# NOSOCOMIAL PNEUMONIA- APPROACH, PREVENTION & MANAGEMENT

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# DEFINITIONS

- Hospital Acquired Pneumonia (HAP)
  - *≥48 h after hospital admission (excluding an incubating infection)*
  - *Early onset HAP vs Late onset HAP*

- Ventilator Associated Pneumonia (VAP)
  - *≥48-72 h after endotracheal intubation*
  - *Early onset VAP vs Late onset VAP*

- Health Care Associated Pneumonia (HCAP)
  - *hospitalized in an acute care hospital ≥ 2days in preceeding 90 days;*
  - *nursing home or long-term care facility resident;*
  - *recent iv chemotherapy, or wound care within past 30 days*
  - *attended a hospital or hemodialysis clinic*

*MMWR Recomm Rep 2004;53(RR-3):1-36*

# EPIDEMIOLOGY

- 15% of all hospital associated infection → 2nd common nosocomial infections worldwide
- 9 - 27% of all ICU acquired infection & > 50% of antibiotic prescribed
- Mechanical ventilation ↑ risk by 6 - 21 times & incidence of VAP increases with duration of ventilation
- Risk of VAP highest early in the course of hospital stay
  - 3%/day for first 5 days,2%/day from 5 to 10 days & 1%/day thereafter
- Increases hospital stay (7-9 days/pt) & extra cost burden ($40,000/pt)
- Mortality rate 24%-70% & Attributable mortality: 33-50%
- Crude mortality rate >20 % if high risk pathogen involved .
- Mortality in Pt with VAP twice than pts without VAP
- At PGI there were 77 episodes of infection in 67 of the 201 patients.

  Pneumonia was the most common infection (46/201 patients, 23%), which constituted 59.7% of all nosocomial infections.

*CDC Guideline for Prevention of Healthcare Associated Pneumonias 2003*
*Am J Respir Crit Care Med 2005;171;388-416*
*Crit Care Med 2005;33(10):2184-93.*
Journal of Infection (2006) 53, 98e105

# MORTALITY RATES & RISK RATIOS FOR DEATH ATTRIBUTABLE TO NOSOCOMIAL PNEUMONIA IN MATCHED CASE-CONTROL STUDIES

| First Author | Ref. | Diagnostic Criteria | Type of Patient | No. of Cases | Crude Mortality | | Attributable Mortality (%) | Risk Ratio | p Value |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | Cases (%) | Controls (%) | | | |
| Craig | 83 | Clinical | ICU | 54 | 20.4 | 5.6 | 14.8 | 3.6 | < 0.01 |
| Fagon | 81 | PSB + BAL | Ventilated | 48 | 54.2 | 27.1 | 27.1 | 2.0 | < 0.01 |
| Cunnion | 84 | Clinical | Surgical | 20 | 55.0 | 5.0 | 50.0 | 23.2* | < 0.002 |
| | | | ICU | 20 | 55.0 | 7.5 | 47.5 | 15.1* | < 0.002 |
| Baker | 44 | PSB/BAL | Medical | 62 | 24.0 | 24.0 | 0 | 1 | NS |
| Papazian | 85 | PSB | ICU | 85 | 40.0 | 38.8 | 1.2 | 1.3 | NS |
| Heyland | 86 | PSB/BAL | Trauma | 177 | 23.7 | 17.9 | 5.8 | 1.3 | NS |
| Bercault | 87 | PSB | Ventilated | 135 | 41.0 | 14.0 | 27.0 | 2.7* | 0.03 |

*Definition of abbreviations*: BAL = bronchoalveolar lavage; ICU = intensive care unit; NS = not significant; PSB = protected specimen brush.

* Odds ratio.

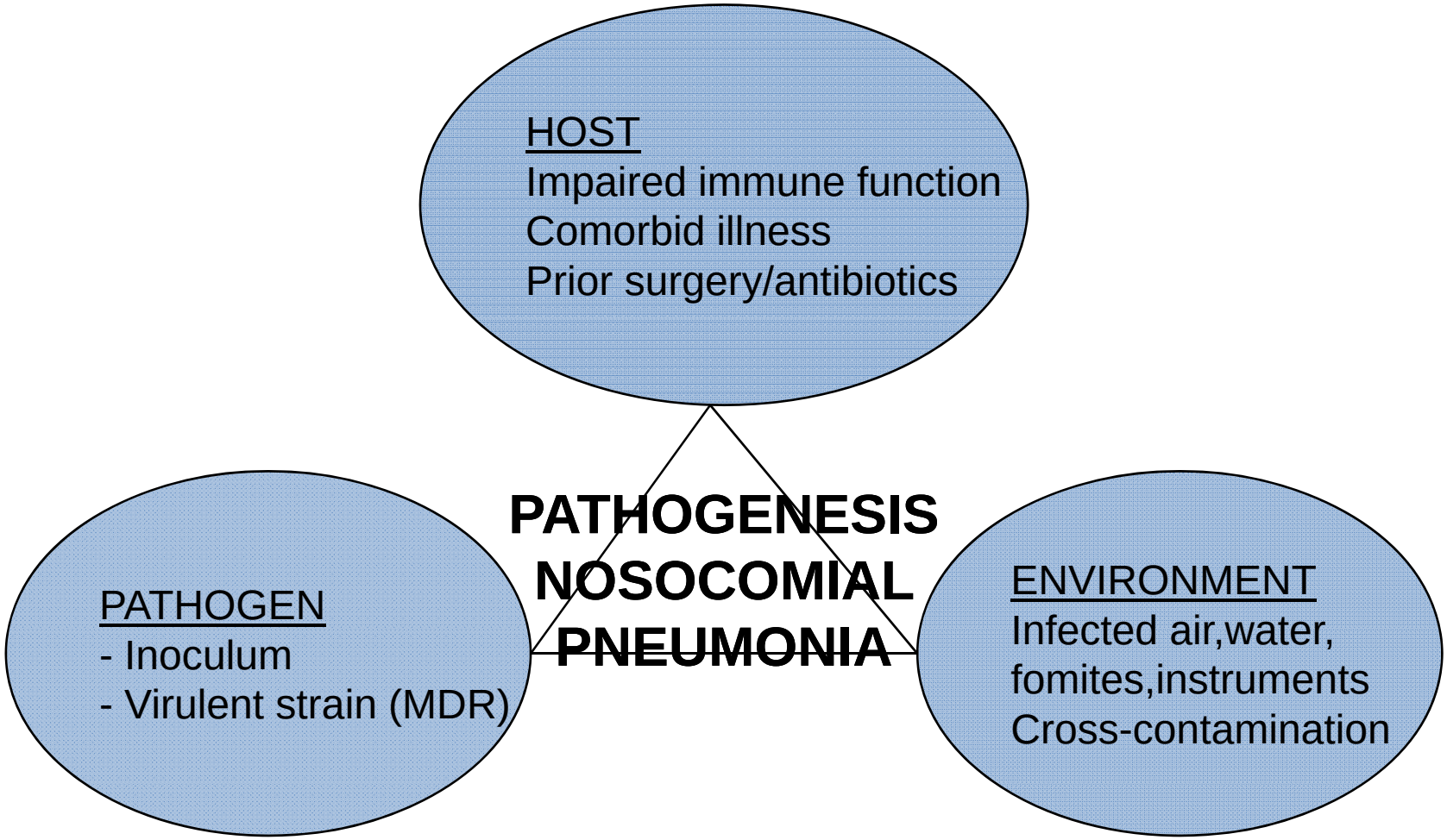
*Am J Resp Crit Care Med 2002: 165;867-903*

# INDIAN SCENARIO

| Study | Yr | Study design | Dur$^{n}$ | Diagnostic criteria | Type of pt | CFU/ ml | N | Incidence of HAP / VAP(%) | Mortality (%) (Attributable mortality) |
|---|---|---|---|---|---|---|---|---|---|
| SGPGI, Lucknow | 03 | Prospective | 1 yr | Clinical +PSB +BAL | SICU | $>10^3$ | 241 | 53.9 | 47.3 (72.3) |
| Escort, Delhi | 03 | Prospective | 3 m | Clinical | CSIC U | - | 952 | 2.6 | 16 |
| GMC, Mumbai | 04 | Prospective | 1 yr | Clinical | CCU | - | 51 | 47 | 37 |
| AIIMS | 05 | Retrospective | 1 yr | Protected BAL | ICU | $>10^4$ | 478 | 35.77 | - |
| KMC, Manipal | 07 | Prospective | 9 m | Clinical ETA* | MICU | $>10^5$ | 97 | 45.4 | - |
| Pgi chandigarh | 06 | Prospective | 1.5 yr | Clinical + ETA | ICU | $>10^5$ | 201 | 23% | - |

*Endotracheal aspirate

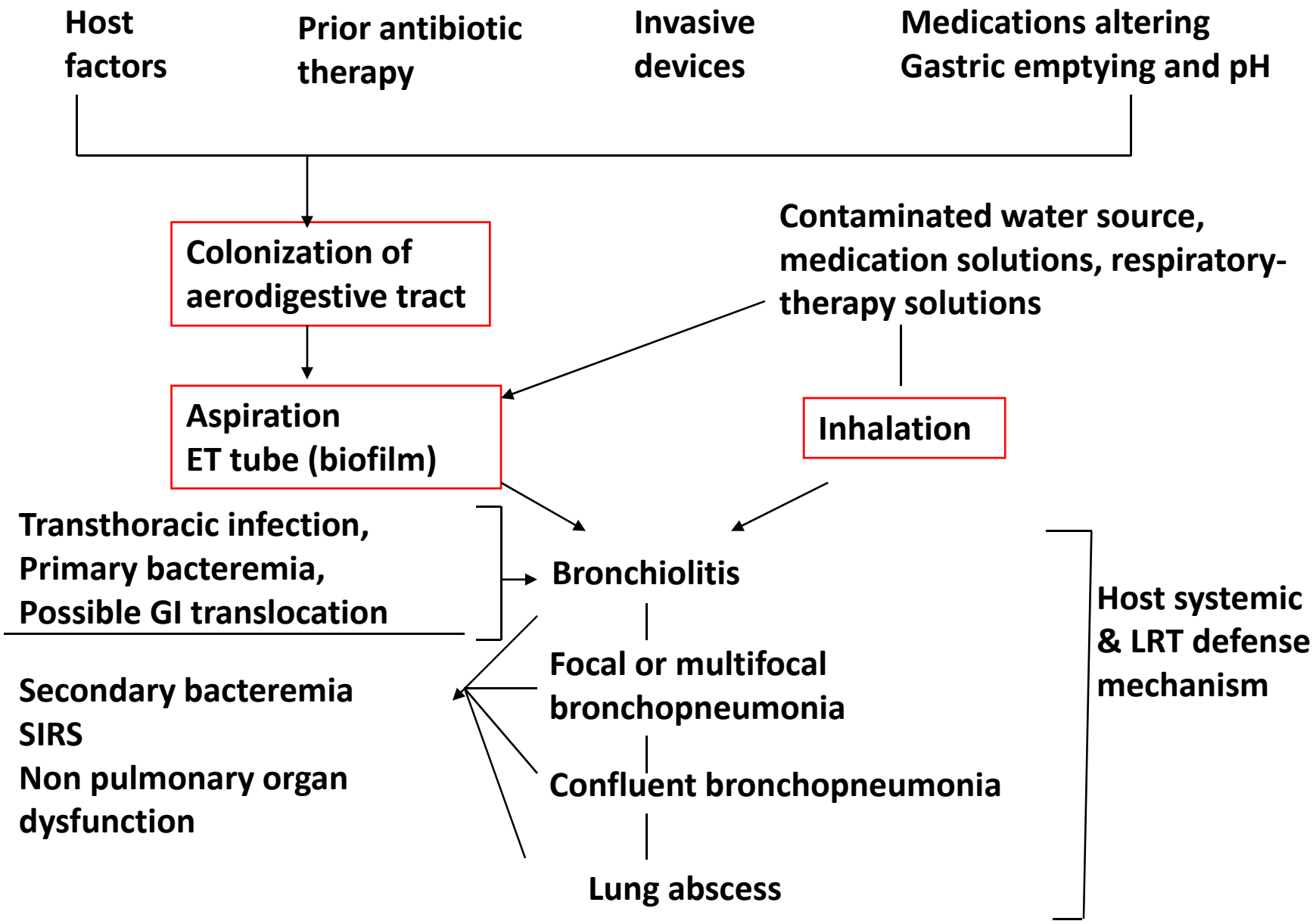
*Indian J Med Res 2003:118;229-235*
*Chest / 126 / 4 / Oct, 2004 Supplement*
*IJCCM 2004*
*Indian J Med Res 2005:121;63-64*
*Ann Thorac Med 2007;2:52-55*


HOST
Impaired immune function
Comorbid illness
Prior surgery/antibiotics
PATHOGENESIS
NOSOCOMIAL
PNEUMONIA
PATHOGEN
- Inoculum
- Virulent strain (MDR)
ENVIRONMENT
Infected air,water,
fomites,instruments
Cross-contamination

# RISK FACTORS

| Host Factors | Intervention Factors | Infection Control related factors |
|---|---|---|
| Age ≥ 60 yrs<br>ARDS<br>COPD, pulmonary disease<br>Coma / impaired consciousness<br>Burns, trauma<br>Organ failure<br>Severity of illness<br>Large-volume gastric aspiration<br>Serum albumin <2.2g/dl<br>Gastric colonization & pH<br>Upper respiratory tract colonization<br>Sinusitis | Endotracheal intubation<br>$H_2$ blockers ± antacids<br>Paralytic agents, continuous iv sedation<br>ICP monitoring<br>Mechanical ventilation > 2days<br>PEEP<br>Frequent ventilator circuit changes<br>Reintubation<br>Nasogastric tube<br>Supine head position<br>Transport out of the ICU<br>Prior antibiotic or no antibiotic therapy | Cross contamination |

*Am J Respir Crit Care Med 2002:165:867-903*




*NEJM 1999;340:627-634*

# MICROBIOLGY

- Different spectrum than CAP
- Different in different regions
- Organisms depend on:
  - Time of onset (Early Vs Late)
  - Severity of illness
  - Presence of Risk factors

| **Severe NP** |
| --- |
| Admission to ICU |
| Respiratory failure (need of ventilator) |
| Rapid CxR progression |
| Evidence of sepsis or end organ dysfunction |

# MICROBIOLGY

| Mild/Moderate HAP with anytime onset, no risk factors or early onset severe HAP | Early Severe HAP with risk Factors or late onset severe HAP |
|---|---|
| ➢ *Enteric GNB*<br>*Enterobactor species*<br>*E.coli*<br>*Klebsiella species*<br>*Proteus species*<br>*Serratia marcescens*<br>*H. influenzae*<br>➢ *MSSA*<br>➢ *S. pneumoniae* | *Pseudomonas aeruginosa*<br>*Acinetobactor species*<br>*MRSA* |

*Am J Respir Crit Care Med 1995;153:1711-1725*

# *Risk factors*

| *Pathogens* | Risk factors |
|---|---|
| Anaerobes | Abdominal surgery, aspiration, foreign body |
| S.aureus | Coma, head trauma, DM, renal failure, iv drug abuse, influenza |
| Legionella | Corticosteroid, malignancy, neutropenia, chemotherapy, renal failure, contaminated coolers/towers |
| Pseudomonas | Long ICU stay, corticosteroids, underlying lung disease, prior abx use |
| Aspergillus /Candida | Immunocompromised pts, neutropenia, organ transplant |
| Viruses | Seasonal (Influenza, parainfluenza, adenovirus, RSV) |

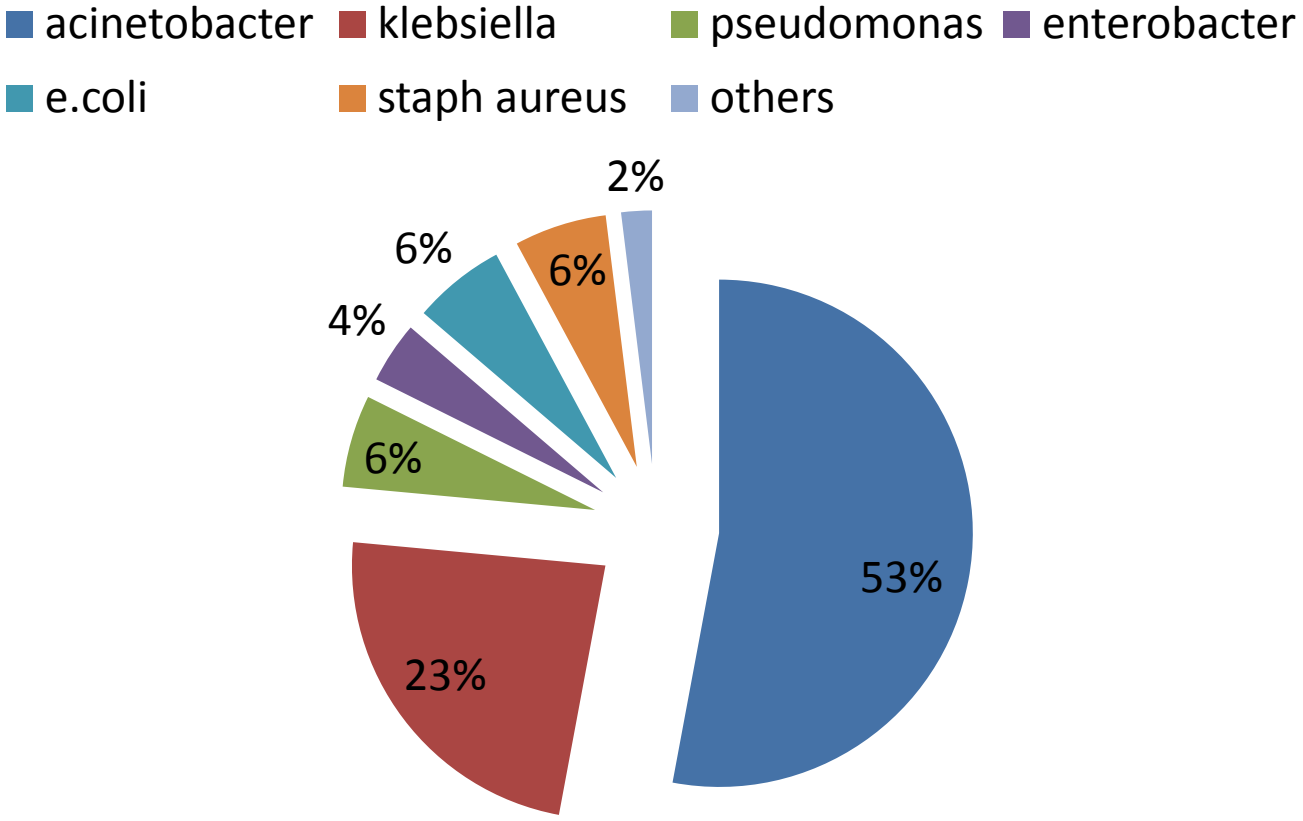
*Am J Respir Crit Care Med 1995;153:1711-1725*

# % incidence of organisms causing VAP in US & INDIA (tertiary care centre)

| | USA | AIIMS | PGI |
|---|---|---|---|
| P. aeruginosa | 24.4 | 40.1 | 32 |
| Acinetobactor spp | 7.9 | 44.8 | 44 |
| Enterobacteriaciae* | 14.1 | 14 | 6 |
| H.influenzae | 9.8 | - | - |
| S.maltophilia | 1.7 | - | - |
| $MSSA_+$ MRSA | 20.4 | 1.04 | 10 |
| Streptococci | 8.0 | - | - |
| S.pneumoniae | 4.1 | - | - |
| Neisseria | 2.6 | - | - |

*Arch Bronconeumol 2005;41:439–456*
*Indian J Med Res 2005;21:63-64*
Journal of Infection (2006) 53, 98e105

# % incidence of organisms causing VAP at RICU, PGI (Oct09-Jan10)



# Emergence of selected MDR bacteria

| Pathogen | Mechanism of resistance | Resistant Antibiotics |
|---|---|---|
| P. aeruginosa | Multiple efflux pumps | Piperacillin, ceftazidime, cefepime, carbapenem, aminoglycosides,fluroquinolones |
| | Decreased expression of OprD* | Imipenem (but not beta-lactams) |
| | Plasmid mediated metallobeta-lactamase | Carbapenems , ceftazidime, cephalosporins |
| Enteric GNB (Klebsiella, E.coli, Enterobactor) | Extended beta-lactamases | Cephalosporins, aztreonam,a minoglycoside |
| | AmpC-type enzyme | Above + carbapenems |
| Acinetobactor | IMP-type metalloenzymes | Carbapenems |
| | OXA-type carbapenemase | |
| MRSA | mecA coded Penicillin binding proteins | Beta-lactams |

*Outer membrane porin channel

# Risk factors for MDR pathogens

1. Antimicrobial therapy in preceding 90 days
2. Current hospitalization of ≥ 5 days
3. High frequency of antibiotic resistance in the community or in the specific hospital unit
4. 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 antibiotics)
   - Chronic dialysis within 30 days
   - Home wound care
   - Family member with MDR pathogen
5. Immunosuppressive disease and/or therapy
6. Acinetobacter baumanni, pseudomonas aeruginosa
7. HA-MRSA, CA-MRSA

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

# DIAGNOSIS OF HAP

Clinical + Chest X ray + Microbiology

- New onset fever
- Purulent expectoration
- Tachycardia
- Tachypnoea
- Leukocytosis / Leukopenia
- Need of higher $FiO_2$

- Clinical diagnosis
  - high sensitivity, low specificity
  - empiric treatment

- Microbiology
  - to identify etiology
  - de-escalate therapy
  - decide duration of therapy

# CXR

- AP films difficult to interpret in ICU
  - 26% of infiltrates by CT scan missed by CXR
  - If underlying CXR abnormal (e.g. ARDS), locating new process difficult

- Sensitivity
  - Air bronchogram 58-83%
  - New/worsening infiltrate 50-78%

- Many pneumonia mimics

| | |
|---|---|
| Aspiration | Alveolar hemorrhage |
| Atelectasis | Pulmonary edema |
| ARDS | Pleural effusion |
| Pulmonary infarcts | BOOP |

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

# METHODS

Proximal Airways

**Sputum**
**Tracheal aspirate**

Simple
No expertise required
Non-quantitative culture
- high sensitivity
- low specificity

NPV 93% for ETA $<10^3$ CFU/ml

Distal Airways

**Non bronchoscopic**

**PSB**
**BAL**
**Protected BAL**

ADV:
Non invasive
Low cost
No expertise required
Less complication

DISADV:
Blind procedure
Sampling error

**Bronchoscopic**

**PSB**
**BAL**
**Protected BAL**

ADV:
Proper sampling from desired bronchus
Less contamination

DISADV
Hypoxia
Expertise
Expensive

## Sputum Stain

- Only 33% of pts colonized →HAP
- Recovery of pathogen from tracheal secretion not diagnostic for pneumonia (exception: Legionella)
- Gram stain
  - If no bacteria, <5% probability HAP
  - If >10/oil immersion field - 50% HAP
- DDx purulent sputum:
  - sinusitis, tracheobronchitis, aspiration

## BAL fluid stain

- Cell Counts

< 50% neutrophils has 100% NPV

- Gram stain

| Presence of bacteria | LR* |
|---|---|
| Blind Bronchial aspirate | 2.1 |
| Mini BAL | 5.3 |
| BAL | 18 |

Likelihood ratio

# Sensitivity & Specificity

| **Methods** | **Quantitative culture** | **Sensitivity** | **Specificity** |
|---|---|---|---|
| Endotracheal aspirate | $\geq 10^5$CFU/ml | 76±9% | 75±28% |
| Bronchoscopy | | | |
| BAL | $10^4$-$10^5$CFU/ml | 73±18% | 82±19% |
| PSB | $\geq 10^3$ CFU/ml | 66±19% | 90±15% |
| Blind Bronchial suction | $\geq 10^4$CFU/ml | 74-97% | 74-100% |
| Blind mini BAL | $\geq 10^4$CFU/ml | 63-100% | 66-96% |
| Blind PSB | $\geq 10^3$ CFU/ml | 58-86% | 71-100% |

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

# BRONCHOSCOPY

- Quantitative cultures important
- Positive culture: $10^3$ or $10^4$ CFU/ml
- Prior antibiotic exposure often causes false negatives
- Invasive lower airway sampling consistently results in changes to antibiotic management among patients with suspected VAP. Despite these changes, however , regular use of bronchoscopy for the diagnosis of VAP does not alter mortality since it does not directly affect the initial antibiotic prescription

**Crit Care Med 2005;33:46–53**

- Culture results below threshold may represent early disease
  - 30% of patients with $>10^2$ but $< 10^3$ CFU eventually developed HAP

•Improves decision making

•De-escalalation of antibiotics

•Stopping antibiotics

•Associated with lower mortality rate

*Chest 1999;115:1076*

# Modified Clinical Pulmonary Infection Scale (CPIS)

| CPIS Point | 0 | 1 | 2 |
|---|---|---|---|
| Tracheal secretions | Rare | Abundant | Abundant + Purulent |
| CxR infiltrates | No infiltrate | Diffuse | Localized |
| Temp, $^0$C | ≥36.5 and ≤38.4 | ≥38.5 and ≤38.9 | ≥39 or ≤36 |
| Leukocytes count, /mm$^3$ | ≥4000 to ≤11000 | <4000 and >11000 | <4000 and >11000 + band forms ≥ 500 |
| PaO2/Fio2, | >240 or ARDS | | ≤240 and no evidence of ARDS |
| Microbiology (Gram stain & culture) | No growth or <1+ | >1+ growth with same pathogen stained | >1+ growth with same pathogen stained > 1+ |

A CPIS score > 6 → good correlation with pneumonia diagnosed bronchoscopically or non-bronchoscopically

Sensitivity 77% & Specificity 44%

Modified CPIS score of ≤6→ good prediction to discontinue antibiotic therapy after 3 days in pts with low suspicion for pneumonia and who are otherwise clinically improving

# Biomarkers to diagnose VAP

- sTREM-1
  - Triggering receptor expressed on myeloid cells
  - Neutrophils express TREM-1 on exposure to infected tissue
  - Gibot et al studied soluble TREM-1 in BAL fluid by rapid immunoblot assay in 148 mechanically ventilated pts with suspected pneumonia
    - Sensitivity 98% & specificity 90%

    *NEJM 2004;350:451–8*
  - Nonspecific to bacterial or fungal pneumonia

- Procalcitonin

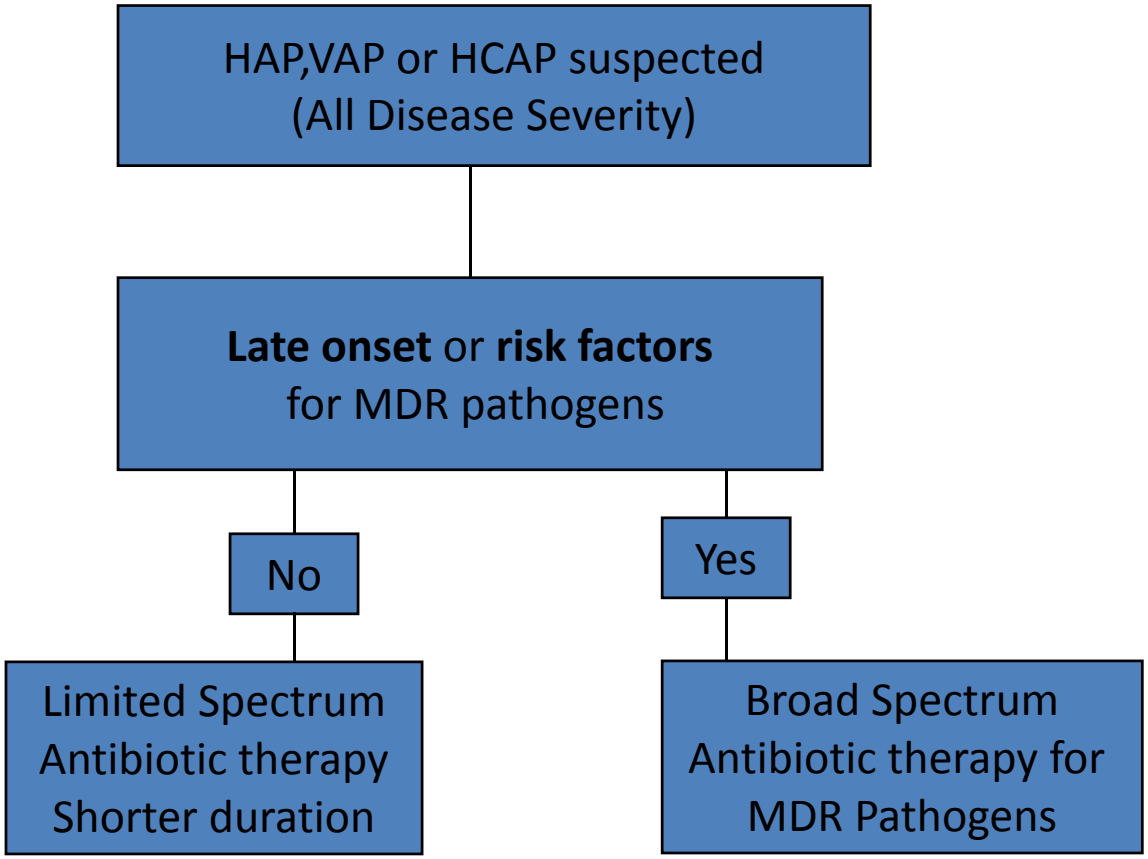
- C-Reactive Protein

# APPROPRIATE INITIAL EMPIRIC ANTIBIOTIC TREATMENT

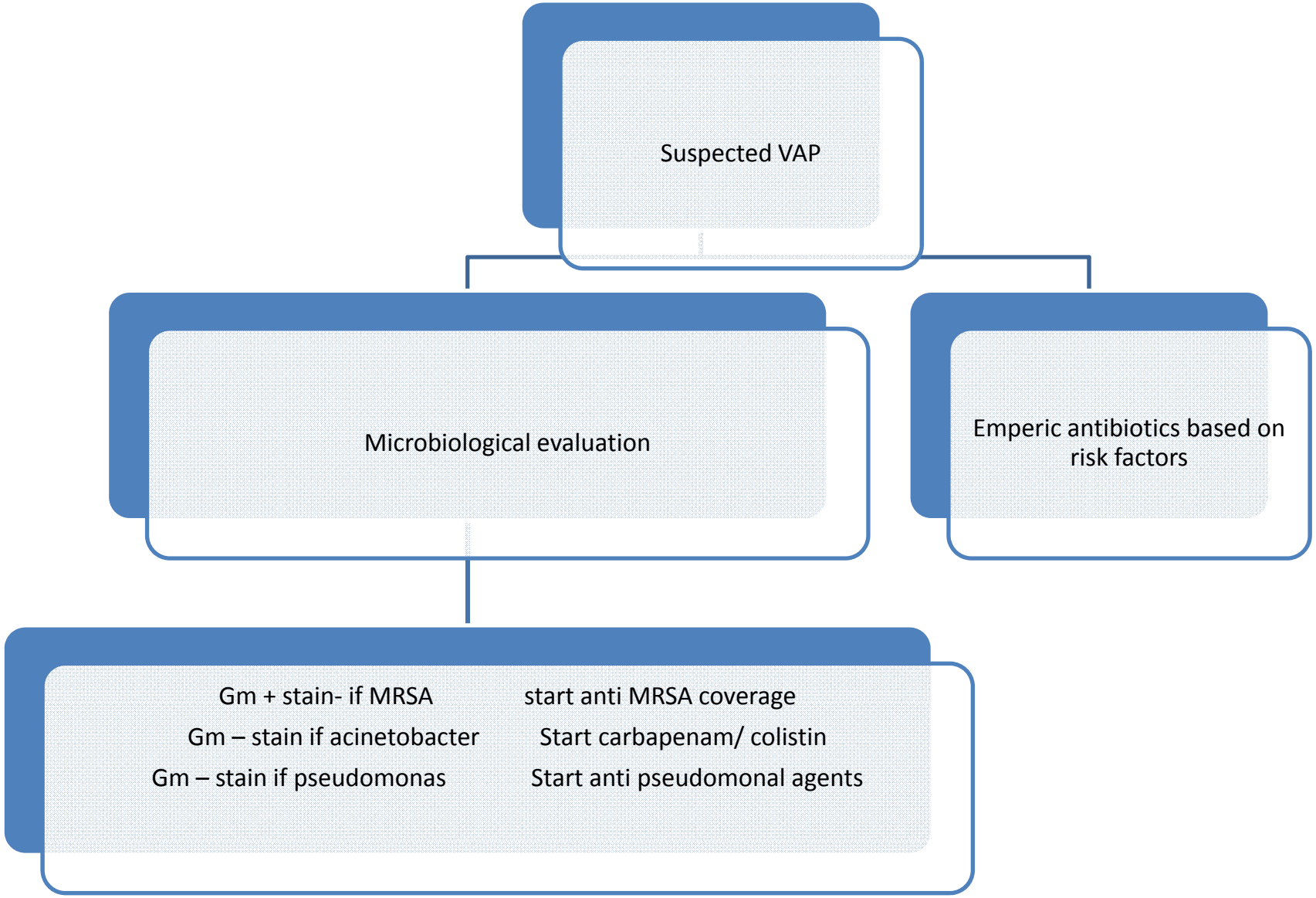
- INAPPROPRIATE INITIAL EMPIRIC ANTIBIOTIC TREATMENT
- De-escalation
- Assessment for risk for MDR organisms
- Colonization pressure→ the higher the MRSA colonization rate in ICU, the higher the MRSA acquisition risk by other patients.

**Infect Control Hosp Epidemiol 2000;21:718-23.**

# Empiric antibiotic therapy

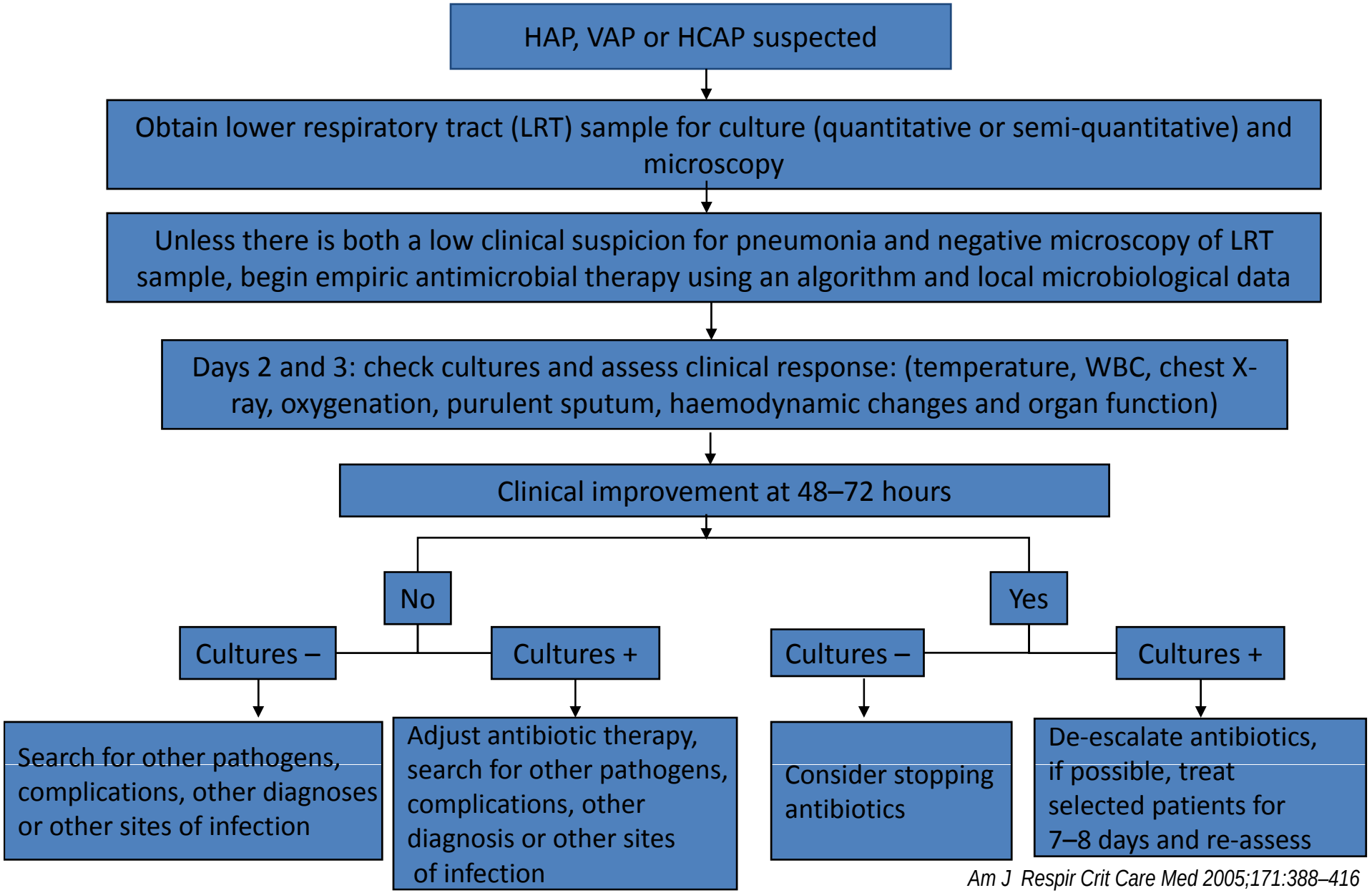



*Am J Respir Crit Care Med 2005;171:388–416*


Suspected VAP
Microbiological evaluation
Emperic antibiotics based on risk factors
Gm + stain- if MRSA
start anti MRSA coverage
Gm – stain if acinetobacter
Start carbapenam/ colistin
Gm – stain if pseudomonas
Start anti pseudomonal agents

| Patient category | Antibiotic Treatment in Pt with VAP |
|---|---|
| No risk for MDR organisms | Ceftriaxone<br>Levofloxacin, moxifloxacin,cipro<br>Ampicillin/sulbactam<br>Ertapenem<br>Amoxicillin-Clavulanate |
| At risk for : Pseudomonas aeruginosa | Initial emperic antibiotic tratment<br>Imipenam/cilastatin: 2 hr infusion<br>Meropenam: 3 hr infusion<br>Doripenam: 4hr infusion<br>Piperacillin- tazobactum:4 hr infusion<br>Ceftazidime/cefipime: continous infusion combination with ciprofloxacin |
| MRSA | Linezolid<br>Vancomycin: continous infusion to trough levels of 15-20 microgm/ml |
| Acinetobacter baumanni | Carbapenam<br>Sulbactam<br>Colistin |
| Previously treated with | recommendation |
| Beta lactam<br>Ciprofloxacin<br>Carbapenam | Carbapenam<br>Avoid imipenam<br>Piperacillin- tazobactam |

# Management strategies summary




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

# Pharmacokinetics-Pharmacodynamics considerations

- HOST FACTORS sepsis→ third spacing
  renal failure
  shock→ fluid therapy
  hypoalbuminemia
- ANTIBIOTICS FACTOR
  time dependent (infusion) → beta lactams, carbapenams & glycopeptides
  concentration dependent (OD)→ FQS, AG, macrolides

# CURRENT ATS-IDSA RECOMMENDATIONS FOR ANTIBIOTIC THERAPY

- Use short duration (5 days) of aminoglycoside combined with a β-lactam to treat *P. aeruginosa* pneumonia (III)
- HCAP treated for MDR pathogen regardless of onset of pneumonia (II)
- De-escalate on results of LRT cultures & patient's clinical response
- Shorter duration of antibiotic therapy (7–8 days) for uncomplicated HAP(I)
- If ESBL+ Enterobacteriaceae isolated – avoid monotherapy with 3$^{rd}$ gen. cephalosporins; use carbapenems (II)
- Aerosolised antibiotics (tobramycin, polymyxin) may have value as adjunctive therapy (II)
- Linezolid can be used as alternative to vancomycin for MRSA VAP (II)

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

# BSAC RECOMMENDATIONS FOR ANTIBIOTIC THERAPY

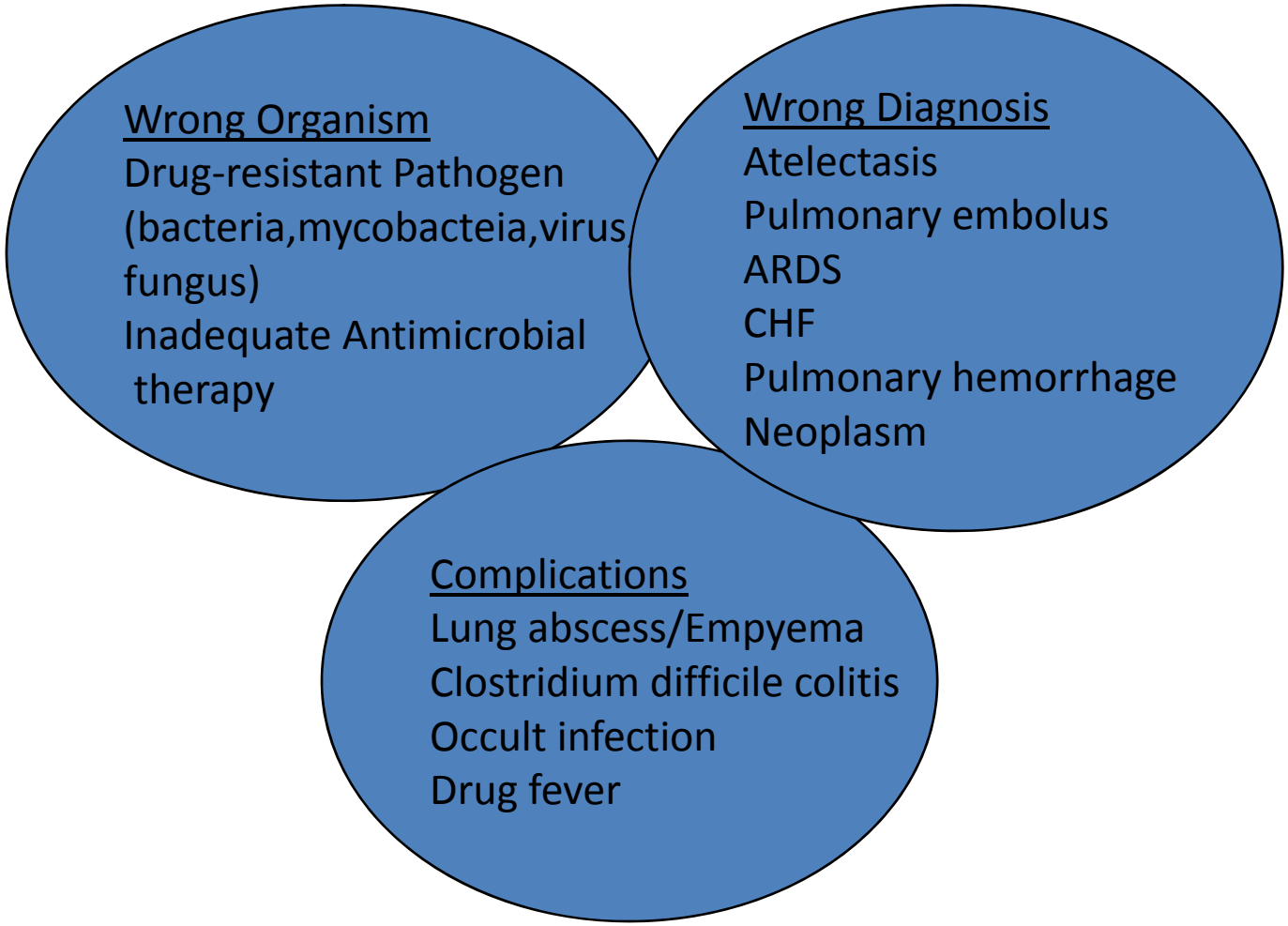
- Duration for empirical therapy in patients who have responded should no longer than 8 days.
- Antimicrobial monotherapy should be used wherever possible for the management of bacterial HAP.

Journal of Antimicrobial Chemotherapy (2008) 62, 5–34

# RESPONSE TO THERAPY

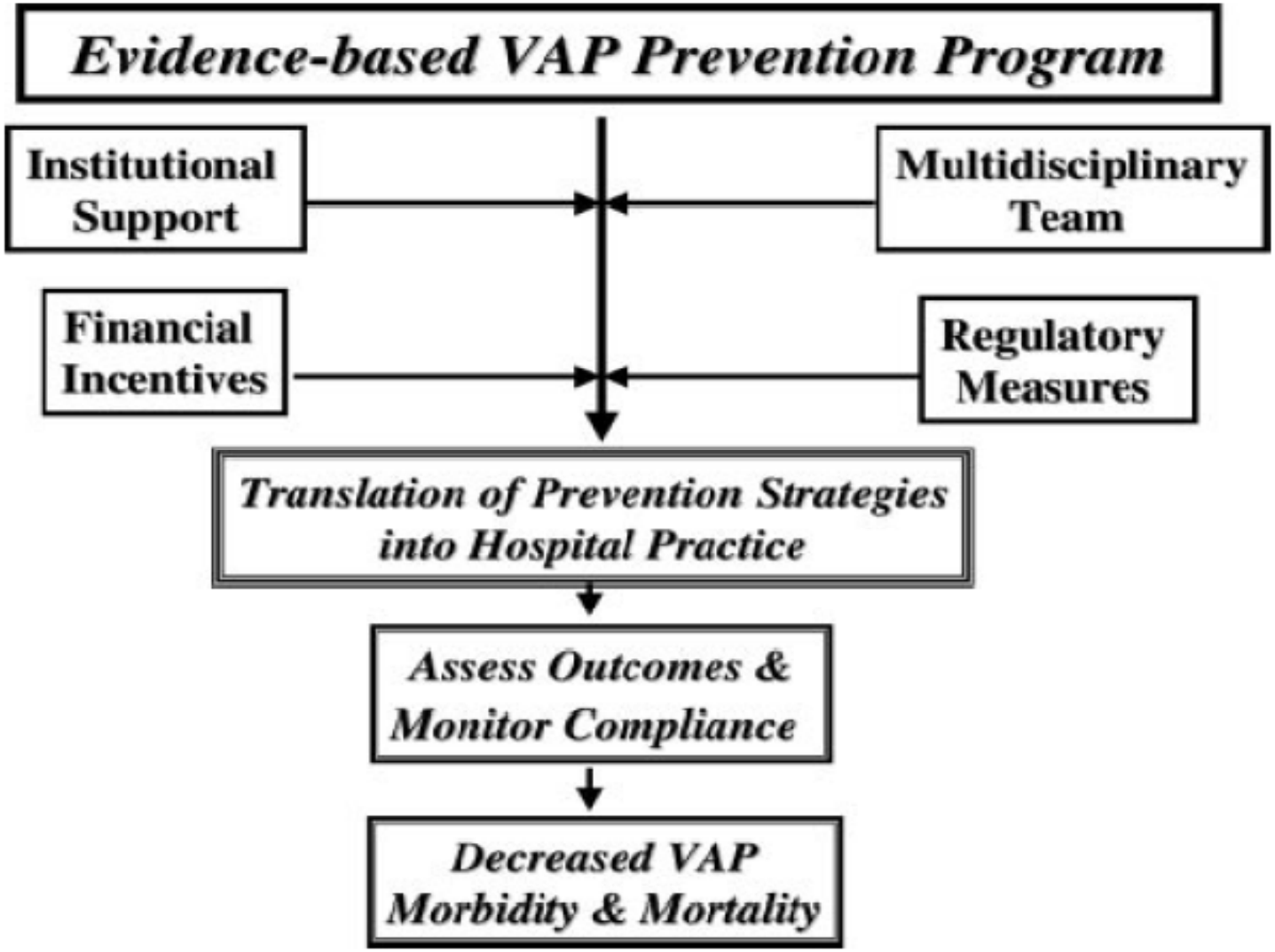
| Parameter | Variables | Outcome |
|---|---|---|
| Clinical | Temperature<br>Total leukocyte count<br>$PaO_2/FiO_2$<br>CXR<br>“CPIS” | Improvement<br>Resolution<br>Delayed Resolution<br>Relapse<br>Failure<br>Death |
| Microbiologic | Serial tracheal aspirate/BAL culture | Eradication<br>Superinfecion<br>Recurrent infection<br>Persistence |

# Assessment of Nonresponders



# PREVENTIVE STRATEGIES


*CHEST 2006; 130:251–260*




*CHEST 2006; 130:251–260*

# Recommended Strategies

| Risk Factors | Intervention/strategy | Evidence |
|---|---|---|
| Infection control measures | Staff education; staffing levels<br>Hand washing<br>Surveillance of ICU infection | Level I<br>Level I<br>Level II |
| Intubation & mechanical ventilation | Avoid intubation/reintubation<br>NIV use (selected pts)<br>Orotracheal intubation & orogastric tubes preferred<br>Continuous aspiration of subglottic secretions<br>ET tube cuff pressure≥20 cm $H_2O$<br>No change of ventilatory circuit<br>Sedation vacation | Level I<br>Level I<br>Level II<br>Level I<br>Level II<br>Level II<br>Level II |
| Stress bleeding prophylaxis | Increases HAP/VAP<br>(Sucralfate<H2-blocker or PPIs) | Level I |

Am J Respir Crit Care Med 2005;171(4):388–416

# Recommended Strategies

| Risk Factors | Intervention/strategy | Evidence |
|---|---|---|
| Aspiration, body position & enteral feeding | Semirecumbent position ($30^0$-$45^0$)<br>Enteral nutrition preferred over parenteral nutrition | Level I<br>Level I |
| Modulation of colonization | Oral care with chlorhexidine (selected pts) [more data reqd for routine use]<br>Selective Decontamination of Digestive tract has reduced VAP, but concern about MDR pathogen<br>Prophylactic antibiotic for 24 hrs at the time of emergent intubation but routine use not advocated at present | Level I<br>Level I<br>Level I |
| Transfusion | Leukocyte depleted RBCs reduce VAP | Level I |
| Hyperglycemia | Intensive insulin therapy (RBS <180mg/dl) | Level II |

# PRONOVOST PROTOCOAL

- Hand wash with soap before procedure
- Skin preparation with chlorhexidine
- Full body  drape
- Avoid femoral line
- Remove unnecessary lines

# Closed versus open suctioning

- No one superior
- Safety of health care worker better in closed suction
- the closed-tracheal suction system did not reduce VAP incidence, even for exogenous pneumonia.

***Crit Care Med 2005; 33:115–119***

# Antibiotic Rotation/Cycling

- Altering antibiotic pattern/class leads to decline in resistance
- A class of antibiotic or specific antibiotic is stopped for a defined period and then re-introduced
- A 4 year study on 3455 ICU patients :

  Rotation of antibiotics and Restriction of Ceftazidime and ciprofloxacin led to decrease in incidence of VAP from 22 to 16% (p=<01)

*Gruson. Am J Respir Crit Care Med 2000;162;837:43*

# RECOMMENDATIONS FOR HEALTH CARE WORKER

- Data from two cohort studies showed that education programs are effective in reducing the incidence of VAP by 51%and 56%, respectively.

J Hosp Infect 2004; 57: 223–7.

Crit Care Med 2002; 30: 2407–12.

- PPE
- Pneumococcal vaccine

Journal of Antimicrobial Chemotherapy (2008) 62, 5–34

# “Ventilator Bundle”

- Four components:
  1. Elevation of the head of the bed to between 30 and 45 degrees,
  2. Daily “sedation vacation”
  3. Peptic ulcer disease (PUD) prophylaxis
  4. Deep vein thrombosis (DVT) prophylaxis (unless contraindicated).

# CARRY HOME MESSAGE

- Nosocomial Pneumonias are  frequent & associated with excess mortality →initiate prompt appropriate & adequate therapy
- Pathogens distinct from one hospital to another, specific sites within the hospital, and from one time period to another
- Either semi-quantitative or quantitative culture data → appropriate for management of HAP /VAP/HCAP
- Avoid overuse of antibiotics by focusing on accurate diagnosis, tailoring therapy to recognized pathogen and shortening duration of therapy to the minimum effective period
- Apply prevention strategies aimed at modifiable risk factors