ± 1.1	−0.2 (−0.4 to 0.02)	0.082
At 14 days				
SOFA score	3.9 ± 4.1	4.3 ± 4.3	−0.4 (−1.3 to 0.6)	>0.2
ODIN score	1.2 ± 1.2	1.2 ± 1.2	−0.03 (−0.3 to 0.2)	>0.2
Antibiotic-free days at 14 days, *d*‡	5.0 ± 5.1	2.2 ± 3.5	2.8 (1.9 to 3.6)	<0.001
Antibiotics per day at 14 days, *n*	1.2 ± 0.8	1.5 ± 0.7	−0.3 (−0.5 to −0.2)	<0.001
Antibiotic-treatment days at 14 days, *d*	8.7 ± 5.4	10.9 ± 4.5	−2.2 (−3.2 to −1.2)	<0.001
Secondary				
Mortality at 28 days, *n (%)*	63 (30.9)	81 (38.8)	−7.9 (−17.0 to 1.2)	0.099
Multiple organ dysfunction at 28 days‡§				
SOFA score	3.1 ± 3.4	3.1 ± 3.8	−0.02 (−1.2 to 1.1)	>0.2
ODIN score	1.0 ± 1.0	1.0 ± 1.0	−0.06 (−0.4 to 0.3)	>0.2
Antibiotic-free days at 28 days, *d*‡	11.5 ± 9.0	7.5 ± 7.6	−3.9 (−5.5 to −2.3)	<0.001
Antibiotics per day at 28 days, *n*	1.0 ± 1.8	1.3 ± 0.7	−0.3 (−0.45 to −0.16)	<0.001
Antibiotic-treatment days at 28 days, *d*	12.8 ± 8.5	14.9 ± 7.9	−2.1 (−3.7 to −0.5)	0.009
Duration of intensive care unit stay, *d*	19.3 ± 9.0	17.6 ± 9.4	1.5 (−0.3 to 3.2)	0.11
Duration of hospital stay, *d*	26.7 ± 23.9	25.1 ± 28.5	1.6 (−0.3 to 3.4)	>0.2
Mechanical ventilation–free days, *d*‡	7.8 ± 9.8	7.0 ± 9.4	0.8 (−1.0 to 2.9)	>0.2
Emergence of resistant bacteria, *n (%)*	125 (61.3)	125 (59.8)	1.5 (−7.9 to 10.9)	>0.2
Emergence of *Candida* species, *n (%)*	23 (11.3)	47 (22.5)	−11.2 (−18.3 to −4.1)	0.0025

Noninvasive Versus Invasive Microbial Investigation in Ventilator-associated Pneumonia

Evaluation of Outcome

MAURICIO RUIZ, ANTONI TORRES, SANTIAGO EWIG, MARIA ANGELES MARCOS, AMALIA ALCÓN, RAFAEL LLEDÓ, MIGUEL ANGEL ASENJO, and ABEL MALDONALDO

Hospital Clinic i Provincial, Servei de Pneumologia i Al.lergia Respiratoria, Servei de Microbiologia, Servei de Anesthesiologia, Direcció Tècmica, Barcelona, Spain

Randomized study,
76 patients
TBAS vs BAL/PSB

AJRCCM 2000; 162:119-125

TABLE 5

MORTALITY RATES IN BOTH GROUPS AND DIFFERENT SUBGROUPS OF BOTH GROUPS

Mortality	Group 1	Group 2	p Value
Crude	18/39 (46%)	14/37 (38%)	0.46
Attributable to pneumonia	10/18 (56%)	10/14 (71%)	0.36
Adjusted	16%	11%	0.53
According to APACHE II			
< 20	6/19 (32%)	5/18 (28%)	0.80
= 20	12/20 (60%)	8/19 (42%)	0.26
Early-onset pneumonia	3/11 (27%)	0/4 (0%)	0.52
Late-onset pneumonia	15/28 (54%)	14/33 (42%)	0.38
Microbiologically confirmed pneumonia (in respiratory secretion samples and/or blood cultures)	10/23 (44%)	10/23 (44%)	1.0
Respiratory secretion samples			
Growth of PPMs			
Significant growth	8/20 (40%)	10/22 (46%)	0.72
Nonsignificant growth	1/2 (50%)	1/8 (13%)	0.38
Regardless of colony counts	9/22 (41%)	11/30 (37%)	0.76
Community-acquired pathogens			
Significant growth in culture	1/4 (25%)	1/4 (25%)	1.0
Nonsignificant growth in culture	—	0/1 (0%)	—
Regardless of colony counts	1/4 (25%)	1/5 (20%)	1.0
PDRM			
Significant growth in culture	6/16 (38%)	7/16 (44%)	0.72
Nonsignificant growth in culture	1/2 (50%)	2/8 (25%)	1.0
Regardless of colony counts	7/18 (39%)	9/24 (38%)	0.93
Only growth in culture of non-PMMs	9/16 (56%)	3/7 (43%)	0.67
Negative culture	4/9 (44%)	1/3 (33%)	1.0
Initial empiric antimicrobial treatment for VAP			
Adequate	5/15 (33%)	6/13 (46%)	0.49
Inadequate	5/8 (63%)	4/10 (40%)	0.63

TABLE 3

OUTCOME OF INITIAL EMPIRIC ANTIMICROBIAL TREATMENT WITH REGARD TO CULTURE RESULTS OF NONINVASIVE VERSUS INVASIVE INVESTIGATION

Outcome/Diagnostic Results	Group 1 n (%)	Group 2 n (%)
Cured	19 (49)	22 (59)
With significant growth in culture	11 (28)	9 (24)
With adequate treatment	10 (26)	5 (14)
With inadequate treatment	1 (3)	4 (11)
With nonsignificant growth of PPMs	1 (3)	6 (16)
With growth of non-PPMs	2 (5)	3 (8)
With negative cultures	5 (13)	4 (11)
Antimicrobial treatment failure	20 (51)	15 (41)
With significant growth in culture	11 (28)	13 (35)
With adequate treatment	4 (10)	7 (19)
With inadequate treatment	7 (18)	6 (16)
With nonsignificant growth of PPMs	1 (3)	1 (3)
With growth of non-PPMs	4 (10)	1 (3)
With negative cultures	4 (10)	0

p = NS for all comparisons.

1. Similar diagnostic yield for non invasive (51%) and invasive techniques (60%)

2. Length of ICU stay and MV, crude and adjusted 30 day mortality not significantly different

3. Cost for microbial investigation significantly higher using invasive techniques

Impact of quantitative invasive diagnostic techniques in the management and outcome of mechanically ventilated patients with suspected pneumonia

Jorge Solé Violán, MD; Javier Arroyo Fernández, MD; Ana Bordes Benítez, MD;
José A. Cardeñosa Cendrero, MD; Felipe Rodríguez de Castro, MD

Prospective study
91 patients
Quantitative versus non quantitative

1. **Invasive techniques lead to more antibiotic changes**
2. **They do not improve the outcome**

Crit Care Med 2000; 28:2737-2741

The NEW ENGLAND JOURNAL of MEDICINE

A Randomized Trial of Diagnostic Techniques for Ventilator-Associated Pneumonia

The Canadian Critical Care Trials Group*

NEJM 2006; 355:2619-2630

1. Similar clinical outcomes

2. Similar overall use of antibiotics

Table 4. Clinical and Microbial Outcomes at Day 28.*

Outcome	Endotracheal Aspiration (N=374)	Bronchoalveolar Lavage (N=365)	All (N=739)
		number of patients (percent)	
Detailed clinical assessment			
Clinical resolution	214 (57.2)	209 (57.3)	423 (57.2)
Delayed resolution	12 (3.2)	9 (2.5)	21 (2.8)
Relapse or recurrent infection	8 (2.1)	8 (2.2)	16 (2.2)
Superinfection	22 (5.9)	30 (8.2)	52 (7.0)
Clinical failure	8 (2.1)	3 (0.8)	11 (1.5)
Indeterminate outcome	41 (11.0)	37 (10.1)	78 (10.6)
Death	69 (18.4)	69 (18.9)	138 (18.7)
Overall clinical assessment			
Cure	226 (60.4)	218 (59.7)	444 (60.1)
Clinical failure	107 (28.6)	110 (30.1)	217 (29.4)
Indeterminate outcome	41 (11.0)	37 (10.1)	78 (10.6)
Detailed microbial assessment			
Resolution	133 (35.6)	149 (40.8)	282 (38.2)
Relapse or recurrent infection	6 (1.6)	10 (2.7)	16 (2.2)
Superinfection	28 (7.5)	47 (12.9)	75 (10.1)
Clinical failure	17 (4.5)	15 (4.1)	32 (4.3)
Colonization	39 (10.4)	28 (7.7)	67 (9.1)
No positive culture	136 (36.4)	100 (27.4)	236 (31.9)
Indeterminate outcome	15 (4.0)	16 (4.4)	31 (4.2)
Overall microbial assessment†			
Cure	172 (77.1)	177 (71.1)	349 (73.9)
Failure	51 (22.9)	72 (28.9)	123 (26.1)

p=0.9

p=0.1

EDITORIALS

Diagnosis of Ventilator-Associated Pneumonia

Marin H. Kollef, M.D.

The exclusion of patients colonized or infected with MRSA, *P. aeruginosa*, and other multidrug-resistant pathogens diminishes the usefulness of the results of Heyland et al. for clinical decision making. There is less concern about administering inappropriate initial antimicrobial therapy when the risk of infection with resistant pathogens is low, thus allowing for the initial use of more narrow-spectrum antimicrobial agents. The

NEJM 2006; 355:25

[Intervention Review]

Quantitative versus qualitative cultures of respiratory secretions for clinical outcomes in patients with ventilator-associated pneumonia

Types of interventions

Invasive and non-invasive methods using quantitative or qualitative cultures of respiratory secretions from patients with suspected VAP.

Cochrane Database Syst Rev 2008; (4):CD006482

Figure 2. Forest plot of comparison: 2 Invasive versus non-invasive method, outcome: 2.1 Mortality.

Study or Subgroup	Invasive Events	Invasive Total	Non-invasive Events	Non-invasive Total	Weight	Risk Ratio M-H, Fixed, 95% CI
CCCTG 2006	69	365	69	374	37.6%	1.02 [0.76, 1.38]
Fagon 2000	63	204	81	209	44.1%	0.80 [0.61, 1.04]
Ruiz 2000	14	37	18	39	9.7%	0.82 [0.48, 1.40]
Sanchez-Nieto 1998	11	24	7	27	3.6%	1.77 [0.82, 3.83]
Solé Violán 2000	10	45	9	43	5.1%	1.06 [0.48, 2.36]
Total (95% CI)		**675**		**692**	**100.0%**	**0.93 [0.78, 1.11]**
Total events	167		184			

Heterogeneity: $Chi^2 = 4.68$, $df = 4$ ($P = 0.32$); $I^2 = 14\%$

Test for overall effect: $Z = 0.76$ ($P = 0.45$)

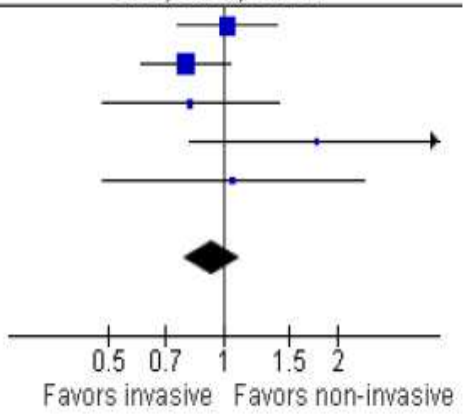


Figure 5. Forest plot of comparison: 2 Invasive versus non-invasive method, outcome: 2.2 Antibiotic change.

Study or Subgroup	Invasive Events	Invasive Total	Non-invasive Events	Non-invasive Total	Weight	Risk Ratio M-H, Random, 95% CI
CCCTG 2006	271	365	279	374	36.7%	1.00 [0.91, 1.08]
Ruiz 2000	10	37	7	39	22.6%	1.51 [0.64, 3.54]
Sanchez-Nieto 1998	10	24	4	27	19.4%	2.81 [1.01, 7.81]
Solé Violán 2000	15	45	5	43	21.3%	2.87 [1.14, 7.21]
Total (95% CI)		**471**		**483**	**100.0%**	**1.67 [0.87, 3.21]**
Total events	306		295			

Heterogeneity: $Tau^2 = 0.30$; $Chi^2 = 10.93$, $df = 3$ ($P = 0.01$); $I^2 = 73\%$

Test for overall effect: $Z = 1.55$ ($P = 0.12$)

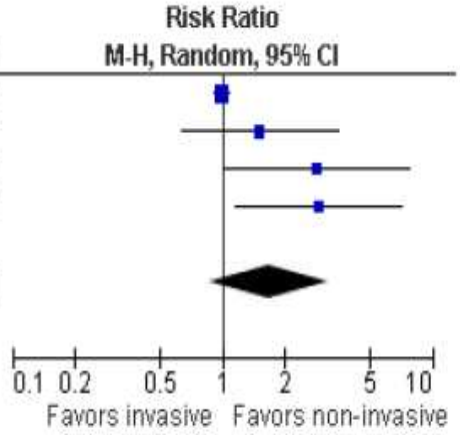


Figure 7. Forest plot of comparison: 2 Invasive versus non-invasive method, outcome: 2.3 Duration on mechanical ventilation (days).

Study or Subgroup	Invasive Mean	SD	Total	Non-invasive Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CCCTG 2006	8.9	16.6	365	8.8	18.34	374	18.2%	0.10 [-2.42, 2.62]
Ruiz 2000	19	15	37	20	24	39	1.4%	-1.00 [-9.95, 7.95]
Sanchez-Nieto 1998	23	12	24	20	17	27	1.8%	3.00 [-5.01, 11.01]
Solé Violán 2000	19.9	2.8	45	19.2	3	43	78.5%	0.70 [-0.51, 1.91]
Total (95% CI)			**471**			**483**	**100.0%**	**0.61 [-0.47, 1.68]**

Heterogeneity: Chi² = 0.64, df = 3 (P = 0.89); I² = 0%
Test for overall effect: Z = 1.11 (P = 0.27)

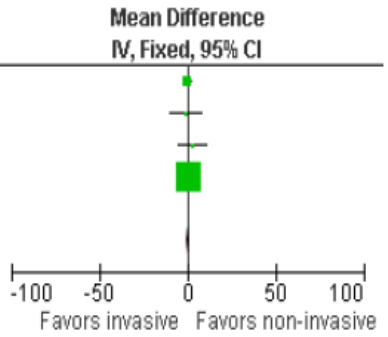


Figure 9. Forest plot of comparison: 2 Invasive versus non-invasive method, outcome: 2.4 ICU stay (days).

Study or Subgroup	Invasive Mean	SD	Total	Non-invasive Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
CCCTG 2006	12.3	14.1	365	12.2	16.3	374	23.8%	0.10 [-2.10, 2.30]
Fagon 2000	26.7	23.9	204	25.1	28.5	209	4.5%	1.60 [-3.47, 6.67]
Ruiz 2000	21	15	37	21	18	39	2.1%	0.00 [-7.43, 7.43]
Sanchez-Nieto 1998	28	17	24	26	18	27	1.2%	2.00 [-7.61, 11.61]
Solé Violán 2000	23.6	3.1	45	22.4	3.1	43	68.4%	1.20 [-0.10, 2.50]
Total (95% CI)			**675**			**692**	**100.0%**	**0.94 [-0.13, 2.01]**

Heterogeneity: Chi² = 0.89, df = 4 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.72 (P = 0.09)

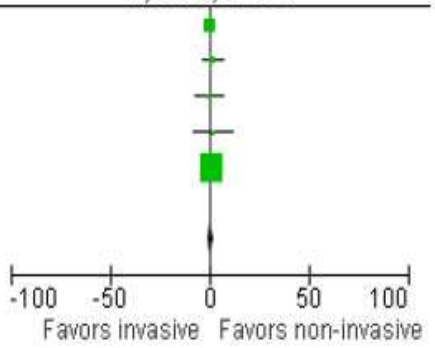
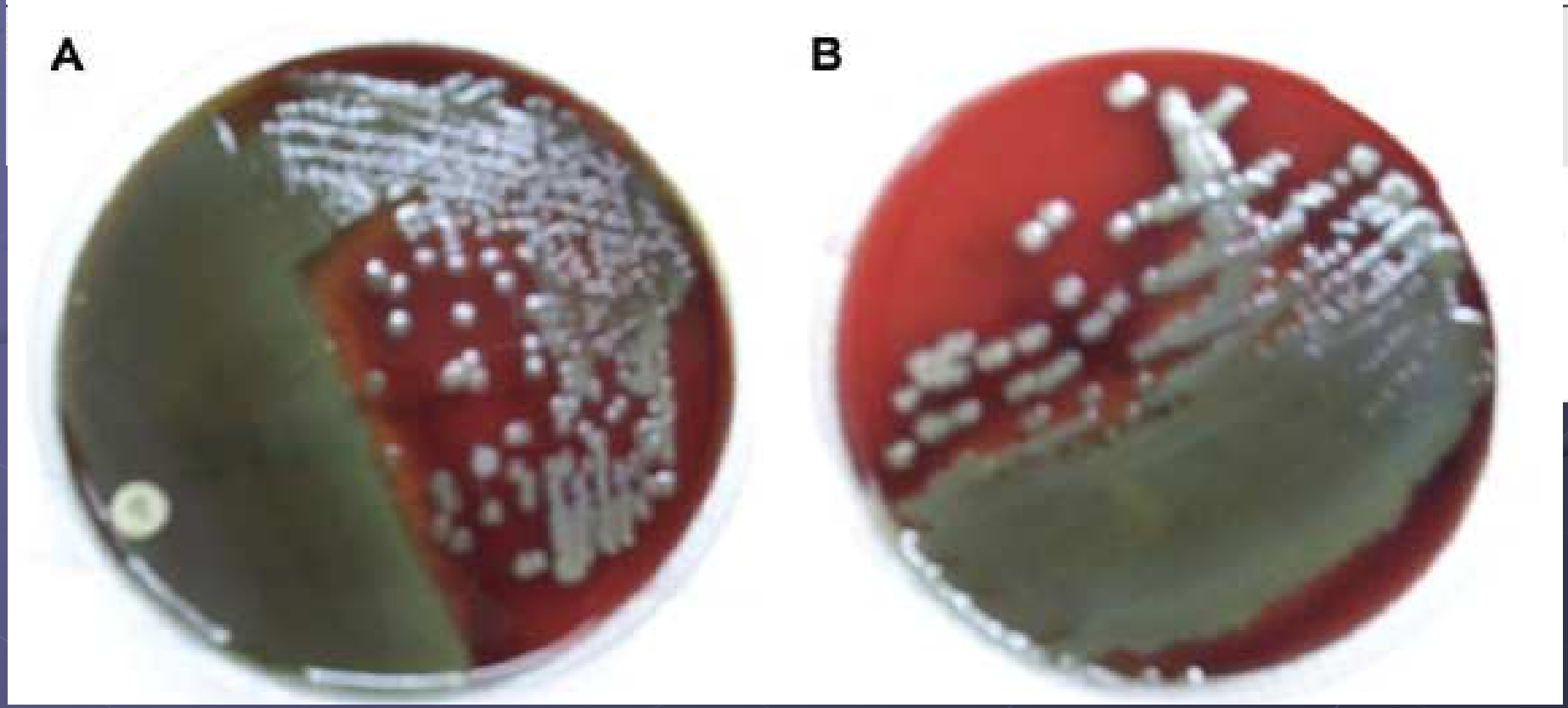


Table 1. Barriers and Potential Solutions to the Performance of Accurate and Applicable Clinical Trials in Hospital-Acquired Pneumonia (HAP) and Ventilator-Associated Pneumonia (VAP)



Clin Infect Dis 2010; 51:S29-S35

Utility of Gram stain in the clinical management of suspected ventilator-associated pneumonia
Secondary analysis of a multicenter randomized trial

M. Albert MD[a], J.O. Friedrich MD, DPhil[b], N.K.J. Adhikari MDCM, MSc[b], A.G. Day MSc[d], C. Verdant MD[a], Daren K. Heyland MD, MSc[c,*], for the Canadian Critical Care Trials Group

Table 3 Agreement between Gram stain and culture results for pathogenic organisms

Gram stain result	Pathogenic organism				Total
	Neither	GP	GN	Both	
Neither	232 (32.9)	25 (3.6)	60 (8.5)	14 (2.0)	331 (47.0)
GP	43 (6.1)	39 (5.5)	16 (2.3)	23 (3.3)	121 (17.1)
GN	7 (1.0)	1 (0.1)	84 (12.0)	5 (0.7)	97 (13.6)
Both	42 (6.0)	16 (2.3)	64 (9.1)	34 (4.8)	156 (22.3)
Total	324 (46.0)	81 (11.5)	224 (31.8)	76 (10.8)	705 (100.0)

Values are shown as n (overall%). Pooled data for BALs and EAs.

J Crit Care 2008; 23:74-81

CHEST ONLINE

Microscopic Examination of Intracellular Organisms in Protected Bronchoalveolar Mini-Lavage Fluid for the Diagnosis of Ventilator-Associated Pneumonia*

Josep-Maria Sirvent, Loreto Vidaur, Susana Gonzalez, Pilar Castro, Jordi de Batlle, Antoni Castro and Alfons Bonet

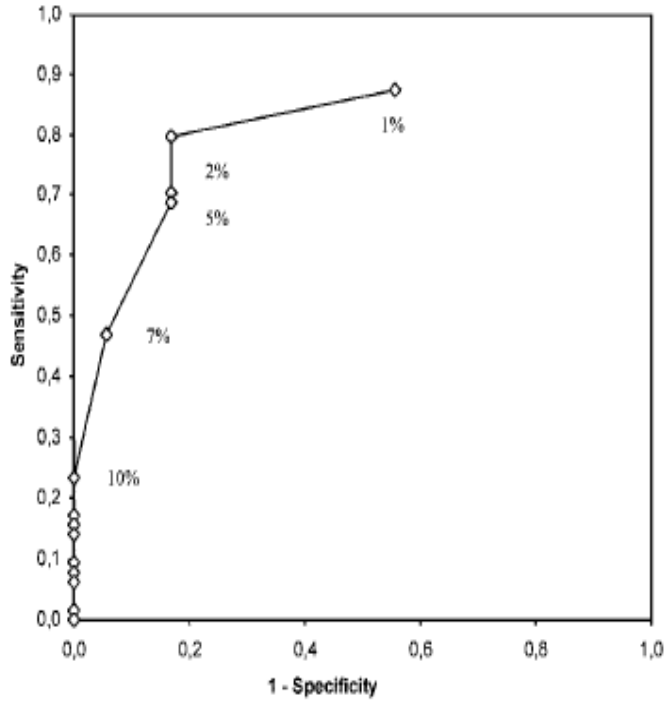
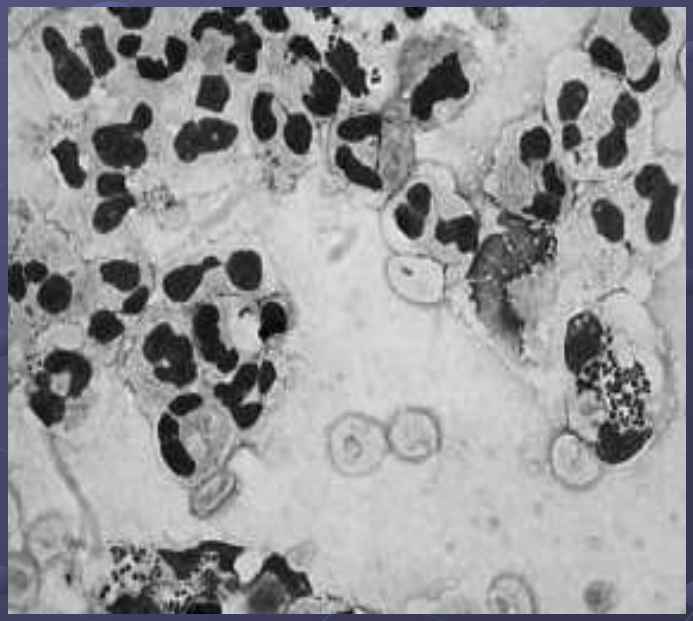


FIGURE 1. ROC curve for the percentage of ICOs.

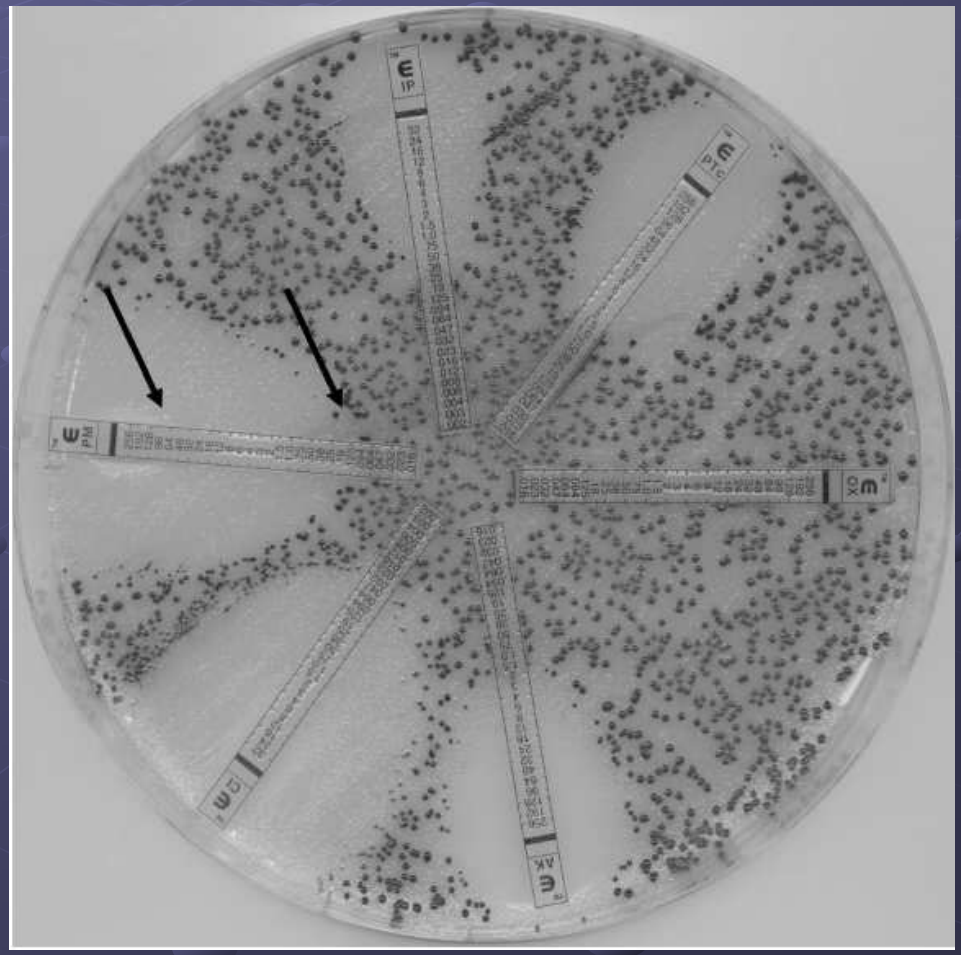


Chest 2003; 123:518-523

Rapid Detection of Microorganism Resistance in Patients With Ventilator-Associated Pneumonia

Patricia Muñoz, MD, PhD, Emilia Cercenado, PharmD, Maddalena Giannella, MD, and Emilio Bouza, MD, PhD

DIRECT E-TEST ON LOWER RESPIRATORY TRACT SAMPLES



An early report based on the results obtained directly by plating LRT secretions with 6 E-test strips is associated with better antibiotic use, less antimicrobial misuse, and a decrease in antimicrobial-related adverse events.

Clin Pulm Med 2009; 16:302-308

Recommendations for Treatment of Hospital-Acquired and Ventilator-Associated Pneumonia: Review of Recent International Guidelines

Thomas M. File, Jr.

Northeastern Ohio Universities College of Medicine, Rootstown, and Summa Health System, Akron, Ohio

Table 2. Key Recommendations for Diagnosis of Hospital-Acquired Pneumonia (HAP) and/or Ventilator-Associated Pneumonia (VAP) from Recent Guidelines

Clin Infect Dis 2010; 51:S42-S47

Guidelines

vs.

Guidelines

American Thoracic Society and Infectious Diseases Society of America (2005)	• All patients should have comprehensive evaluation to define severity and exclude other sources of infection and reveal conditions that can influence the likely etiology (II) • A new or progressive pulmonary infiltrate and ≥2 of fever, leukocytosis, or sputum purulence is most accurate clinical criteria (II) • Patients should have blood cultures performed (II) • Obtain LRT secretions for culture before initiating antimicrobial therapy (II) • Negative culture result of appropriate LRT specimen in absence of change in antimicrobial therapy in preceding 72 h virtually rules out pyogenic bacterial infection; exception includes Legionella (II) • Reliable tracheal aspirate Gram stain can be used to direct initial antimicrobial therapy and may increase the diagnostic value of CPIS (II) • Quantitative cultures can be performed on endotracheal samples collected bronchoscopically or no bronchoscopically (the choice depends on local expertise, experience, availability, and cost (II) • Modified CPIS of ≤6 for 3 days is a criterion to select patients at low risk for early discontinuation of empirical therapy of HAP (I)
British Society for Antimicrobial Chemotherapy (2008)	• CPIS is useful for selecting patients for short-course therapy (C) • Chest radiograph should be performed and compared with previous chest radiographs (D) • CT may assist in diagnosis of HAP (GPP) • Endotracheal aspirate samples are not useful for diagnosis of VAP (A) • There is no evidence that any 1 invasive method is best (A) • Recommend the least expensive, least invasive method requiring minimal expertise be used for microbiological diagnosis (GPP) • Quantitative culture of PSB or BAL specimen should not be relied on for diagnosis of HAP/VAP (A) • Quantification of intracellular organisms in BAL specimen can be used to guide therapy (A)

Review of Recent Clinical Trials of Hospital-Acquired Pneumonia and Ventilator-Associated Pneumonia: A Perspective from Academia

Marin H. Kollef

By some accounts, we are approaching a pre-antibiotic era in which patients infected with specific pathogens, including methicillin resistant *Staphylococcus aureus*, *Acinetobacter* species, *Pseudomonas aeruginosa*, and MDR *Enterobacteriaceae*, frequently receive inappropriate initial antimicrobial treatment

Clin Infect Dis 2010; 51:S29-S35

Diagnosis of Ventilator-Associated Pneumonia

Marin H. Kollef, M.D.

- **the narrowing of initially prescribed broad-spectrum antimicrobial regimens on the basis of microbiological data and the shortening of the duration of antibiotic treatment is an important component of de-escalation…**

NEJM 2006; 355:25

Conclusions

1. Delays in the initiation of appropriate therapy
can increase mortality of VAP and
thus therapy should not be postponed
for the purpose of performing diagnostic studies
in patients clinically unstable

2. The knowledge of local micro-organism patterns
and the optimization of initial empiric treatment
could be more important
than the methods used to obtain and cultivate pulmonary secretions
in reducing the morbidity and mortality in patients with VAP

3. The most recommended sample for the diagnosis of VAP
is the one that can be conducted most rapidly at each center
by a physician with experience in the technique

American Thoracic Society Documents

Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY AND THE INFECTIOUS DISEASES SOCIETY OF AMERICA WAS APPROVED BY THE ATS BOARD OF DIRECTORS, DECEMBER 2004 AND THE IDSA GUIDELINE COMMITTEE, OCTOBER 2004

Am J Respir Crit Care Med Vol 171. pp 388–416, 2005
DOI: 10.1164/rccm.200405-644ST
Internet address: www.atsjournals.org

IDSA

UPDATE IN PROGRESS*

*Projected Publication, Fall 2012

Σας ευχαριστώ πολύ