Management of Hospital-acquired Pneumonia

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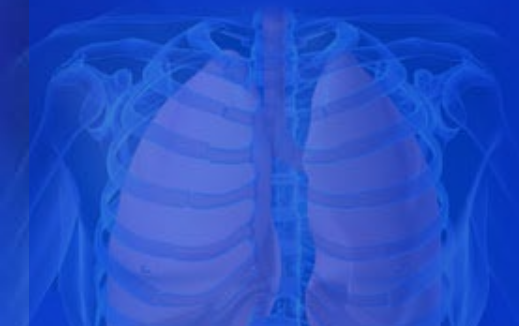
Introduction

- Definitions:
  - Hospital-acquired pneumonia (HAP) refers to the development of parenchymal lung infection after at least 48 hours of hospitalization
  - Ventilator-associated pneumonia (VAP) refers to the development of parenchymal lung infection after the patient has undergone intubation and received mechanical ventilation after at least 48 hours.
  - Health-care-associated pneumonia (HCAP) refers to pneumonia that develops inside or outside the hospital in the presence of risk factors for multi-drug-resistant pathogens because of prior contact with health-care environment

Niederman M, CID 2010

Epidemiology of HAP

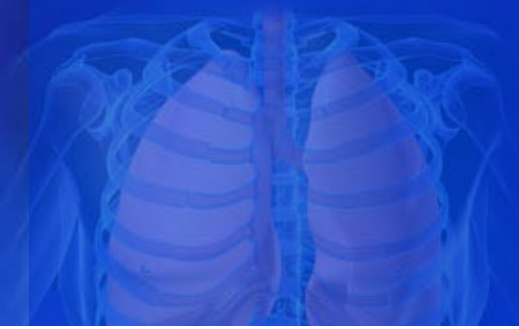
- HAP is the second most common nosocomial infection and accounts for approximately 25% of all infection in the Intensive Care Unit (ICU)



Torres A, et al. Int Care Med, 2009

Epidemiology of HAP

- The incidence of VAP is 10-30% among patient who require mechanical ventilation for more than 48 hours

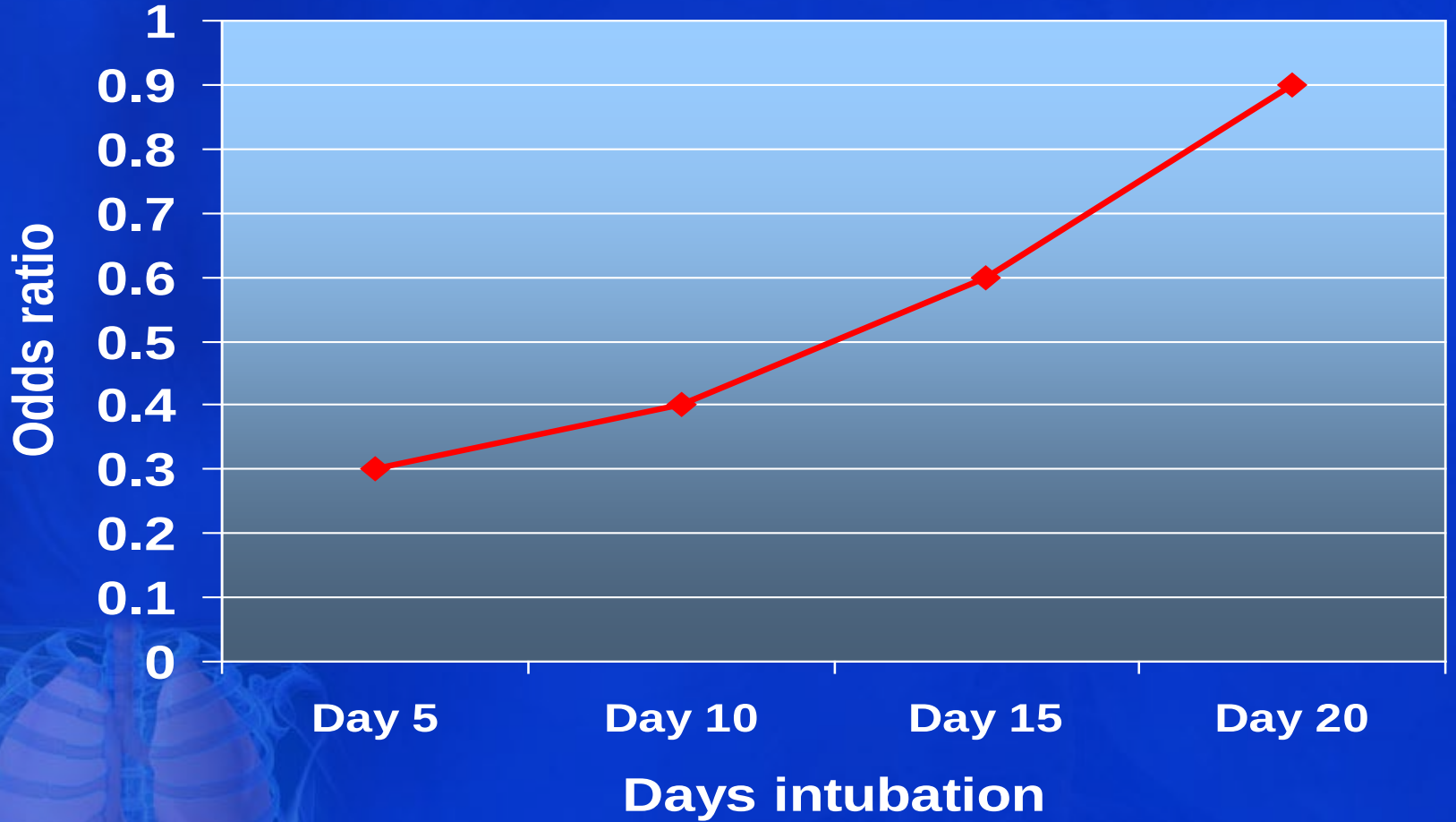


Chastre J. Am J Resp Crit Care Med, 2002

Epidemiology of HAP

- Probability to develop VAP is directly related to duration of mechanical ventilation and intubation

Probability of development of ventilator-associated pneumonia and duration of mechanical ventilation



Rello J, et al. Crit Care Med, 2003

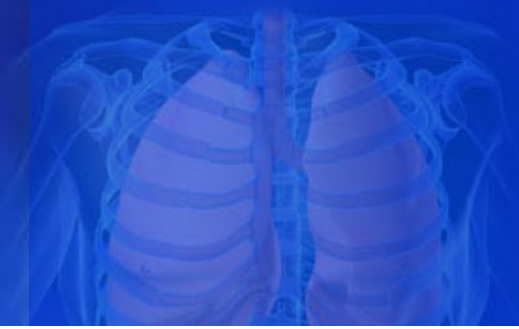
HAP Introduction

- The risk of VAP is highest early in the course of hospital stay, and estimated to be 3% per day during the first 5 days of ventilation, 2% per day during 5-10 days of ventilation, 1% per day during days afterwards.

Cook D. et al. Ann Int Med 1998; Niederman M. et al. AJRCCM, 2005

Epidemiology of HAP

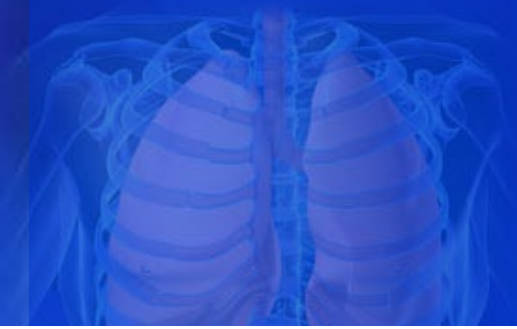
- Time of onset: Early vs. Late
  - For HAP-early onset: Diagnosed 2-5 day after hospitalization
  - For HAP-late onset: Diagnosed ≥ 5 days after hospitalization



Am J Res Crit Care Med, 2005

HAP Introduction

- Usually HAP will increase hospital stay by 7-9 days per patient, and has been reported to produce an excess cost of more than 49,000$ per patient.



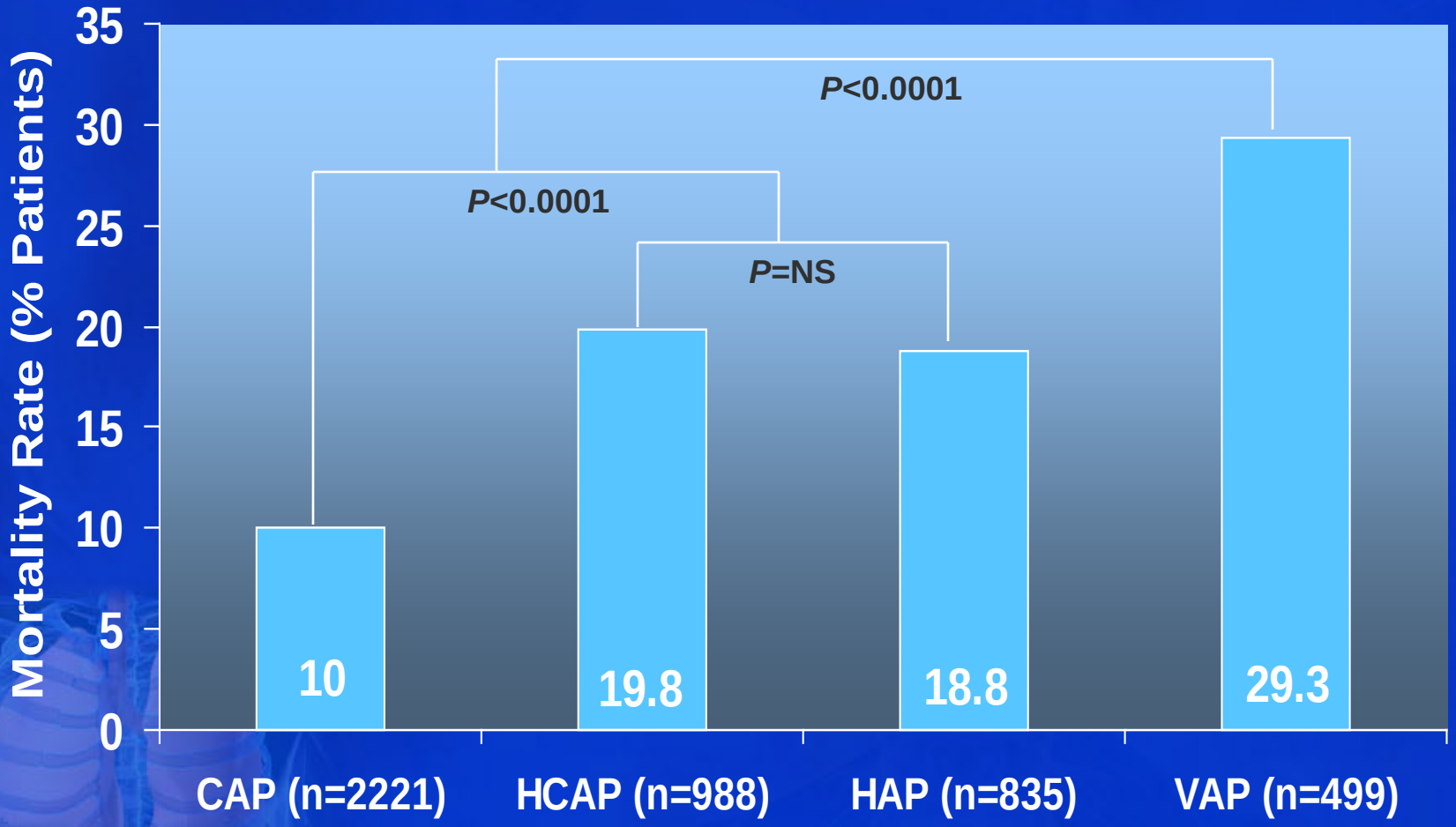
Chastre J. AJRCCM, 2002; Rello J, et al. Chest, 2002

Introduction:
Risk Factors for Development of HAP

- Patient related in:
  - Male sex
  - Pre-existing pulmonary disease
  - Multiple organ system failure

- Treatment related in:
  - Intubation
  - Enteral feeding

Mortality among patients with pneumonia (Percentage of hospital mortality by classification)



Am J Res Crit Care Med, 2005

Mortality Associated with Ventilator-Associated Pneumonia (VAP) in Unmatched Studies

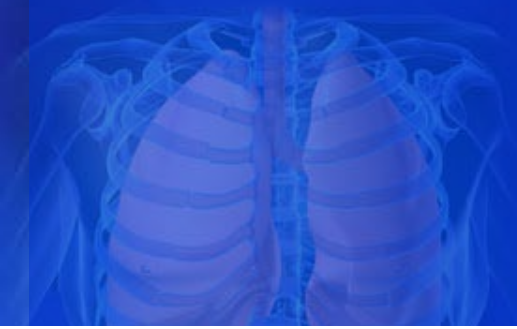
VAP related mortality has been demonstrated by Muscedere et al

Study (year)	# of patients	Population	Mortality in group without VAP, no (%)	Mortality in group with VAP, no (%)
Ibrahim et al (2001)	880	Medical-surgical	283 (32.2)	400 (45.5)
Tejada et al (2001)	103	Trauma	19 (18.8)	45 (43.5)
Moine et al (2002)	764	Medical-surgical	168 (22.0)	359 (47.0)
Kanafani et al (2003)	70	Medical-surgical	21 (30.0)	27 (39.0)
Warren et al (2003)	819	Medical-surgical	278 (34.0)	410 (50.0)
Alp et al (2004)	2402	Medical-surgical	288 (12.0)	1561 (65.0)
Myny et al (2005)	287	Medical-surgical	57 (20.0)	89 (31.0)
Noor et al (2005)	250	Medical-surgical	80 (32.0)	143 (57.1)
Moreno et al (2006)	2172	Medical-surgical	391 (18.0)	760 (35.0)
Hyllienmark et al (2007)	221	Medical-surgical	35 (16.0)	73 (33.0)
Suka et al (2007)	8892	Medical-surgical	889 (10.0)	1823 (20.5)
Valles et al (2007)	101	Medical-surgical	27 (27.0)	45 (45.0)
Van Der Kooi et al (2007)	1533	Medical-surgical	353 (23.0)	399 (26.0)
Cuellar et al (2008)	1290	Medical-surgical	181 (14.0)	497 (38.5)
Da Rocha et al (2008)	275	Medical-surgical	128 (46.5)	88 (32.1)
Total	20,059	…	3200 (16.0)	6719 (33.5)

Muscedere J, et al. CID, 2010

Microbiology

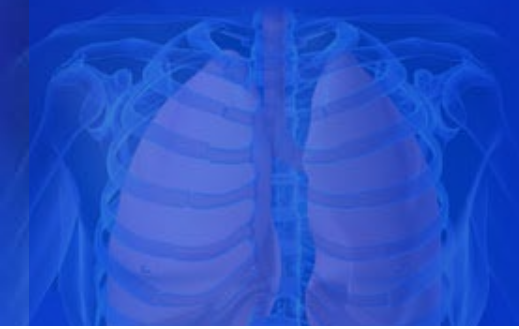
- HAP and VAP can be caused by a wide variety of bacteria that originate from the patient flora as the health care bacteria



Am J Res Crit Care Med, 2005

Microbiology

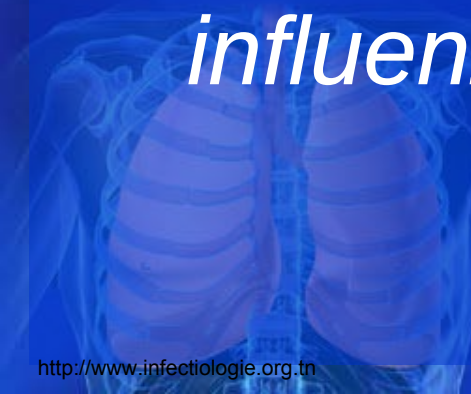
- In several studies, a consistent organisms caused nearly 80% of HAP and VAP episodes:
  1. *Staphylococcus aureus* 28%
  2. *Pseudomonas aeruginosa* 21.8%
  3. *Klebsiella spp* 9.8%
  4. *E.coli* 6.9%
  5. *Acinetobacter spp* 6.8%, and
  6. *Enterobacter spp* 6.3%



Jones R, CID, 2010

Microbiology

- The rest of HAP episodes with positive bacterial culture (>20% of all cases) are caused by *Serratia spp, Stenotrophomonas maltophilia,* and community-acquired pathogens (*Pneumococci, Haemophilus influenzae).*



Risk factors for MDR pathogens in HAP

Risk Factors for multidrug-resistant pathogens causing hospital-acquired pneumonia, healthcare-associated pneumonia, and ventilator-associated pneumonia

- Antimicrobial therapy in preceding 90 d
- Current hospitalization of 5 d or more
- High frequency of antibiotic resistance in the community or in the specific hospital unit
- Presence of risk factors for HCAP:
  - Hospitalization for 2 d or more in the preceding 90 d
  - Residence in a nursing home or extended care facility
  - Home infusion therapy (including antibiotics)
  - Chronic dialysis within 30 d
  - Home wound care
  - Family member with multidrug-resistant pathogen
- Immunosuppressive disease and/or therapy

Regional Incidence of Pathogens Isolated from Patients Hospitalized with Pneumonia in the Last 5 Years of the SENTRY Antimicrobial Surveillance Program (31,436 Cases)

Pathogens	Incidence, %			
	All regions	United States	Europe	Latin America
Staphylococcus aureus	28.0	36.3	23.0	20.1
Pseudomonas aeruginosa	21.8	19.7	20.8	28.2
Klebsiella species	9.8	8.5	10.1	12.1
Escherichia coli	6.9	4.6	10.1	5.5
Acinetobacter species	6.8	4.8	5.6	13.3
Enterobacter species	6.3	6.5	6.2	6.2
Serratia species	3.5	4.1	3.2	2.4
Stenotrophomonas maltophilia	3.1	3.3	3.2	2.3
Streptococcus pneumoniae	2.9	2.5	3.6	2.4
Haemophilus influenzae	2.7	2.5	3.7	1.3

Jones R, CID, 2010

Variations in Drug Susceptibility Rates between Hospital-Acquired Bacterial Pneumonia (HABP) and Ventilator-Associated Bacterial Pneumonia (VABP) Isolates from All SENTRY Antimicrobial Surveillance Program Regions, 2004-2008

Antimicrobial agent	Susceptibility, % (HABP / VABP)					
	Staphylococcus aureus	*Pseudomonas aeruginosa*	*Klebsiella* species	*Escherichia coli*	*Acinetobacter* species	*Enterobacter* species
Oxacillin	41/49[a]	…	…	…	…	…
Gentamicin	87/78	**72/66**	**82/71**	85/84	**25/18**	**87/81**
Levofloxacin	42/52[a]	60/58	**84/76**	72/74	**16/11**	88/89
Cefepime	41/49	**70/65**	**87/76**	91/87	**27/20**	93/91
Ceftazidime	41/49	**68/63**	**77/68**	**84/78**	12/10	62/64
Meropenem	41/49	**72/66**	>99/99	100/100	**58/46**	100/99
Piperacillin-tazobactam	41/49	**76/71**	**76/71**	86/82	**19/11**	71/70

NOTE. Boldface indicated ≥5% decrease in susceptibility for VABP isolates, compared with HABP isolates. More than a 10% lower susceptibility occurred with 3 drug-pathogen analyses.

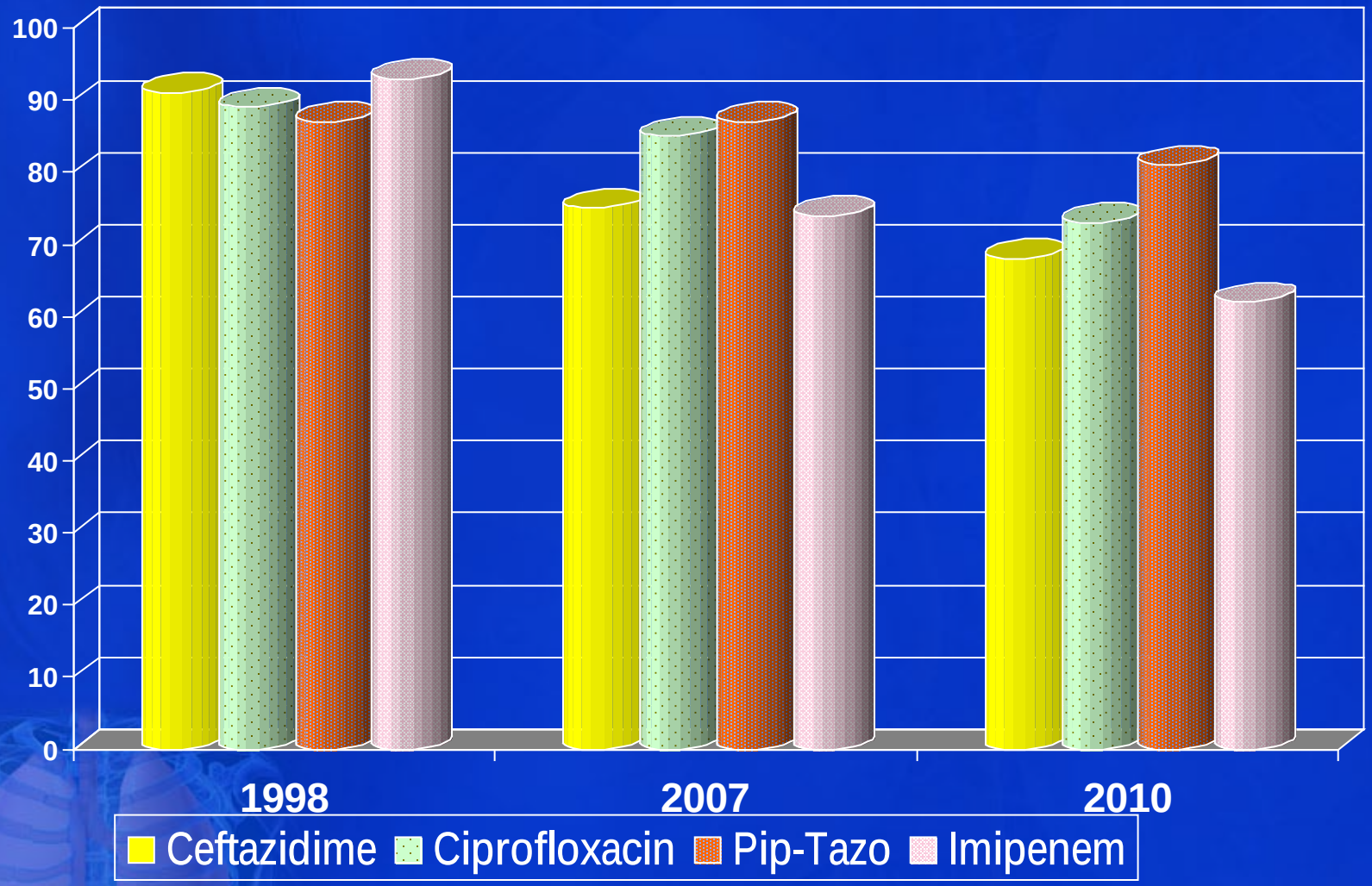
[a]VABP *S. aureus* isolates were generally more susceptible to oxacillin and fluoroguinolones.

Jones R. S Resp Crit Care Med, 2003; Gales A, et al. Diag Micro Inf Dis, 2002; Habon D, et al. Diag Micro Inf Dis, 2003

Comparison of Abx susceptibility of GNRs in KAMC Riyadh on 1998, 2007 and 2010

GNRs	Ceftazidime %			Ciprofloxacin %			Pip-Tazo %			Imipenem %		
	1998	2007	2010	1998	2007	2010	1998	2007	2010	1998	2007	2010
E.Coli	93	70	88	87	71	69	92	86	86	100	99	98
Klebsiella spp	68	69	69	91	79	66	83	81	68	100	98	94
Pseudomonas spp	91	75	68	89	85	73	87	87	81	93	74	62
Acinetobacter spp	43	17	25	52	19	22	70	15	21	98	28	31

Pseudomonas spp in KAMC



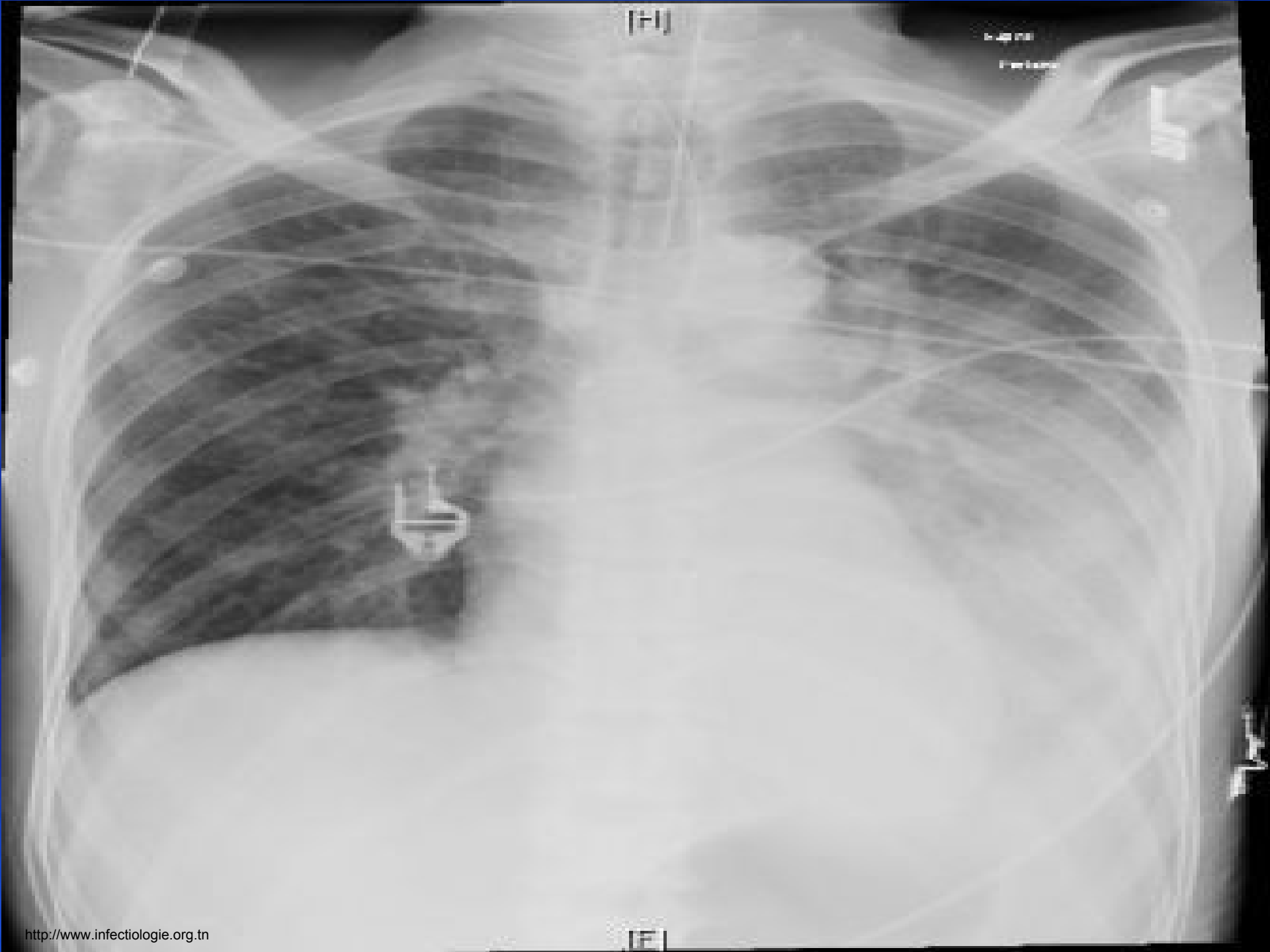
Diagnosis of HAP and VAP

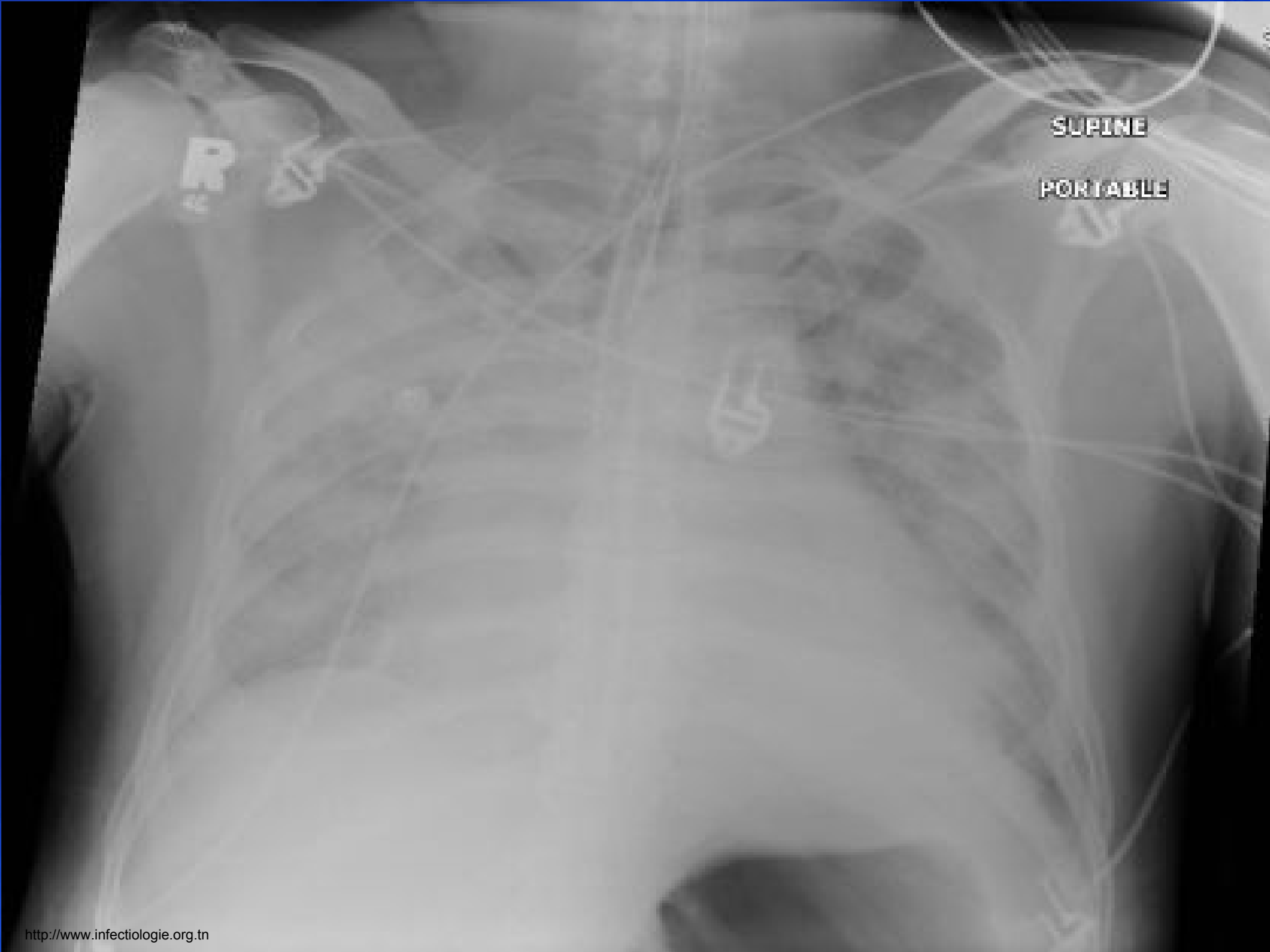
- Niederman. ATS + IDSA Guidelines, AJRCCM, 2005
- Retstein C. Can J Inf Dis Med Microbiol, 2008

Diagnosis

The diagnosis of HAP is suspected if the patient has a radiographic infiltrate that is new or progressive, along with clinical findings suggesting infection, which include the new onset of fever, leukocytosis, and decline in oxygenation. When fever, leukocytosis, purulent sputum, and a positive culture of sputum or tracheal aspirate are present without a new lung infiltrate, the diagnosis of nosocomial tracheobronchitis should be considered.

Nsier S. et al. Eur Resp J, 2002 / Niederman M. et al. Am J resp Crit Care Med, 2005





Microbiologic Diagnosis of HAP

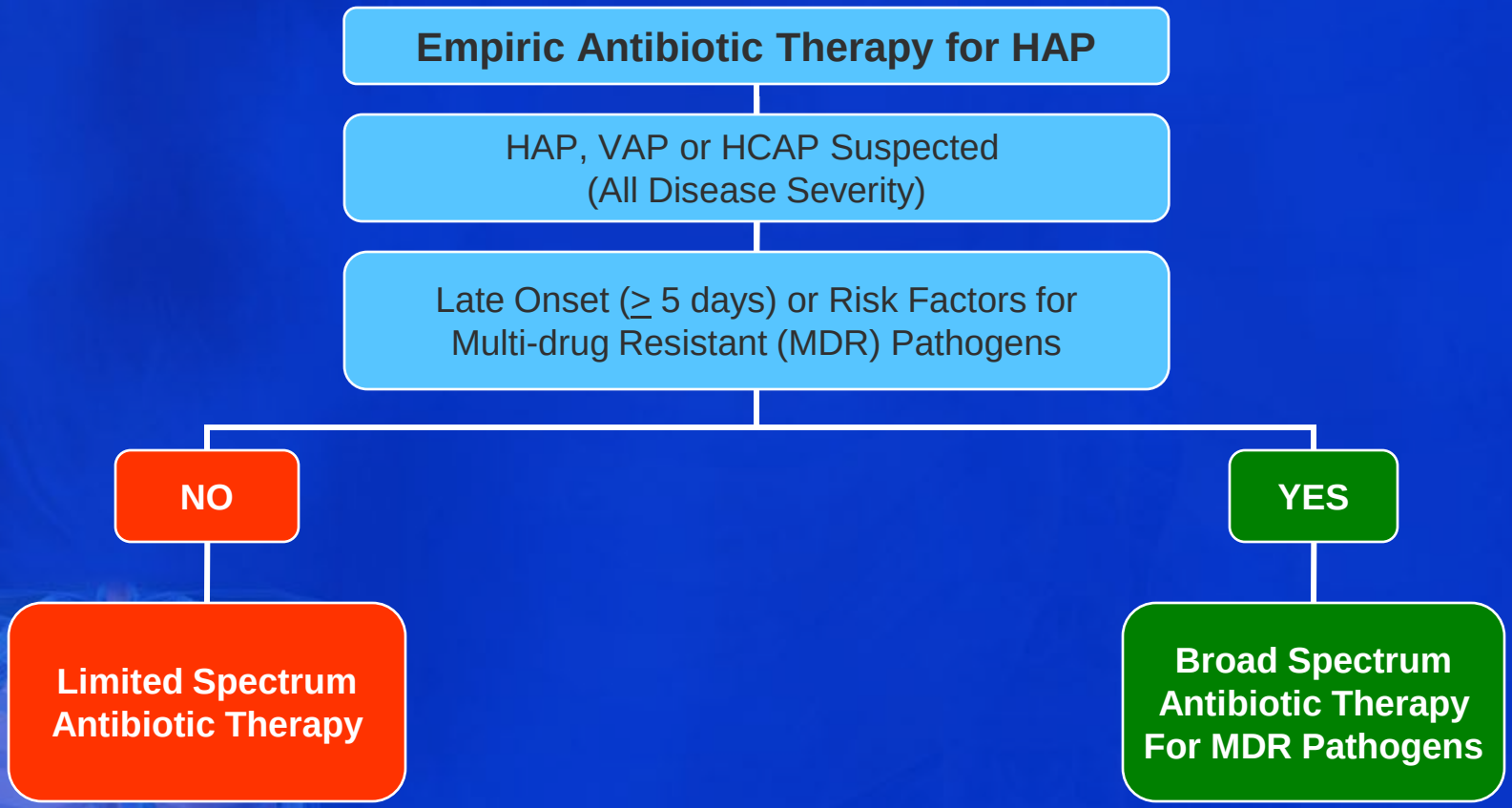
- Blood culture
- Samples of lower respiratory tract secretion should be obtained including:
  - Endotracheal aspirate
  - BAL, or
  - Protected specimen brush sample

- If there a complicating empyema, a pleural aspirate should be obtained.

Chastre J. AJRCCM, 2002; Rello J, et al. Chest, 2002

Treatment of HAP

Once the clinical decision has been made to initiate therapy, the overall approach to therapy is summarized in the following algorithm.



Niederman M. et al. AJRCCM, 2005

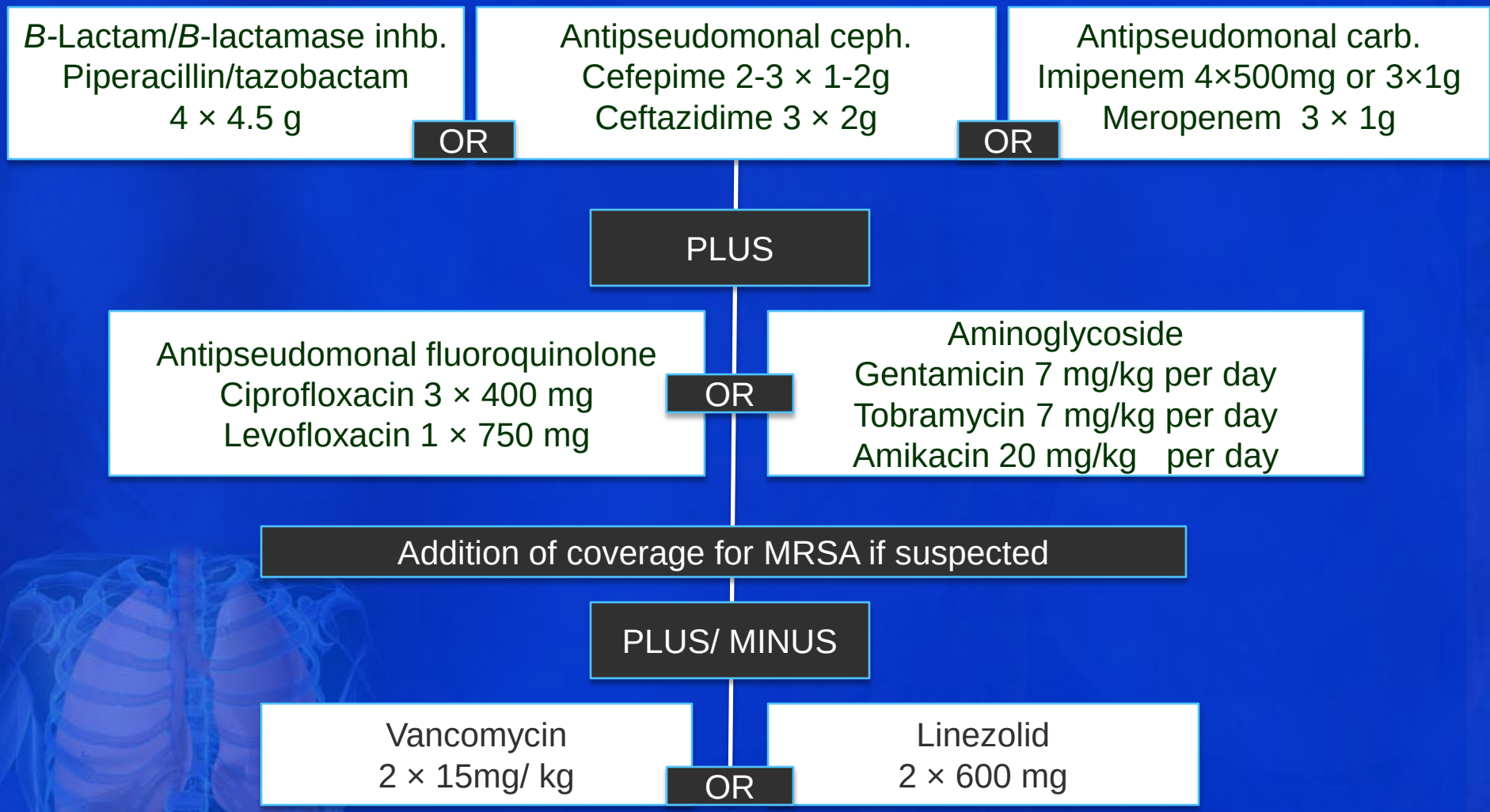
ATS/IDSA GUIDELINES FOR HAP 2005

Am J Respir Crit Care Med Vol 171. pp 388–416, 2005

American Thoracic Society Documents

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

IDSA Initial empiric AB therapy for HAP/VAP in patients with late-onset disease or risk factors from multidrug-resistant pathogens and all disease severity.



IDSA Initial empiric AB therapy for HAP/VAP in patients with NO risk factors for multidrug-resistant pathogens, early onset, and any disease severity

Ampicillin-Sulbactam
4 × 3g

OR

Ceftriaxone 1 × 2g

OR

Levofloxacin 1 × 750 mg
Moxifloxacin 1 × 400 mg
Ciprofloxacin 3 × 400 mg

OR

Ertapenem 1 × 1g

EUROPEAN GUIDELINES FOR HOSPITAL ACQUIRED PNEMONIA

Intensive Care Medicine (2009) 35:9-29

Defining, treating and preventing hospital acquired pneumonia: European perspective

1. European Respiratory Society (ERS),
2. European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and
3. European Society of Intensive Care Medicine (ESICM)

ESCMID 2009 Antimicrobial treatment of early onset pneumonia without any additional risk factors

Aminopenicillin plus *B*-lactamase-inhibitor
Amoxi-Clav 3 × 2.2g
Amp- Sulb 3 × 3g

OR

2nd G. Cep.
Cefuroxime 3 ×1.5g

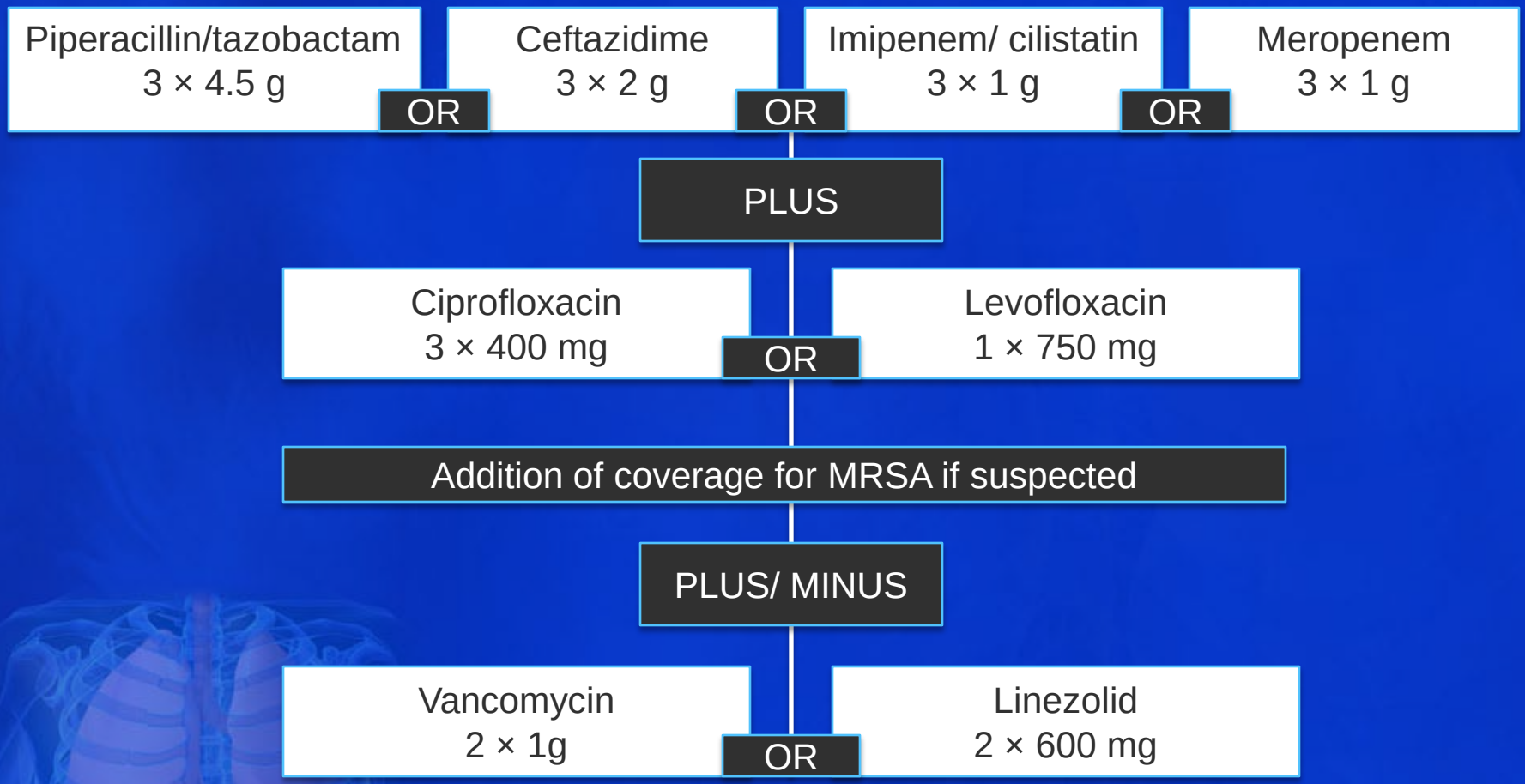
OR

3rd G. Cep.
Cefotaxime 3 × 2g
Ceftriaxone 1 × 2g

OR

Respiratory quinolone (not ciprofloxacin)
Levofloxacin 1 × 750 mg
Moxifloxacin 1 × 400 mg

ESCMID Antimicrobial treatment of late onset pneumonia



Initial Empirical Antimicrobial Treatment

Initial Empirical Antimicrobial Treatment for Patient with Hospital-Acquired, Ventilator-Associated, or Health Care-Associated Pneumonia, according to the 2005 American Thoracic Society and Infectious Disease Society of America Guidelines

Potential Pathogen	Recommended antibiotic treatment
No risk factors for MDR, early onset, and any disease severity	Ceftriaxone; levofloxacin, moxifloxacin, ciprofloxacin; ampicillin-sulbactam; or ertapenem
Streptococcus pneumoniae	…
Haemophilus influenzae	…
MSSA	…
Antibiotic-susceptible, enteric gram-negative bacilli	…
Escherichia coli	…
Klebsiella pneumoniae	…
Enterobacter species	…
Proteus species	…
Serratia marcescens	…
Late onset disease or risk factors for MDR pathogens and all disease severity	Combination antibiotic therapy: antipseudomonal cephalosporin (cefepime or ceftazidime), antipseudomonal carbapenem (imipenem or meropenem), or ß-lactam or ß-lactamase inhibitor (piperacillin-tazobactam) plus antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) plus linezolid or vancomycin (if risk factors present)
Pseudomonas aeruginosa	…
K. pneumoniae (ESBL)	…
Acinetobacter species	…
Legionella pneumophila	…
MRSA	…

NOTE. ESBL, extended-spectrum ß-lactamase; MDR, multidrug resistant, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *S. aureus*

Torres A, et al. CID, 2010

Initial Intravenous Adult doses of Antibiotics

Initial Intravenous, adult doses of antibiotics for empiric therapy of hospital-acquired pneumonia, including ventilator-associated pneumonia, and health care-associated pneumonia in patients with late-onset disease or risk factors for multidrug-resistant pathogens

Antibiotics	Dosage*
Antipseudomonal cephalosporin	
Cefepime	1-2g every 8-12h
Ceftazidime	2g every 8h
Carbapenems	
Imipenem	500mg every 6h or 1g every 8h
Meropenem	1g every 8h
ß-Lactam/ ß-lactamase inhibitor	
Piperacillin-tazobactam	4.5g every 6h
Aminoglycosides	
Gentamicin	5-7mg/kg per d[+]
Tobramycin	7mg/kg per d[+]
Amikacin	20mg/kg per d[+]
Antipseudomonal quinolones	
Levofloxacin	750mg every d
Ciprofloxacin	400mg every 8h
Vancomycin	15mg/kg every 12h[‡]
Linezolid	600mg every 12h

*Doses are based on normal renal and hepatic function/ [+]Trough levels for gentamicin and tobamycin should be less than 1µg/ml, and for amikacin they should be less than 4-5µg/ml/ [‡]Trough levels for vancomycin should be 15-20µg/ml

Niederman M. et al, AJRCCM, 2005

Duration of Antibiotic Therapy

- Pugh R. et al., have done a meta-analysis for 8 studies (1703 patients) to compare short (7 days) and prolonged antibiotic therapy for HAP and VAP.

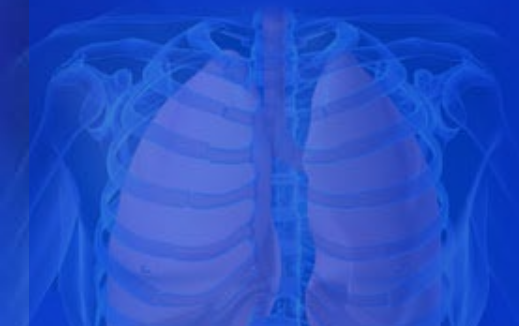
- They concluded that, for patients with HAP and VAP not due to non-fermenting gram-negative bacilli (particularly *P.aeruginosa* and *Acinetobacter* species) a short fixed course (7-8 days) antibiotic therapy may be more appropriate than prolonged course (10-15 days).

Pugh R. et al. Cochrane Database, 2011

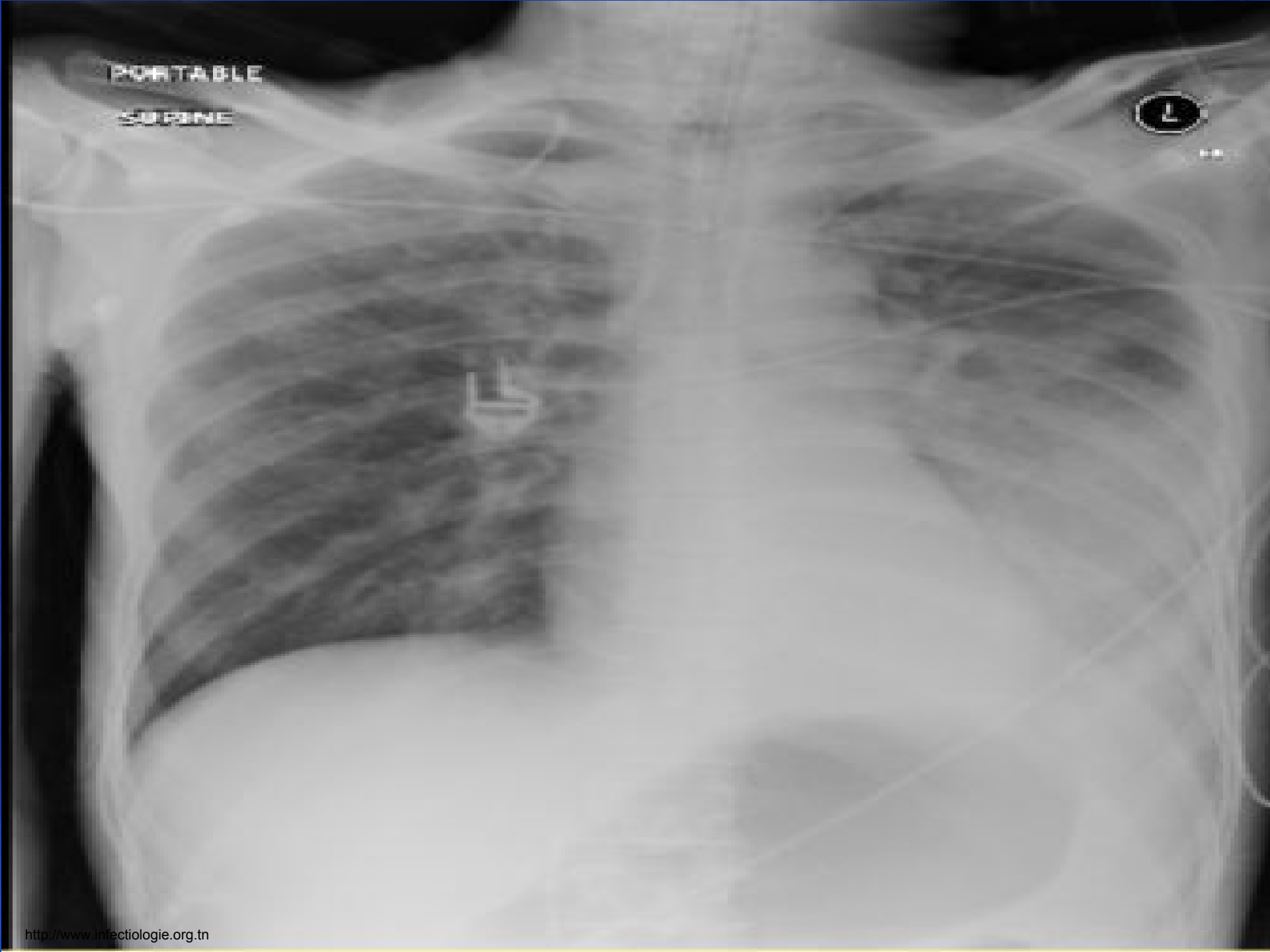
Other Therapeutic modalities

- Although promising, antibiotics aerosolization for treatment of VAP has not yet entered the armementarium for daily practice.

- The results of recent investigations emphasize its potential contribution as an interesting adjunctive therapy to intravenous antibiotics, but the clinical impact of such strategy has not yet been definitely established.



Chastre J. et al. CID, 2010 / Wood G. Expert Rev Anti Infect Ther, 2011



Thank You

May 2012