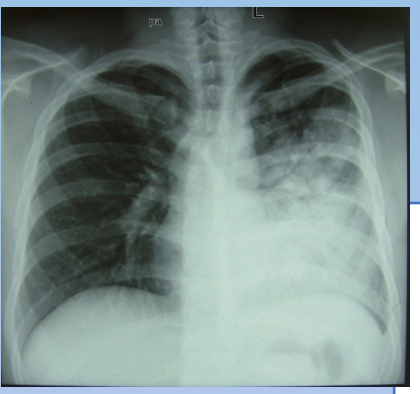
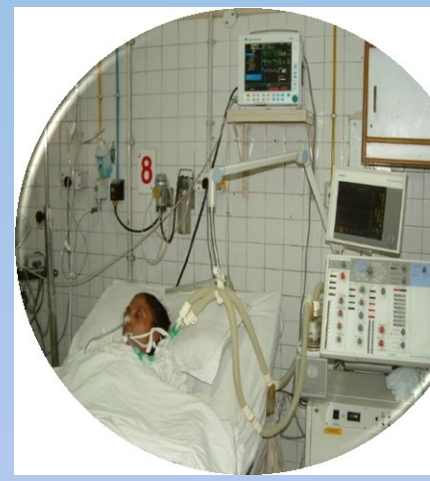


# Management of a patient with Pneumonia




**Prof. G.C. Khilnani**

*M.D. FCCP(USA), FAMS, FNCCP, FICP,FICCM, FISDA*

Chairman, PSRI Institute of Pulmonary, Critical Care and Sleep Medicine

Pushpawati Singhania Hospital & Research Institute, New Delhi

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All India Institute of Medical Sciences
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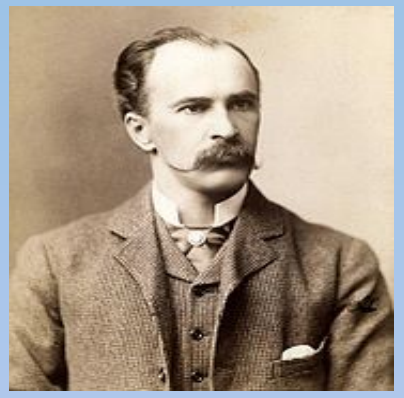
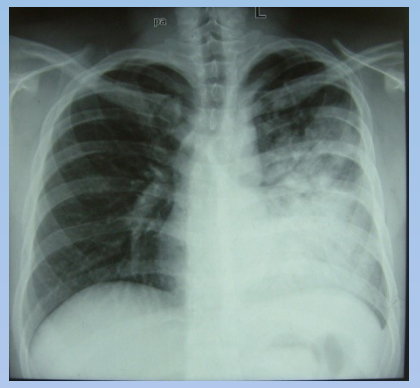


# Sir William Osler

*Principles and Practice of Medicine 1901*



The most widespread and fatal of all the acute diseases, pneumonia, is now ‘’**The Captain of the Men of death**’’…

**More than a century later !!!**

Most common cause of infection related mortality in USA

- Affects 4000000 (4 million) adults per year
- Rate is 8-15/1000 per year
- 6$^{th}$ leading cause of death in USA

National center of Health Statistics 1992

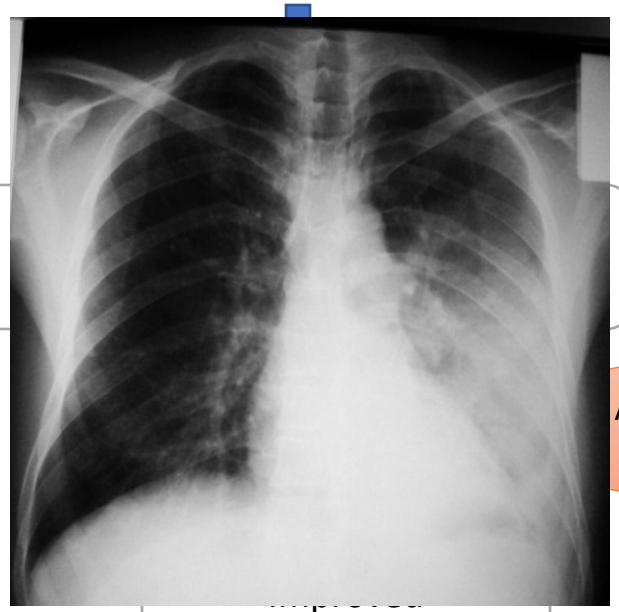
# Major changes during last two decades

*Niederman, M. S. Chest 2007;131:1205-1215*

- Changing spectrum of etiologies (viruses, resistant microorganisms including MRSA)
- Increasing resistance of pathogens to antimicrobial drugs
- Increased number of people in elderly age group and immunosuppressed

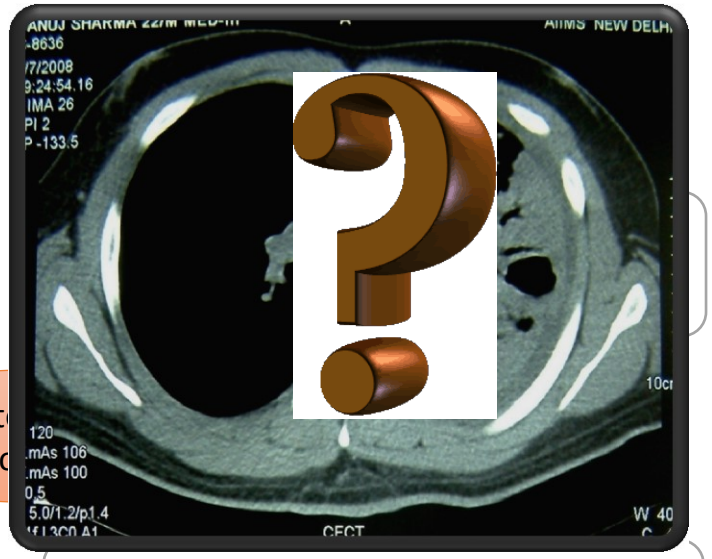
# Community Acquired pneumonia

25/Male, R/O Delhi
Fever, Cough and Expectoration: 7d
Came to OPD



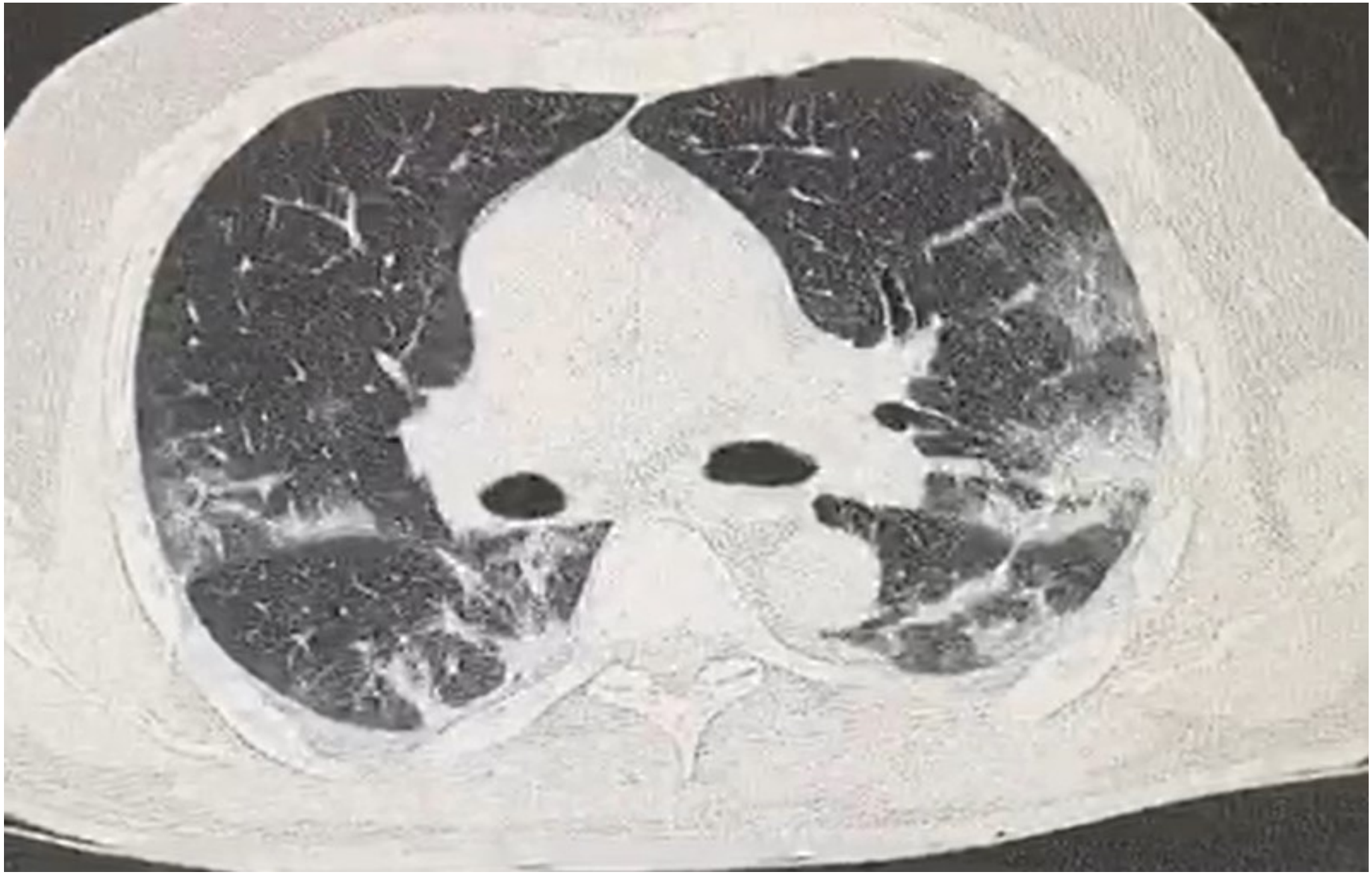
Pneumonia

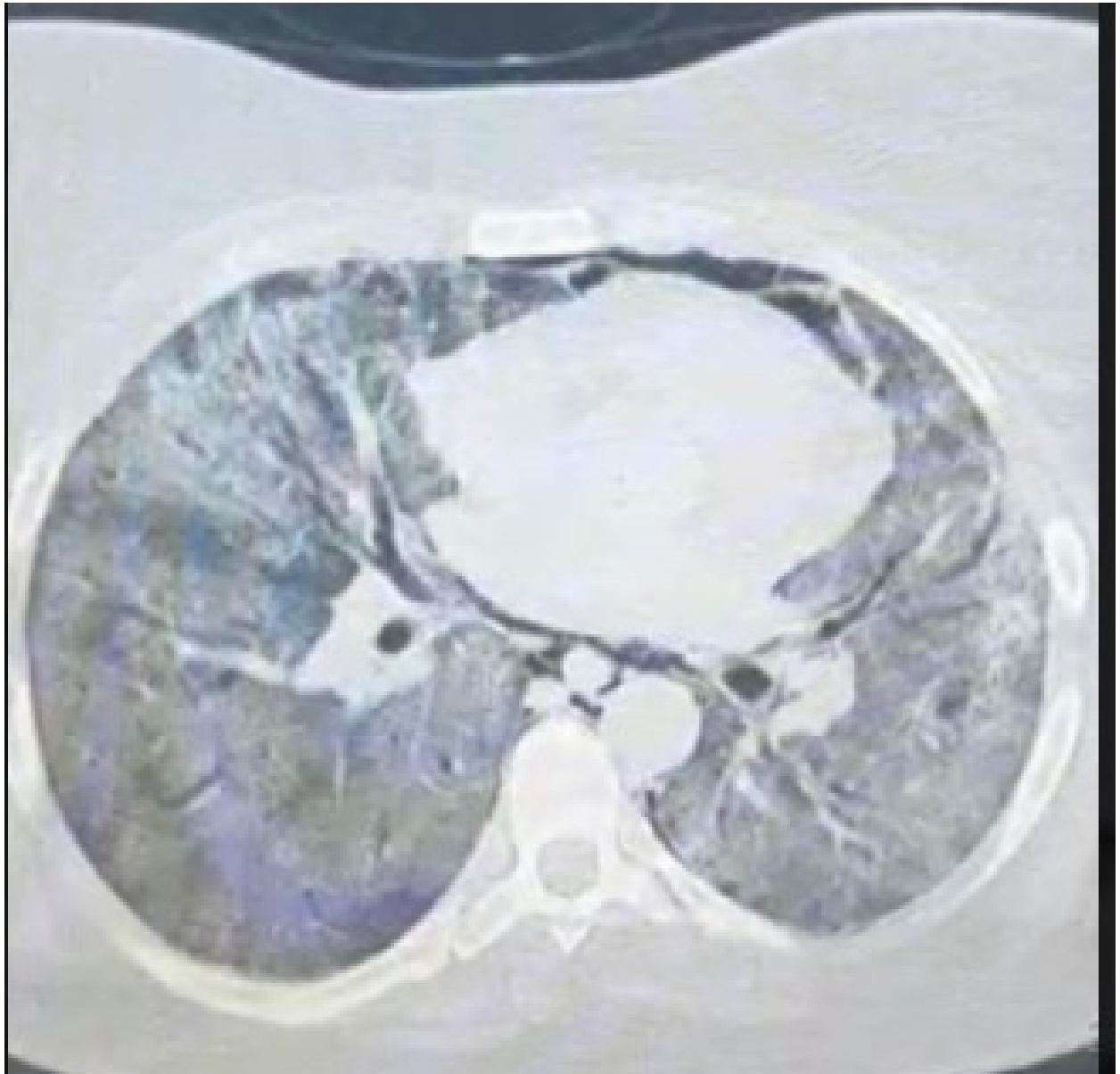
21/Male, of Indian origin r/o UK
Fever, Cough and Expectoration: 7d
Came to OPD




Worsened

AFB+ve:Tuberculosis





# Approach to a patient with Community Acquired Pneumonia

# Case-1

**A 73 yr old male, Never smoker, a known case of hypertension and diabetes, came to OPD with complaints of**

- Fever and cough with expectoration since last 5
- shortness of breath since last 5 days with few episodes of desaturation
- Wife is a Medical doctor and recorded SpO2 of 89% on Room Air and brought him to hospital

## No h/o hospitalisation / iv antibiotics / recent travel

## VITALS:

- BP- 140/90mmhg
- Pulse- 94/min
- Respiratory rate- 21cycle/min

Temperature- Febrile (101° F)

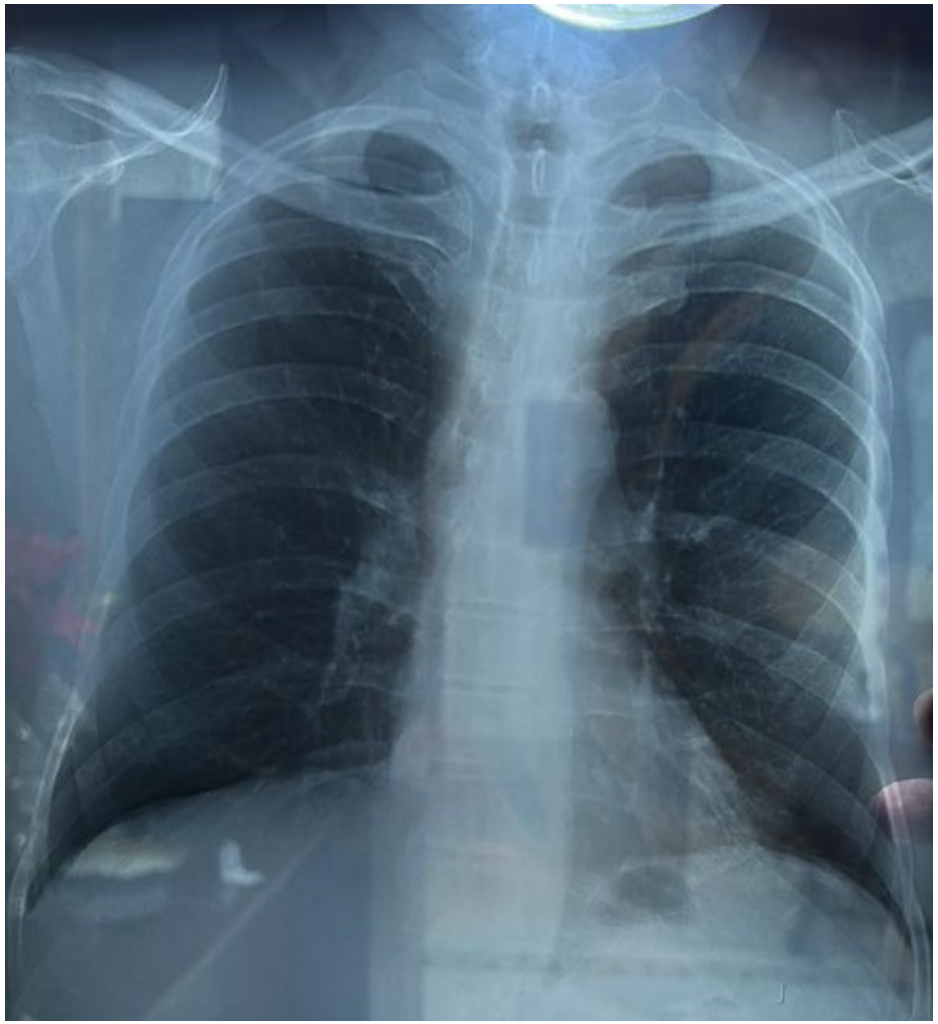
SpO2 89% (recorded at home)

## SYSTEMIC EXAMINATION:

- CVS- ,S1S2 Normal
- RS- B/L AE+
- Left basal crepts+

Abdomen- soft, non-tender

TLC count(24/11/22)- 15190/cu mm



24/11/2022

Does a normal X-ray rule out community acquired pneumonia???

What are the indications of doing a CT Chest in community acquired pneumonia?

J Community Hosp Intern Med Perspect. 2020; 10(1): 19–24.
Published online 2020 Jan 2. doi: 10.1080/20009666.2020.1711639
PMCID: PMC7034517
PMID: 32128054

# Characteristics of pneumonia with negative chest radiography in cases confirmed by computed tomography

Takatoshi Kitazawa,[a] Hisanao Yoshihara,[a] Kazunori Seo,[a,b] Yusuke Yoshino,[a] and Yasuo Ota[a,c]

- 138 patients were divided into two groups, those whose infiltrates were present on CT but absent or inclusive on chest radiography [CR- group] and those whose infiltrates were present on both chest radiography and CT [CR+ group].

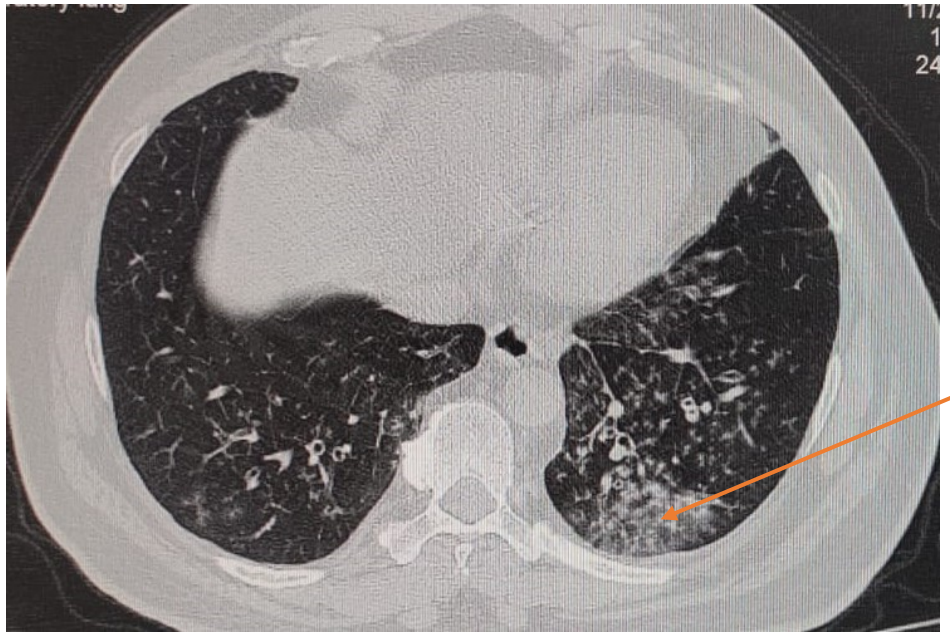
## RESULTS:

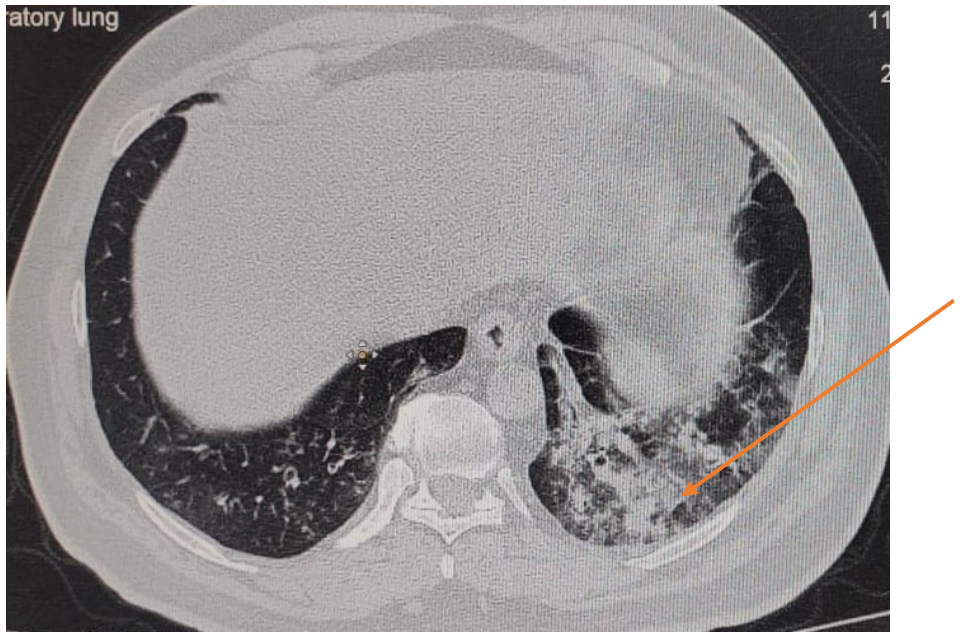
A total of 138 patients were included, with 58 patients in the CR- group and 80 patients in the CR+ group. Mean age was higher in the CR- group than in the CR+ group, and white blood cell counts and C-reactive protein (CRP) levels were lower in the CR- group than in the CR+ group. As for laterality of pneumonia infiltration, patients in the CR- group showed infiltration in the left lung more frequently than those in the CR+ group.

In patients admitted with a clinical diagnosis of CAP, the initial chest radiograph lacks sensitivity and may not demonstrate parenchymal opacifications in 21% of patients.

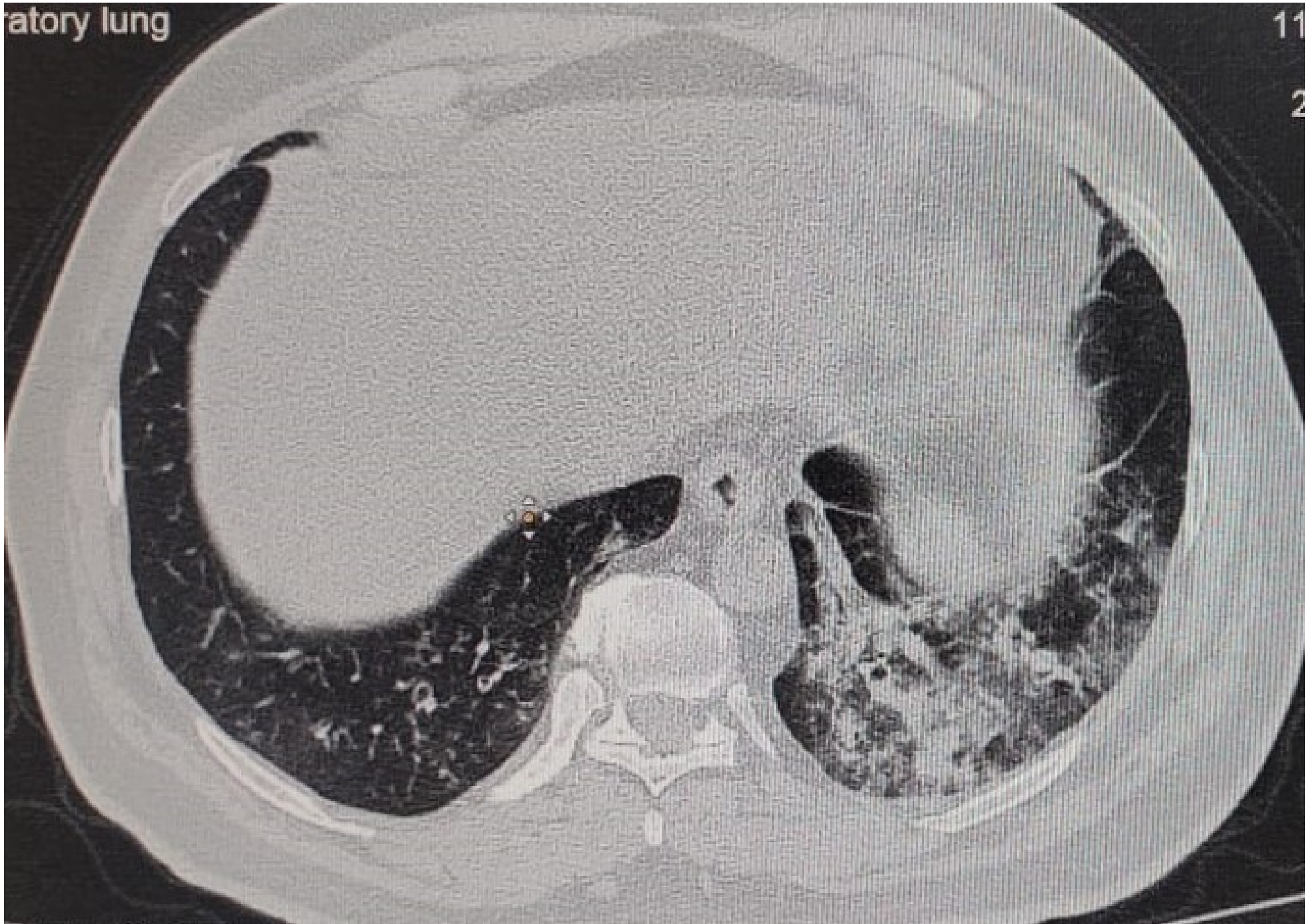
- Since X ray did not show active parenchymal lesions , NCCT Chest was done

He was advised for CT chest,






CT was s/o left lower lobe consolidation with tiny nodules


atory lung
11
2

# INVESTIGATIONS:

- **TLC count:**

| DATE | VALUE |
|---|---|
| 24/11/2022 | **15.91 X $10^3$** |
| Sputum Gram stain | Inconclusive |
| Sputum Culture | Awaited |

| BLOOD CULTURE | negative |
|---|---|
| URINE CULTURE | negative |
| H1N1 test | negative |
| PROCALCITONIN | 0.7ng/ml |

# Microbiology & Laboratory evaluation

URINE ANTIGEN

Procalcitonin

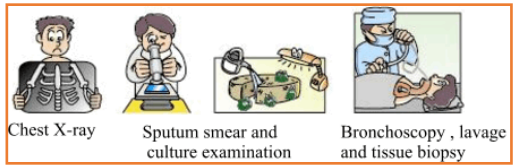
SPUTUM CULTURE

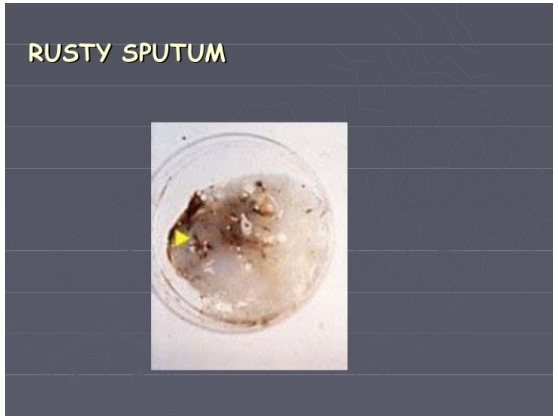
Tests tor TB

BLOOD CULTURE

Bronchoscopy

# Diagnosis of Pneumonia




Microbiology

- Sputum Gram Stain and culture
- Blood Culture
- Bronchoscopy
- Serology
- Urine antigen test
  S pneumonia & Legionella
- PCR for viral diseases
- Others

# Sputum examination

- Sputum C/S and gram stain
  - Yield of sputum cultures34-86%
  - For pneumococcal pneumonia, Sensitivity and Specificity of gram stain 15-100% and 11-100%
  - Useful despite variable results
    - Rapid results
    - Helps narrow down the etiology

**IDSA/ATS guidelines**

**Sputum samples should only be sent ,**

a) If good quality specimen can be obtained

b) If quality measures for collection, transport and processing can be ensured

# Blood Cultures

- Low sensitivity, high specificity
- Yield between 5% to 33%
- Systematic review (Afshar et al, 2009)
  - True positive cultures in 0% to 14%
  - Commonest organism isolated Pneumococcus
  - Doesn't change antibiotic decisions

**IDSA/ATS guidelines**

**Obtain blood cultures only if**

i. Intensive care unit admission
ii. Cavitary infiltrates
iii. Leukopenia
iv. Active alcohol abuse
v. Chronic severe liver disease
vi. Asplenia (anatomic or functional)
vii. Positive pneumococcal UAT
viii. Pleural effusion

Gupta et al. Indian J Chest Dis Allied Sci 2012

# Newer tests

- Urinary Antigen
  - Streptococcus and Gp 1 Legionella
  - Sensitivity – 75%, Specificity - >95%
  - Early(<15 min), no effect with antibi
- Serological tests
  - IgM for Chlamydia and Mycoplasma
- Molecular diagnostics
  - Sensitive but no resistance pattern and costly

Indian Guidelines (2013)

1. Legionella urinary antigen test is desirable in patients with severe CAP (1B)

2. Pneumococcal antigen detection test is not required routinely for the management of CAP (2A).

3. Investigations for atypical pathogens like Mycoplasma, Chlamydia, and viruses need not be routinely done (2A).

4. Pneumococcal PCR is not recommended as a routine diagnostic test in patients with CAP (1A)

# Biomarkers

- Erythrocyte sedimentation rate(ESR)
- C- Reactive Protein(CRP)
- Procalcitonin(PCT)
- Triggering receptor expressed on Myeloid cells(sTREM1)

GUIDELINES

# Guidelines for the Use of Procalcitonin for Rational Use of Antibiotics

Gopi C Khilnani[1], Pawan Tiwari[2], Kapil Gangadhar Zirpe[3], Dhruva Chaudhry[4], Deepak Govil[5], Subhal Dixit[6], Atul Prabhakar Kulkarni[7], Subhash Kumar Todi[8], Vijay Hadda[9], Neetu Jain[10], Manjunath B Govindagoudar[11], Srinivas Samavedam[12], Simant Kumar Jha[13], Niraj Tyagi[14], Madhusudan R Jaju[15], Anita Sharma[16]

*Received on:* 06 July 2022; *Accepted on:* 09 August 2022; *Published on:* XX XX XXXX

**Keywords:** Antibiotics, Guidelines, Procalcitonin, Sepsis, Stewardship.

*Indian Journal of Critical Care Medicine* (2022): 10.5005/jp-journals-10071-24326

## Executive Summary

### Procalcitonin (PCT) In Sepsis

[1]Department of Pulmonary, Critical Care and Sleep Medicine, PSRI Hospital, New Delhi, India

Should procalcitonin be done in hospitalized patients with community acquired pneumonia

Does procalcitonin help I in discriminating bacterial from viral and fungal aetiologies?

# Procalcitonin in LRTI

Questions

**Should baseline procalcitonin values in community-acquired lower respiratory tract infections be used to decide antibiotic initiation?**

## Statement

Baseline procalcitonin levels have not been consistently shown to reduce antibiotic exposure in community-acquired lower respiratory tract infections. Most guidelines recommend against withholding antibiotics in lower respiratory tract infections or CAP based on baseline procalcitonin.

## Recommendation for baseline procalcitonin

Baseline procalcitonin levels alone should not be used to withhold empiric antibiotic therapy in patients with LRTI and CAP.(1A)

Based on clinical judgment, prompt initiation of optimal empiric antibiotic therapy is recommended in patients with LRTI including CAP. (1A)

Evidence Statement or Recommendations

Khilnani GC et al. Guidelines for the use of Procalcitonin for Rational Use of Antibiotics. IJCCM 2022 (Accepted for publication)

# Procalcitonin in LRTI

Questions

**What is the utility and optimal timing of measurement of serum procalcitonin for antibiotic administration in CAP and other LRTIs?**

## Statement

In patients with community-acquired pneumonia, baseline procalcitonin alone has limited utility in clinical decision-making regarding the initiation of antibiotics. In clinical trials, procalcitonin measurements have been performed at randomization or emergency or hospital admission.

## Recommendation for baseline procalcitonin

Should **not be routinely measured** for initiation of antibiotics in all patients with CAP. (1A)

Be obtained in severe CAP for subsequent de-escalation of antibiotics. (2A)

If indicated, baseline serum procalcitonin should be **preferably measured at admission.** (3A)

Evidence Statement or Recommendations

Khilnani GC et al. Guidelines for the use of Procalcitonin for Rational Use of Antibiotics. IJCCM 2022 (Accepted for publication)

# Procalcitonin in LRTI

Questions

**Can procalcitonin levels be used to differentiate between viral and bacterial etiology in community-acquired pneumonia?**

## Statement

Higher procalcitonin levels are strongly associated with typical bacterial infections. Baseline procalcitonin levels have varied sensitivity in differentiating bacterial and viral CAP. There are currently no established threshold values of procalcitonin to discriminate bacterial from viral pneumonia.

## Recommendation for baseline procalcitonin

Procalcitonin levels alone should not be used to differentiate between bacterial and viral etiology in patients with CAP. (1A)

Evidence Statement or Recommendations

Khilnani GC et al. Guidelines for the use of Procalcitonin for Rational Use of Antibiotics. IJCCM 2022 (Accepted for publication)

# *Should a Bronchoscopy be done in CAP*

Original Article

# The impact on community acquired pneumonia empirical therapy of diagnostic bronchoscopic techniques

Effrosyni Manali, Antonios Papadopoulos, Sotirios Tsiodras, Vlasis Polychronopoulos, Helen Giamarellou & Kyriaki Kanellakopoulou

Pages 286-292 | Received 11 Mar 2007, Published online: 08 Jul 2009

Download citation https://doi.org/10.1080/00365540701663373

- This study examined 88 hospitalized patients and compared the diagnostic yield of protected specimen brush (PSB) and bronchoalveolar lavage (BAL) in the immunocompetent patient with CAP with results obtained from conventional sputum cultures.

- Followed by the modification of initial empirical treatment based on the microbiological results.

Effrosyni Manali, Antonios Papadopoulos, Sotirios Tsiodras, Vlasis Polychronopoulos, Helen Giamarellou & Kyriaki Kanellakopoulou (2008) The impact on community acquired pneumonia empirical therapy of diagnostic bronchoscopic techniques, Scandinavian Journal of Infectious Diseases, 40:4, 286-292, DOI: 10.1080/00365540701663373

- Fibreoptic bronchoscopy with quantitative PSB and BAL cultures for common pathogens, mycobacteria and fungi was performed.

- Conventional sputum cultures were also obtained. PSB and BAL quantitative cultures added 26.1% and 36.4%, respectively, more microbiological documentation for CAP compared to conventional sputum cultures.

Effrosyni Manali, Antonios Papadopoulos, Sotirios Tsiodras, Vlasis Polychronopoulos, Helen Giamarellou & Kyriaki Kanellakopoulou (2008) The impact on community acquired pneumonia empirical therapy of diagnostic bronchoscopic techniques, Scandinavian Journal of Infectious Diseases, 40:4, 286-292, DOI: 10.1080/00365540701663373

# Assessing Severity of CAP

# PSI PNEUMONIA SEVERITY INDEX

FINE MJ ET AL: A PREDICTION RULE TO IDENTIFY LOW-RISK PATIENTS WITH COMUNITY ACQUIRED PNEUMONIA.NEJM 1997;336:243

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

as a site-of-care tool. BUN, blood urea nitrogen; CHF, chronic heart failure; SBP, systolic blood pressure.

| CURB-65 | Clinical Feature | Points |
|---|---|---|
| C | Confusion | 1 |
| U | Urea > 7 mmol/L | 1 |
| R | RR ≥ 30 | 1 |
| B | SBP ≤ 90 mm Hg OR<br>DBP ≤ 60 mm Hg | 1 |
| 65 | Age > 65 | 1 |

| CURB-65 Score | Risk group | 30-day mortality | Management |
|---|---|---|---|
| 0 -1 | 1 | 1.5% | Low risk, consider home treatment |
| 2 | 2 | 9.2% | Probably admission vs close outpatient management |
| 3-5 | 3 | 22% | Admission, manage as severe |

# CRITERIA FOR DEFINING SEVERE CAP

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

→ Major criteria (any 1)

- Confusion
- RR > 30 cycles/min
- Hypotension
- Hypothermia
- PO2/Fio2 < 250
- Leukopenia < 4000 cells/ul
- Uremia > 20mg/dl
- Low platelet < 1,00,000
- Multi lobar infiltrates

→ Minor criteria(any 3)

ATS/IDSA guidelines (2019)

# Case continued…

Patient was started on antibiotics (Cefaparazone-sulbactum and Moxifloxacin). Based on clinical presentation and radiology

- Bronchoscopy was done:

**AFB microscopy – negative**

**Genexpert – negative**

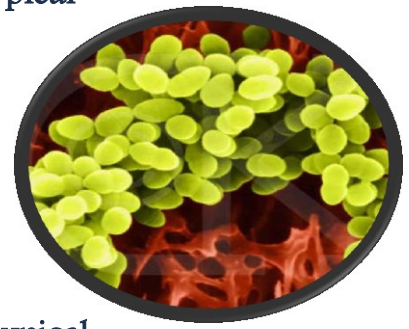
Gram stain – pus cells > 25/low power field.

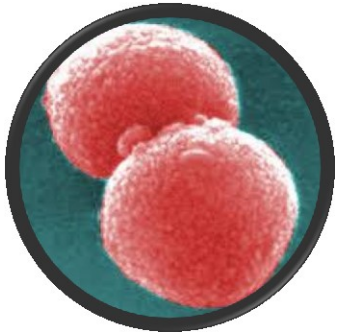
Pyogenic culture – no growth seen.

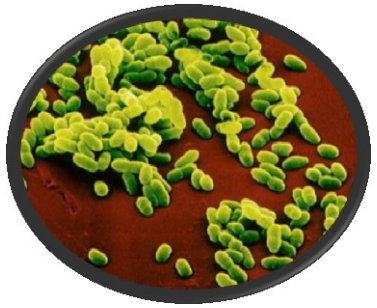
*What are common organisms in CAP?*

# Major Culprits…

Typical







Atypical

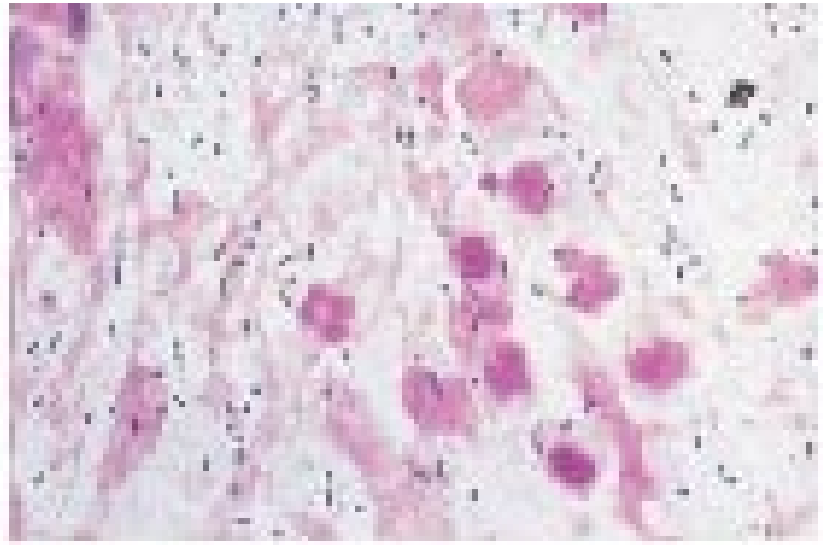
Staphylococci

Pneumococci

H. influenzae

# Most common etiologies of community acquired pneumonia

| Patient type | Etiology |
|---|---|
| Outpatient | Streptococcus pneumoniae<br>Mycoplasma pneumoniae<br>Haemophilus influenzae<br>Chlamydophila pneumoniae<br>Respiratory viruses |
| Inpatient (non-ICU) | S. Pneumoniae<br>M. Pneumoniae<br>C. Pneumoniae<br>H. Influenzae<br>Legionella species<br>Aspiration<br>Respiratory viruses |
| Inpatient (ICU) | S. Pneumoniae<br>Staphylococcus aureus<br>Legionella species<br>Gram-negative bacilli<br>H. influenzae |



IDSA/ATS Guidelines CID2007:44 (Suppl)27-72

# Other causes

- Virus
  - **Influenza,** Adenoviruses, Respiratory syncytial viruses, Parainfluenza viruses, **Coronavirus,** Hantavirus etc.
- Tubercular
- Fungal : Aspergillus, Fusarium etc.
- Parasitic
- Leptospira

# CAP Microorganisms: AIIMS Study (2008-10) (n = 50)

| Organisms | No. of patients |
|---|---|
| Streptococcus pneumoniae | 11(22%) |
| Chlamydophila pneumonia | 10(20%) |
| Mycoplasma pneumonia | 4(8%) |
| **Mycobacterium tuberculosis** | **4(8%)** |
| Klebsiella pneumonia | 3(6%) |
| Pseudomonas aeruginosa | 3(6%) |
| Parainfluenza 3 virus<br>Influenza A virus | 2(4%)<br>1(2%) |
| Escherichia coli | 1(2%) |
| Staphylococcus aureus (CA-MRSA) | 1(2%) |

# What should be initial choice of antibiotics in patients with CAP?

Indian Journal of
Critical Care Medicine

# Indian Guidelines for Antimicrobial Prescription in Critically Ill

Khilnani GC, Zirpe K, Hadda V, Mehta Y, Madan K, Kulkarni A, Mohan A, Dixit S, Guleria R, Bhattacharya P. Guidelines for Antibiotic Prescription in Intensive Care Unit. Indian Journal of Critical Care Medicine 2019;23(Suppl 1): S1-S63

**Expert Committee:** Arti Kapil, Pawan Tiwari, Saurabh Mittal, Dhruva Chaudhary, JC Suri, MK Daga, Yash Zaveri, Suresh Rama Subban, Seema Sood, RK Mani, Narendra Rungta, Anirban Chaudhry, Rajesh Pandey, Neetu Jain, Arvind Baronia, Jaya Kumar, Gyanendra Agarwal, Camilla Rodrigues, BK Rao, Deepak Govil, Sachin Gupta, Ashit Hegde, Pramod Garg, Sandeep Mahajan, Chand Wattal, Rajesh Chawla, Anjan Trikha, Prakash Shastri, Anil Gurnani, Rajesh Mishra, Rohit Bhatia, GC Khilnani, Kapil Zirpe, Vijay Hadda, Anant Mohan, Atul Kulkarni, Karan Madan, Yatin Mehta, Subhal Dixit, Randeep Guleria, Pradeep Bhattacharya

# CHOICE OF ANTIBIOTICS

INITIAL TREATMENT FOR OUT PATIENTS WITH CAP:

| | STANDARD REGIMEN |
|---|---|
| No comorbidities or risk factors for MRSA/ pseudomonas aeruginosa | • Amoxycillin or<br>• Doxycycline or<br>• Macrolides (if local pneumococcal resistance is <25%) |
| With comorbidities | Combination therapy with<br>• Amoxycillin/clavulanate or<br>• Cephalosporins + Macrolides or<br>• Doxycycline<br>Or<br>Monotherapy with<br>• Respiratory fluroquinolones |

Indian guidelines on antibiotic prescription in ICU

# CHOICE OF ANTIBIOTICS

INITIAL TREATMENT FOR INPATIENTS WITH CAP:

| | STANDARD REGIMEN |
|---|---|
| Without risk factors for MRSA/ pseudomonas | Combination therapy with<br>• Beta- lactams and macrolides<br>OR<br>Monotherapy with<br>• Respiratory fluroquinolones<br>**If both macrolides and fluroquinolones are contraindicated**<br>Combination therapy with<br>• Beta-lactam +<br>• Doxycycline |

Indian guidelines on antibiotic prescription in ICU

# Indian guidelines for antibiotic administration in ICU

Questions

For empirical therapy in patients with CAP in ICU, should combination therapy be preferred over monotherapy?

| Recommendation | Patients with CAP requiring ICU admission should initially receive combination of empirical antimicrobial agents covering common causative organisms. (2A) |
|---|---|

What should be the preferred combination therapy for CAP in ICU?

| Recommendation | non-pseudomonal β-lactam (cefotaxime, ceftriaxone) or beta lactam with beta-lactamase inhibitor (amoxicillin–clavulanic acid), ***plus*** a macrolide (azithromycin or clarithromycin) (1A).<br>For penicillin-allergic patients, respiratory fluoroquinolone (levofloxacin, moxifloxacin or ciprofloxacin) and aztreonam (3A) |
|---|---|

If macrolides cannot be used, a fluoroquinolone may be used if no clinical suspicion of TB, after sending sputum or endotracheal aspirate samples to rule out tuberculosis. (3A)

Evidence Statement or Recommendations

# WHEN TO SUSPECT AN ANAEROBIC INFECTION AND PSEUDOMONAS

# Risk factors for anaerobic infection :

- Dysphagia
- Altered sensorium
- Coma,
- Witnessed aspiration,
- Putrid discharge,
- Presence of lung abscess,
- Empyema or
- Necrotizing pneumonia.

# Risk factors for infection with Pseudomonas aeruginosa:

- Chronic pulmonary disease (chronic obstructive pulmonary disease, asthma, bronchiectasis)
- Frequent systemic corticosteroid use
- Prior antibiotic therapy
- Old age
- Immunocompromised states
- Enteral tube feeding,
- Cerebrovascular or cardiovascular disease.
- Prior antibiotic therapy is a risk factor for multidrug-resistant pseudomonal infection.

# WHEN TO SUSPECT COMMUNITY ACQUIRED MRSA ?

# Risk factors for MRSA in CAP:

- Close contact with MRSA carrier or patient,
- Influenza,
- Prisoners,
- Professional athletes,
- Army recruits,
- Men having sex with men (MSM), intravenous (IV)
- Drug abusers,
- Regular sauna users
- Recent antibiotic use.
- MRSA pneumonia should be suspected after influenza or in previously healthy young patients, if there is cavitation or necrotizing pneumonia, along with rapid increase of pleural effusion, massive hemoptysis,neutropenia or erythematous rashes.

SHOULD FLUOROQUINOLONES BE USED AS INITIAL TREATMENT FOR COMMUNITY ACQUIRED PNEUMONIA IN INDIA ?

# Status of quinolones and Linezolid in India

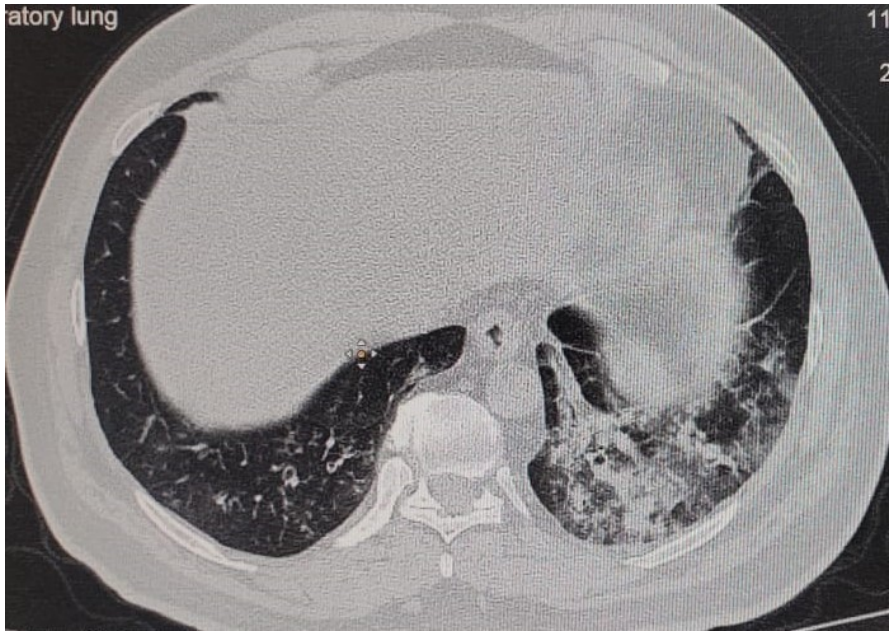
Questions

## How should quinolones be used in severe CAP in India?

| | |
|---|---|
| Statement | For patients with severe CAP requiring ICU admission without risk factors for pseudomonal infection, a combination of beta-lactams along with macrolides is better as compared to beta-lactam fluoroquinolone combination in terms of mortality benefit and length of hospital stay. |
| Recommendation | If macrolides cannot be used, a fluoroquinolone may be used if there is no clinical suspicion of tuberculosis, after sending sputum or endotracheal aspirate for AFB and Genexpert (3A). |

Evidence Statement or Recommendations

Khilnani GC et al. Indian Journal of Critical Care Medicine 2019;23(Suppl 1): S1-S63




# BACK TO OUR CASE

# Sputum culture of the patient

**SPUTUM CULTURE AND SENSITIVITY**

| | |
|---|---|
| **NATURE OF SPECIMEN** | Sputum |
| **ORGANISM** | **Streptococcus pneumoniae** |
| **REMARKS** | Heavy growth |

| **ANTIBIOTICS** | **RESULT** |
|---|---|
| Ampicillin | **Sensitive** |
| Ampicillin/Sulbactam | **Sensitive** |
| Cefaclor | **Sensitive** |
| Cefotaxime | **Sensitive** |
| Ceftizoxime | **Sensitive** |
| Cefuroxime | **Sensitive** |
| Cefdinir | **Sensitive** |
| Cefpodoxime | **Sensitive** |
| Tetracycline | Resistant |
| Ofloxacin | **Sensitive** |
| Chloramphenicol | **Sensitive** |
| Linezolid | **Sensitive** |
| Cotrimoxazole | Intermediate |
| Amoxicillin / Clavulanic Acid | **Sensitive** |
| Benzyl Penicillin | **Sensitive** |
| Ceftriaxone | **Sensitive** |
| Erythromycin | Resistant |
| Azithromycin | Resistant |
| Moxifloxacin | Resistant |
| Vancomycin | **Sensitive** |
| Levofloxacin | Resistant |
| Clindamycin | Resistant |
| Doripenem | **Sensitive** |
| Ertapenem | **Sensitive** |
| Imipenem | **Sensitive** |
| Meropenem | **Sensitive** |

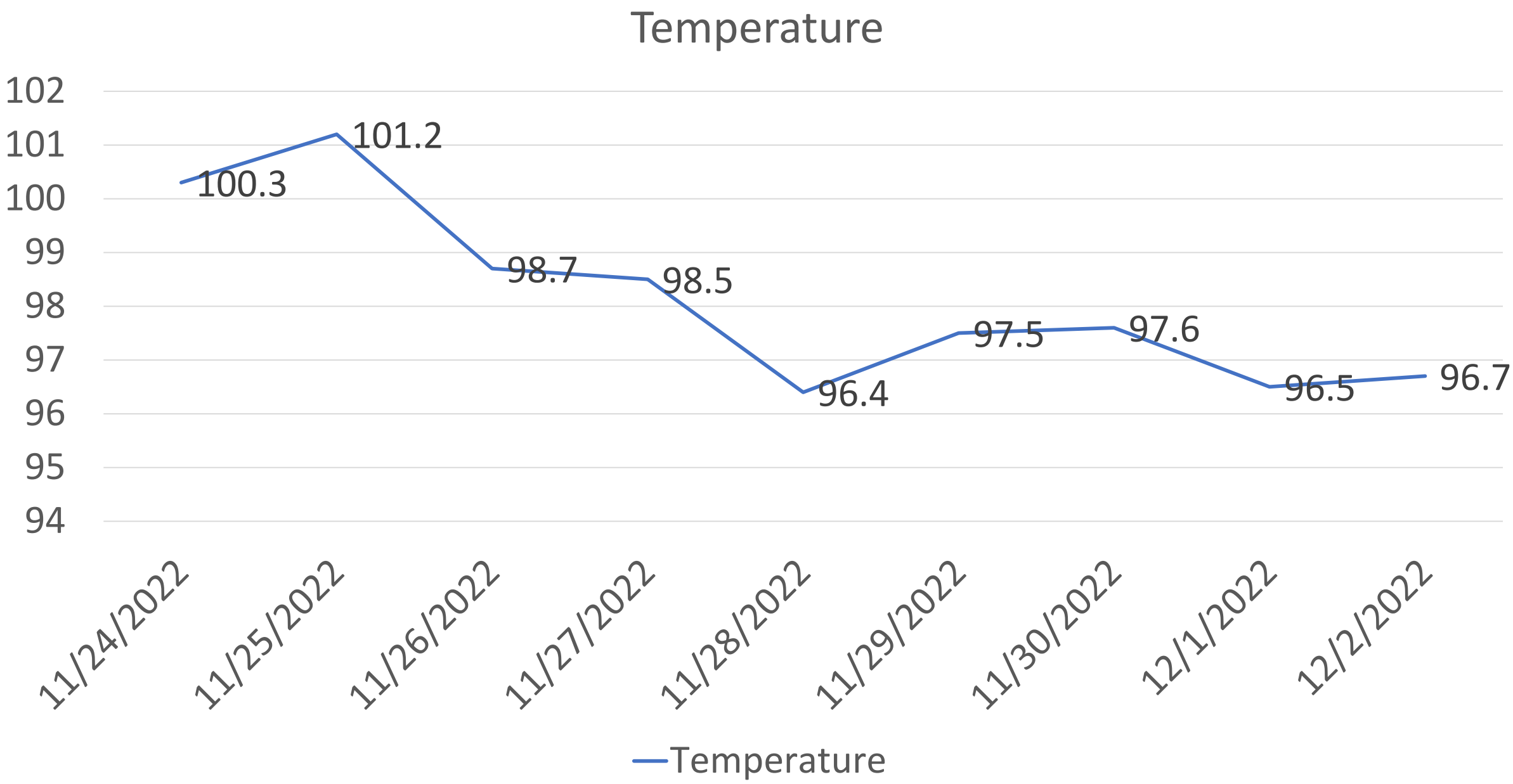
# Case continued…..

Patient was continued on cefaperazone sulbactam and moxifloxacin for 7 days

According to culture sensitivity report, patient was de escalated to azithromycin and continued on cefaperazone.

After 1 week of injectable antibiotics, patients condition improved, follow up USG was done – which showed no pleural effusion.

After a total of 7 days of injectable antibiotics, pt was switched to oral antiobitic - cefpodoxime clavulanate and pt was discharged.

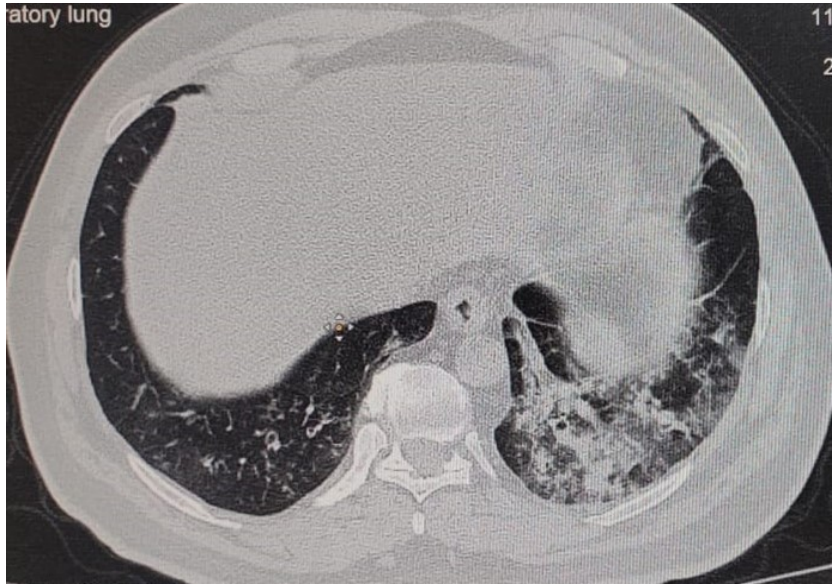

Temperature
102
101
100
99
98
97
96
95
94
100.3
101.2
98.7
98.5
96.4
97.5
97.6
96.5
96.7
11/24/2022
11/25/2022
11/26/2022
11/27/2022
11/28/2022
11/29/2022
11/30/2022
12/1/2022
12/2/2022
Temperature

# Case continued…

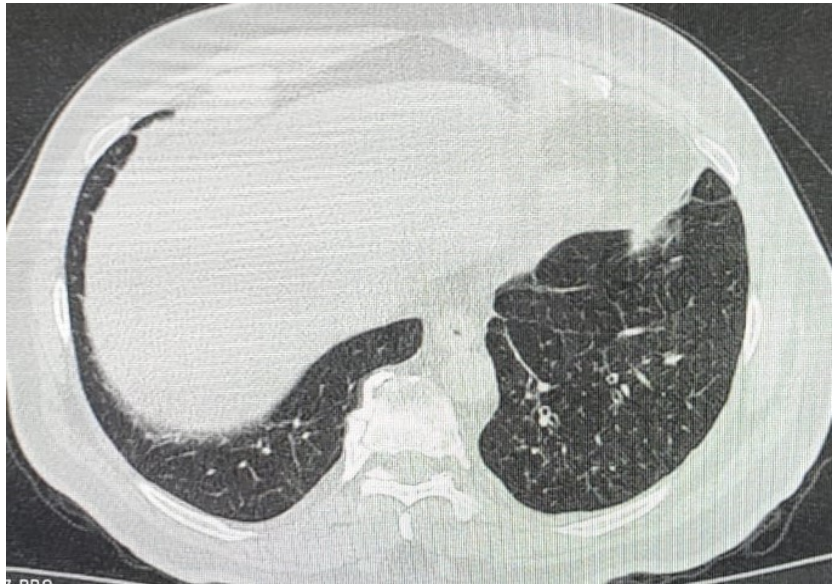
Patient came to OPD for follow up after 7 days of oral antibiotics.

Patient’s symptoms had resolved.

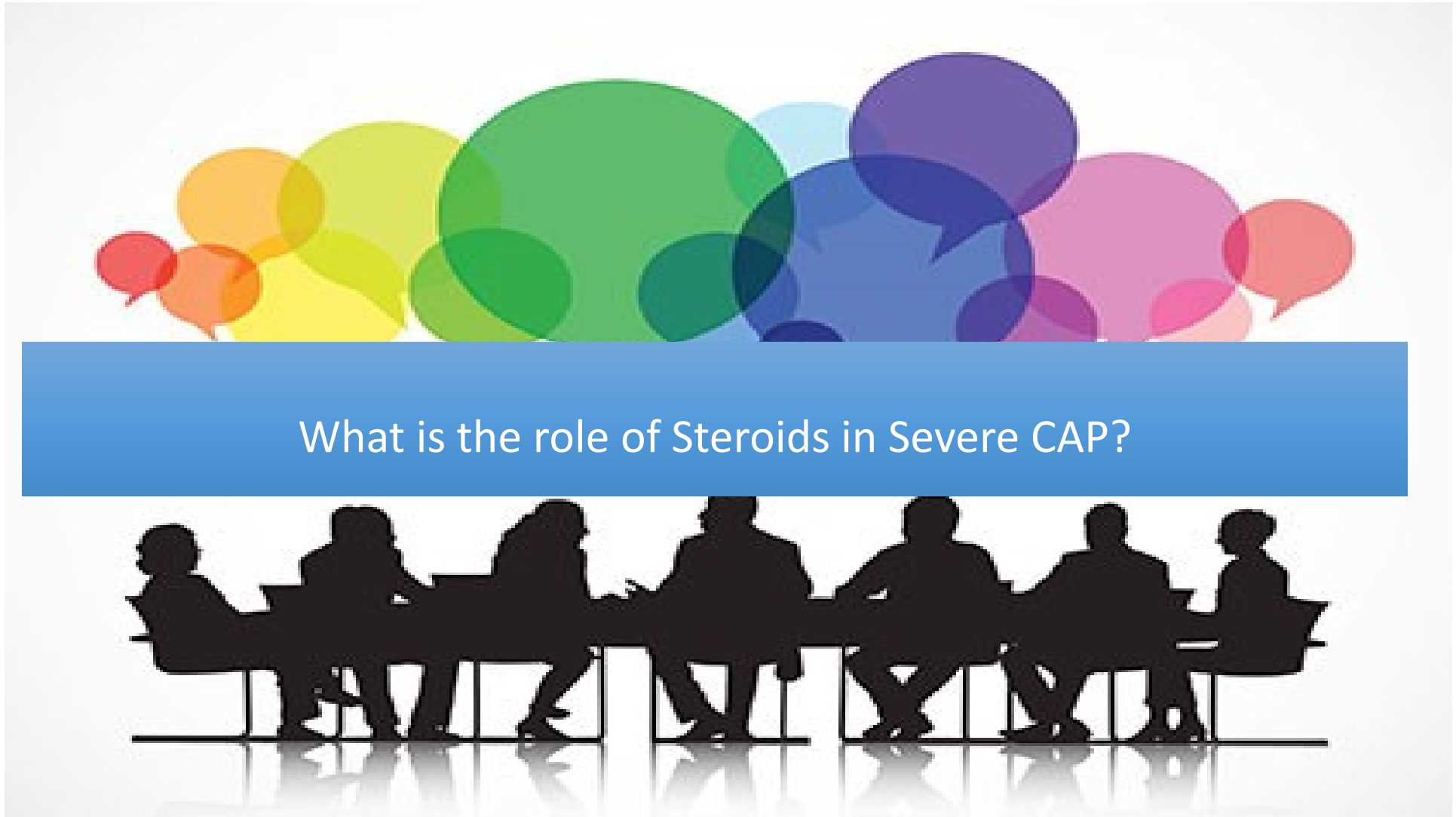
Follow up CT chest was done, which showed clearing of consolidation compared to past CT.




24/11/2022



02/12/2022



# What is the role of Steroids in Severe CAP?

# Role of Steroids

1. No role  in non severe CAP
2. Role in severe CAP with inflammation(CRP>15mg/dL), septic shock or ARDS
3. Mortality risk reduction [1]
4. Contraindications to be ruled out

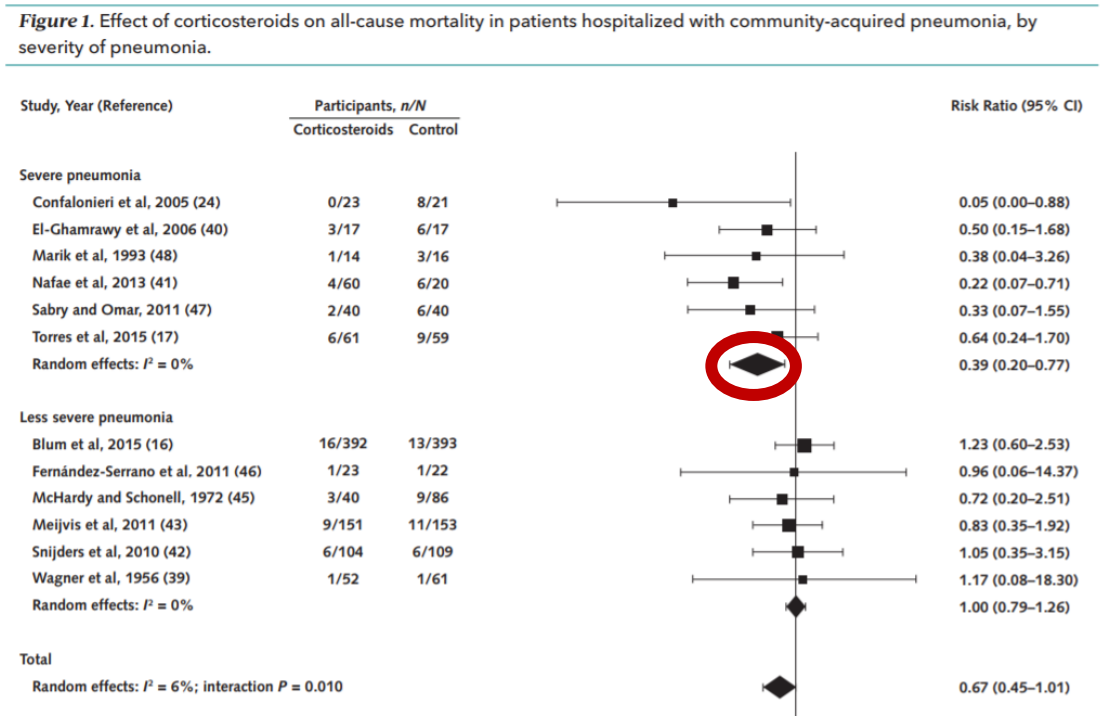


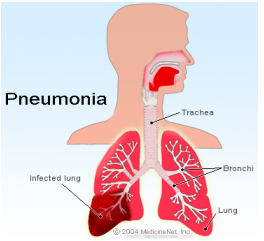
*Figure 1.* Effect of corticosteroids on all-cause mortality in patients hospitalized with community-acquired pneumonia, by severity of pneumonia.

| Study, Year (Reference) | Participants, *n/N* | | Risk Ratio (95% CI) |
|---|---|---|---|
| | Corticosteroids | Control | |
| Severe pneumonia | | | |
| Confalonieri et al, 2005 (24) | 0/23 | 8/21 | 0.05 (0.00–0.88) |
| El-Ghamrawy et al, 2006 (40) | 3/17 | 6/17 | 0.50 (0.15–1.68) |
| Marik et al, 1993 (48) | 1/14 | 3/16 | 0.38 (0.04–3.26) |
| Nafae et al, 2013 (41) | 4/60 | 6/20 | 0.22 (0.07–0.71) |
| Sabry and Omar, 2011 (47) | 2/40 | 6/40 | 0.33 (0.07–1.55) |
| Torres et al, 2015 (17) | 6/61 | 9/59 | 0.64 (0.24–1.70) |
| Random effects: $I^2$ = 0% | | | 0.39 (0.20–0.77) |
| Less severe pneumonia | | | |
| Blum et al, 2015 (16) | 16/392 | 13/393 | 1.23 (0.60–2.53) |
| Fernández-Serrano et al, 2011 (46) | 1/23 | 1/22 | 0.96 (0.06–14.37) |
| McHardy and Schonell, 1972 (45) | 3/40 | 9/86 | 0.72 (0.20–2.51) |
| Meijvis et al, 2011 (43) | 9/151 | 11/153 | 0.83 (0.35–1.92) |
| Snijders et al, 2010 (42) | 6/104 | 6/109 | 1.05 (0.35–3.15) |
| Wagner et al, 1956 (39) | 1/52 | 1/61 | 1.17 (0.08–18.30) |
| Random effects: $I^2$ = 0% | | | 1.00 (0.79–1.26) |
| Total | | | |
| Random effects: $I^2$ = 6%; interaction $P$ = 0.010 | | | 0.67 (0.45–1.01) |

1. Siemieniuk RA et al. Corticosteroid therapy for patients hospitalized with communityacquired pneumonia: a systematic review and meta-analysis. Ann Intern Med. 2015;163:519–28.

# HOSPITAL ACQUIRED PNEUMONIA

# Definition




**CAP**

- Pneumonia in community setting i.e. acquired outside of hospitals or extended health care facilities

**HAP**

- Pneumonia 48 hours or more after admission
- Not intubated at the time of admission

**VAP**

- Pneumonia more than 48–72 hours after endotracheal intubation

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

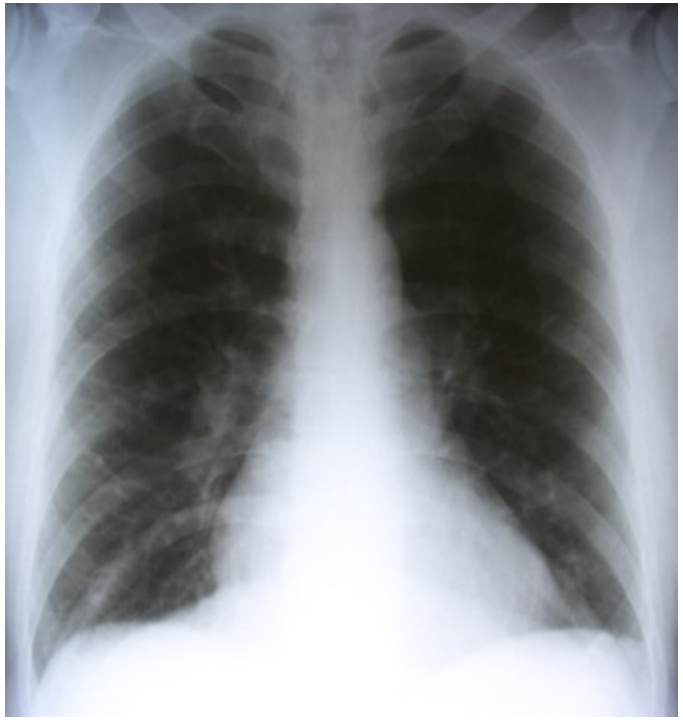
# Nosocomial Pneumonia in ICU

| Non-ventilated | Ventilated |
| --- | --- |
| Incidence | |
| 0.9/1000 patient days | 20.6/1000 patient days<br>3-21 fold higher risk |
| Mortality | |
| Crude mortality rate 20% | 71% |

*Chest 2002;122:2115-21*

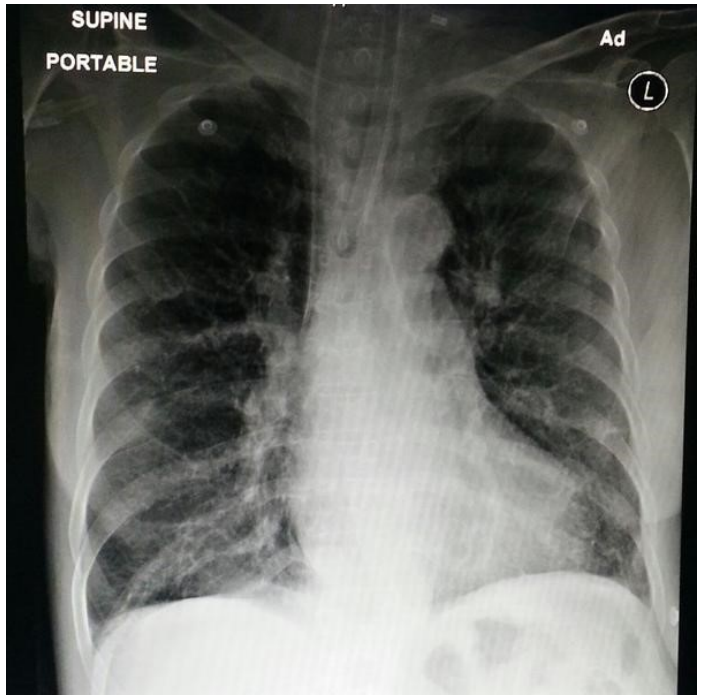
# *Case scenario 2*

- 56 yr old gentleman
- Diagnosed c/o COPD with OSAS (AHI – 68.2/hr)
- Admitted with increased dyspnea and drowsiness – 3 days
- Had Type 2 respiratory failure, started on NIV



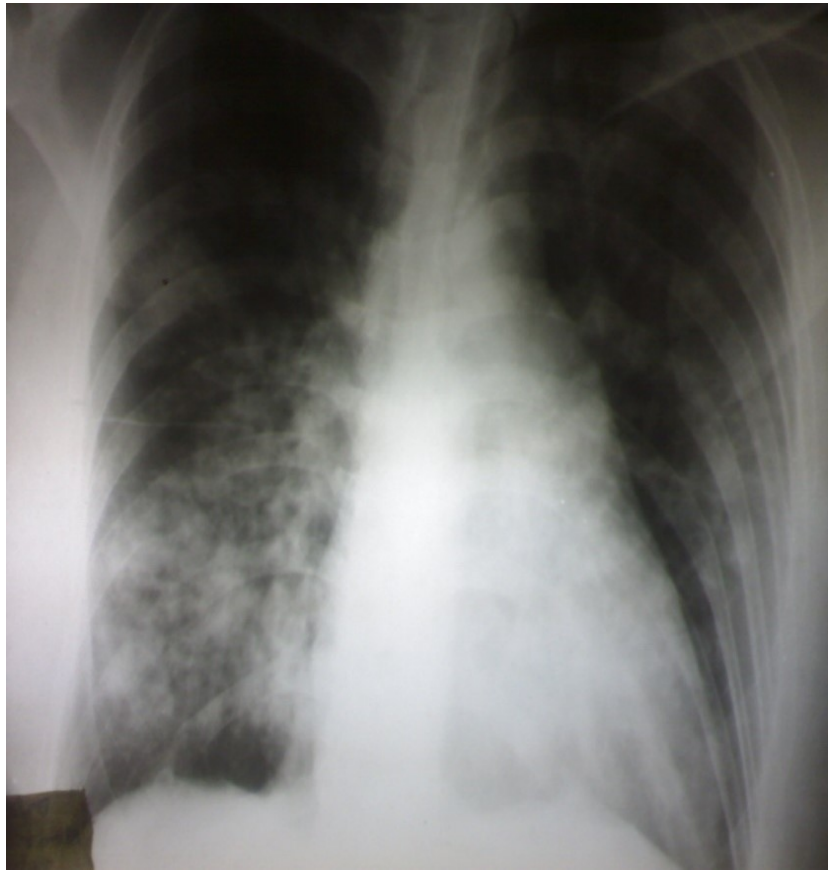
# *After 24 hours*

- Worsening respiratory failure with progressive rise in CO2
- Deterioration in sensorium
- Intubated and mechanically ventilated
- **Pt was started on ceftriaxone and azithromycin**



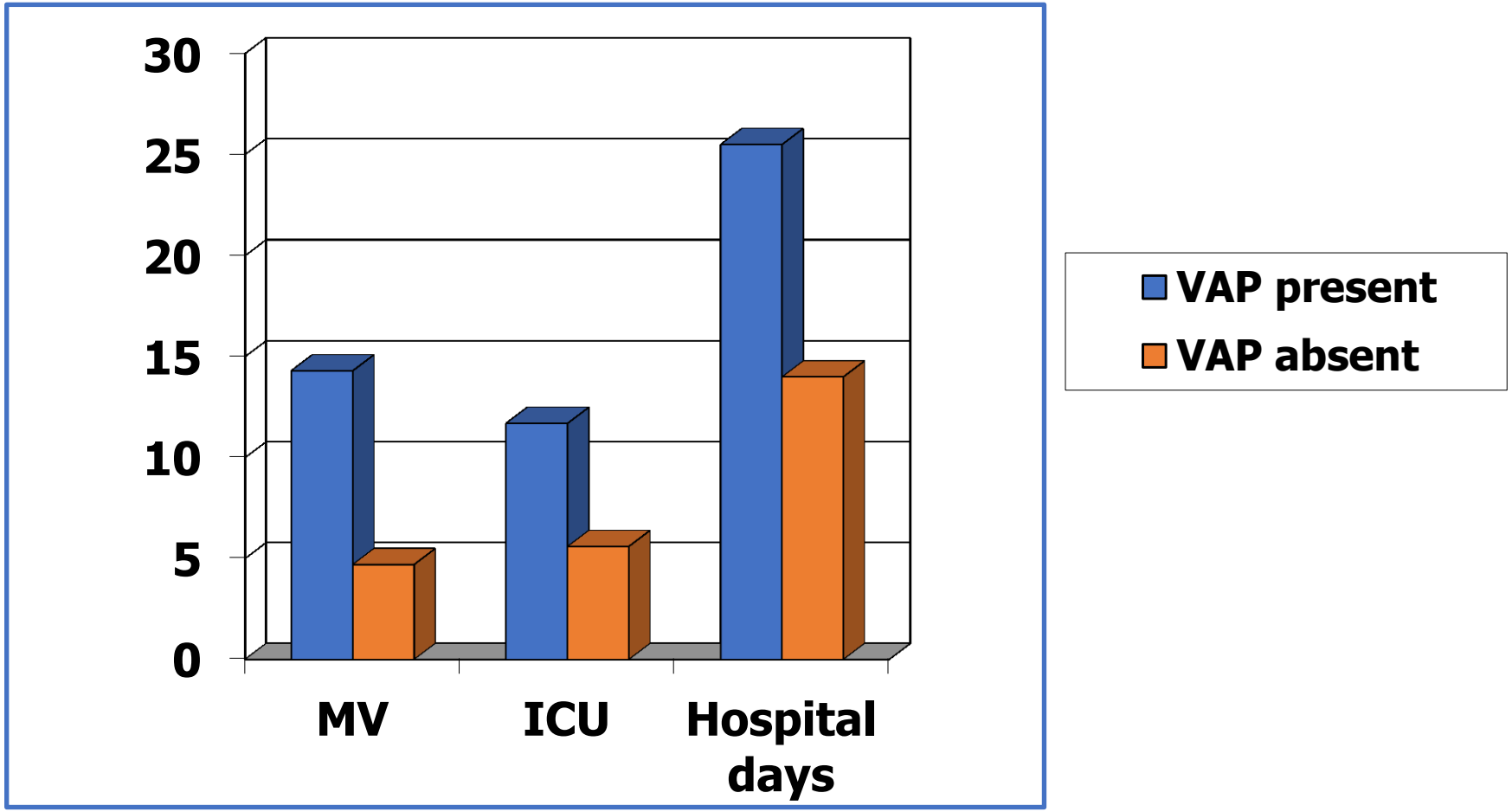
# *Case scenario 2*

- Day 3 worsening hypoxia
- Fever and new infiltrates on CXR
- Increasing inotrope requirement,
- TLC 18300
- Mini BAL done



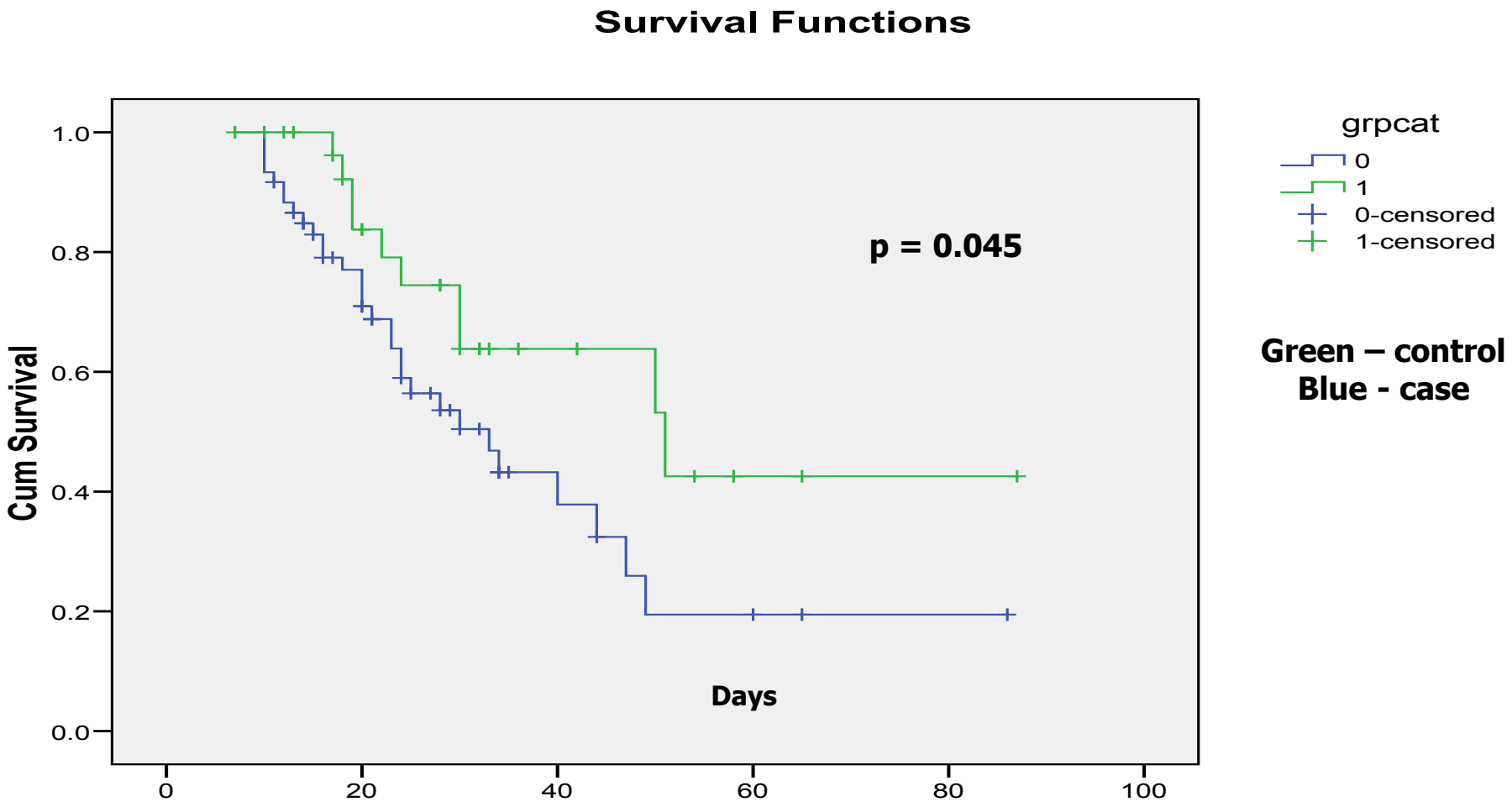
# This Patient has Hospital Acquired Pneumonia (VAP)

# Impact of VAP

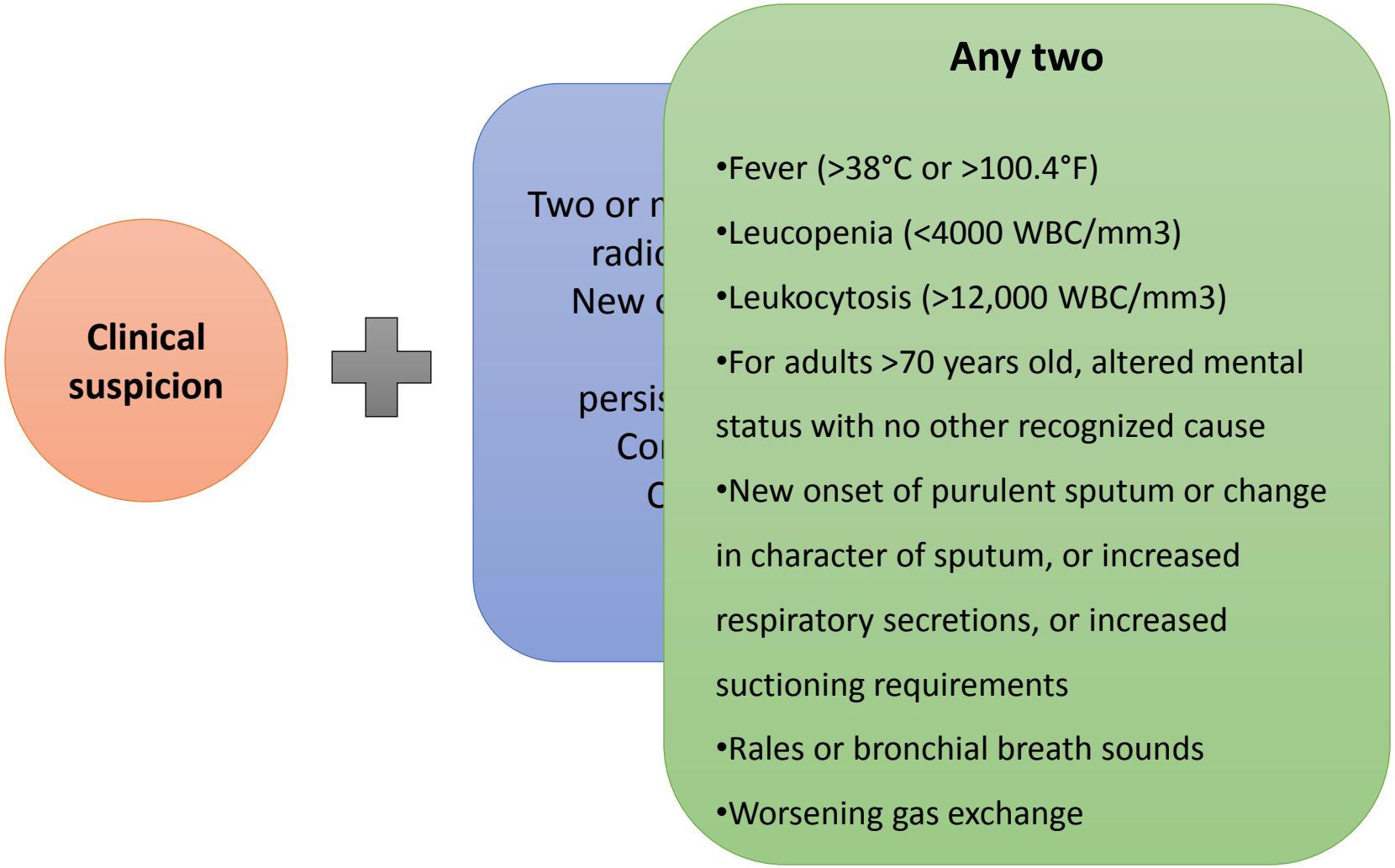



*Chest 2002;122:2115-21*

# Survival Curve in Cases (VAP) and Controls AIIMS study (G.C.Khilnani et al)



# HAP/VAP Dx: Modified CDC Criteria




Am J Respir Crit Care Med 2005;171;388-416
Am J Infect Control 2008; 36: 309-32

# The modified clinical pulmonary infection score

| CPIS Points | 0 | 1 | 2 |
|---|---|---|---|
| Tracheal secretions | Rare | Abundant | Abundant + purulent |
| CXR | No infiltrate | Diffused | Localized |
| | | | > 11,000+ bands≥ 500 |
| $PaO_2/FiO_2$ | > 240 or ARDS | | < 240 and no evidence of ARDS |
| Microbiology | Negative | | Positive |

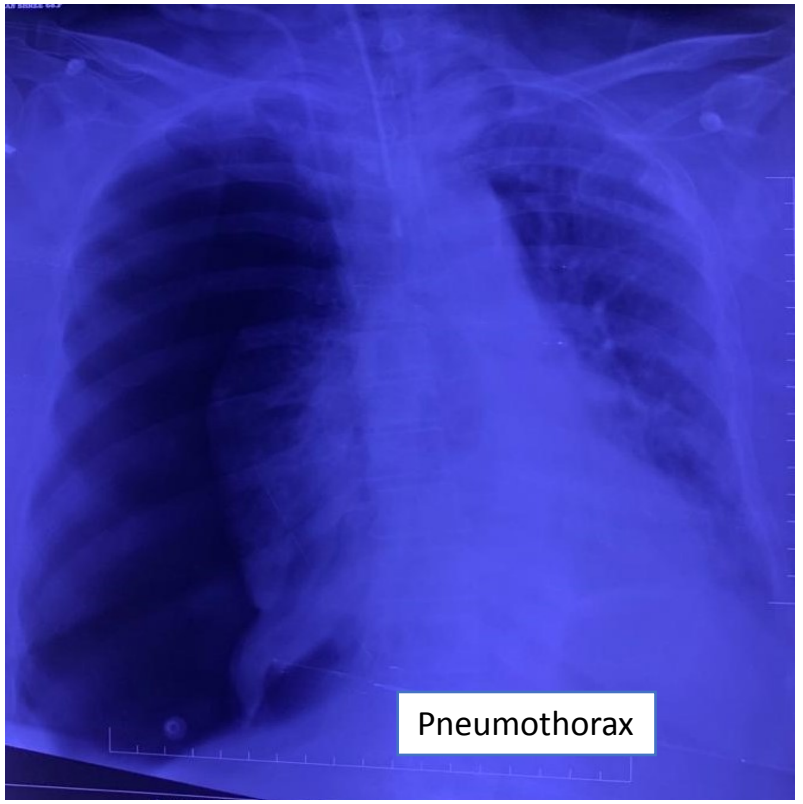
Score > 6 → good correlation with pneumonia

**Sensitivity 78-85% & Specificity 49-56%**

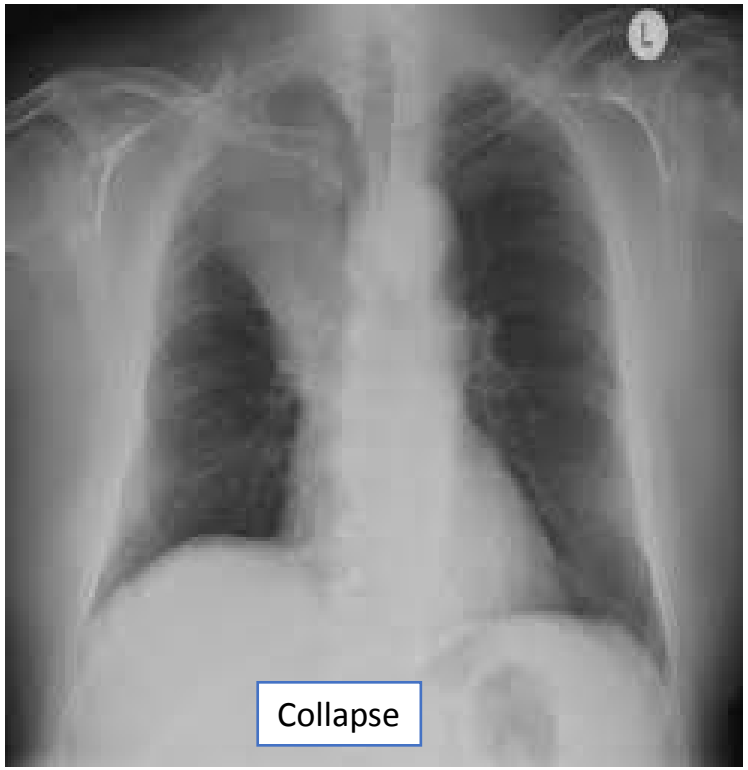
Score ≤6→ good prediction to discontinue antibiotic therapy after 3 days

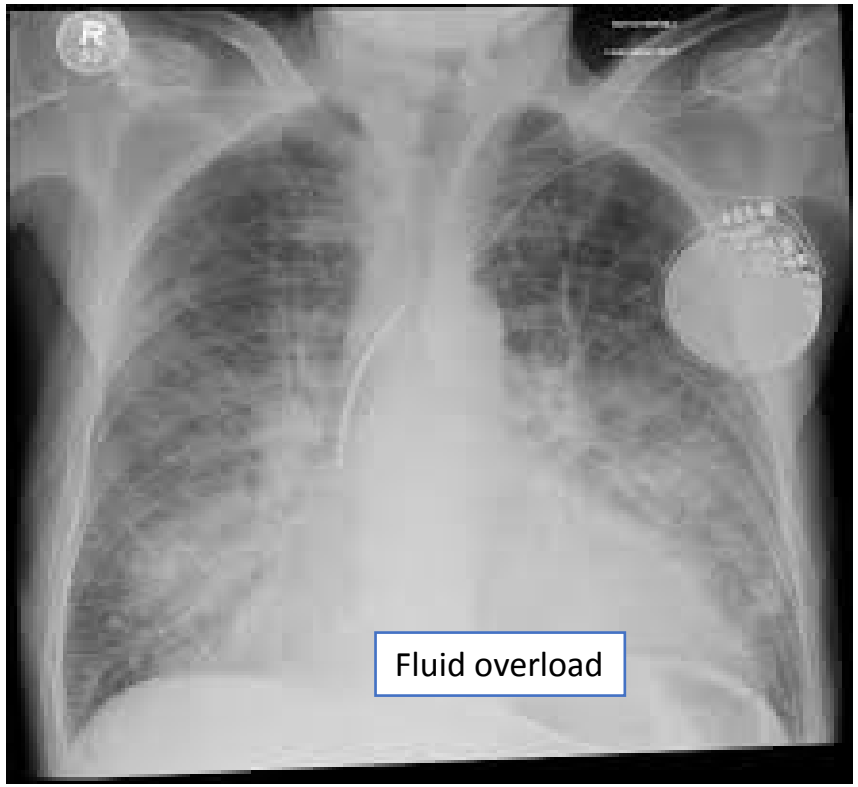
Am J Respir Crit Care Med Vol 168. pp 173–179, 2003

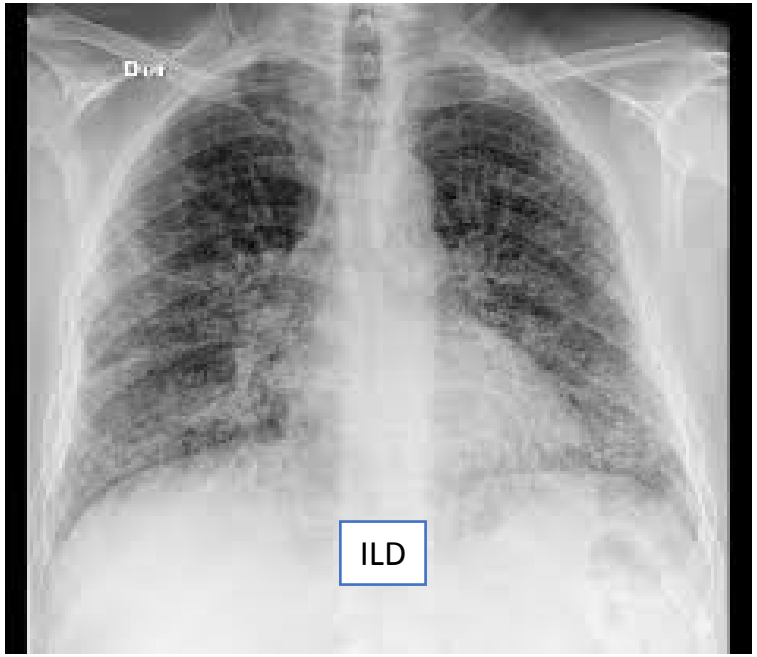
# D/D VAP

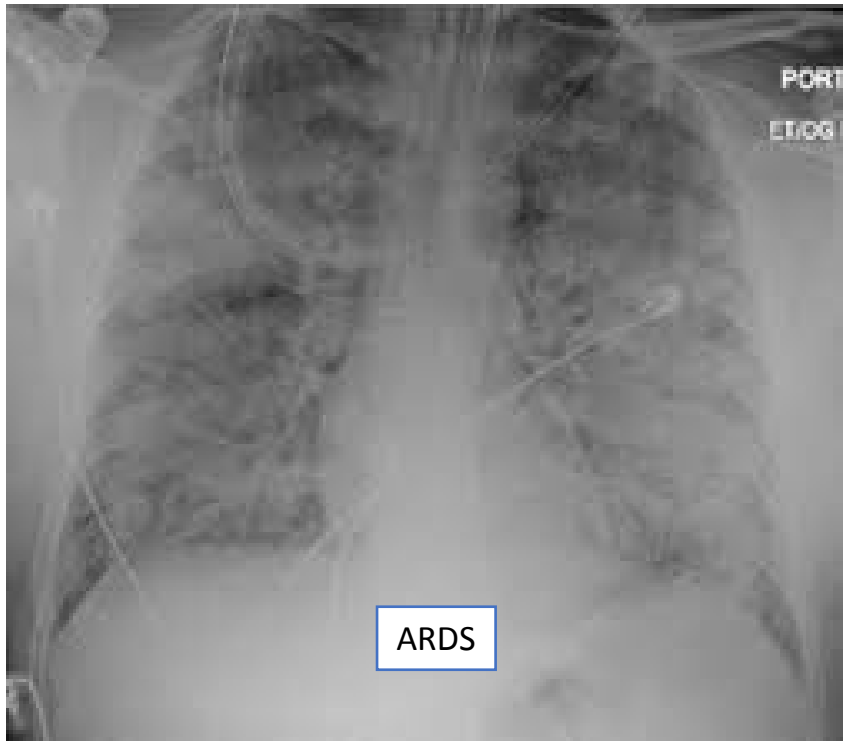



ARDS


Collapse


Fluid overload


ILD


ARDS

# Differential Diagnosis

- Atelectasis (Collapse of Lung)
- Pleural effusion
- Pulmonary embolism
- Cardiogenic Pulmonary oedema
- Lung cancer
- Pulmonary alveolar Haemorrhage

# Microbiologic Diagnosis

# Microbiologic Diagnosis

- Tracheal Aspirate
- Mini BAL, Non-bronchoscopic BAL
- Bronchoscopy

Indian J Crit Care Med, 2011

# Comparison of bronchoscopic and non-bronchoscopic techniques for diagnosis of ventilator associated pneumonia

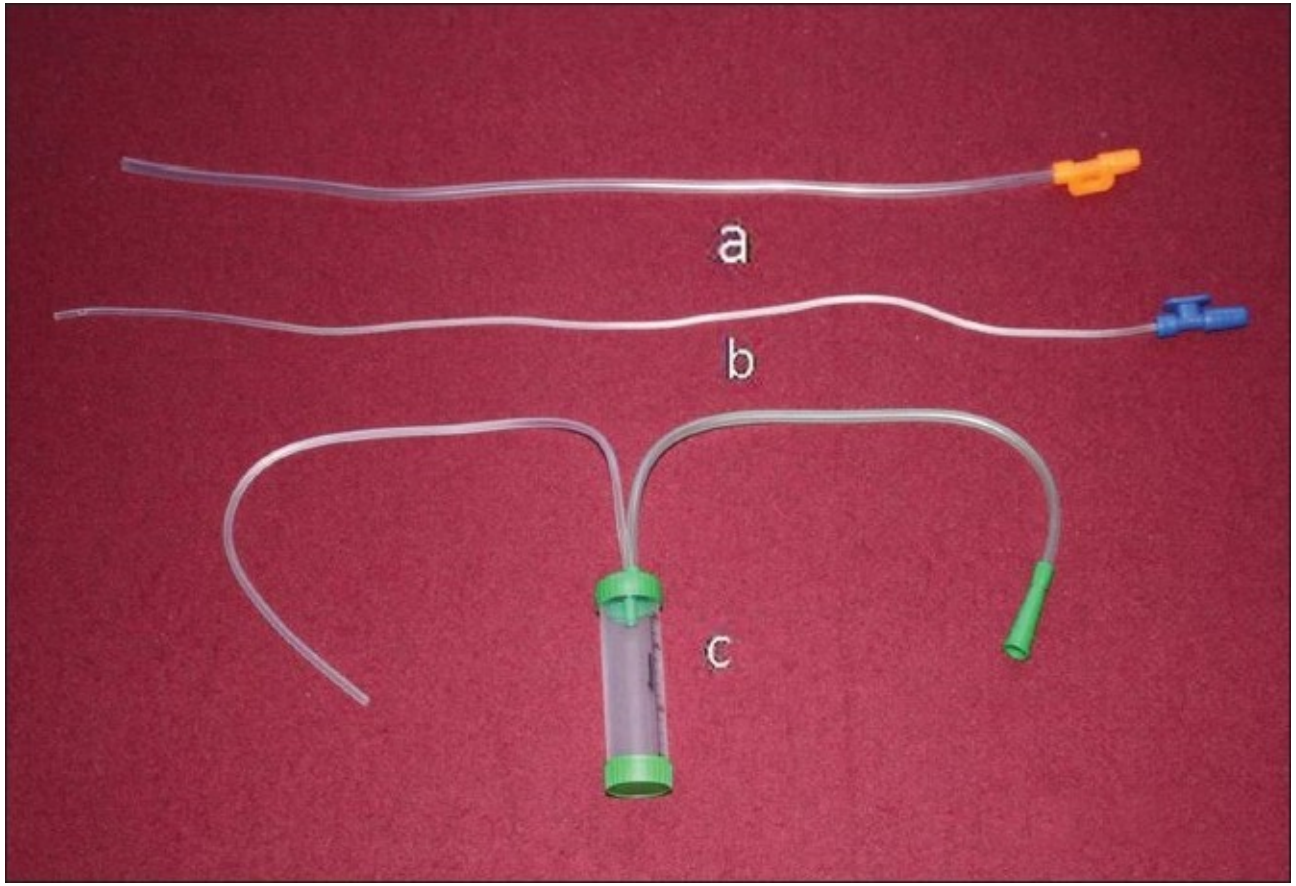
**GC Khilnani[1], T.K Luqman Arafath[1], Vijay Hadda[1], Arti Kapil[2], Seema Sood[2], SK Sharma[1],**

[1] Department of Medicine, All India Institute of Medical Sciences, New Delhi, India

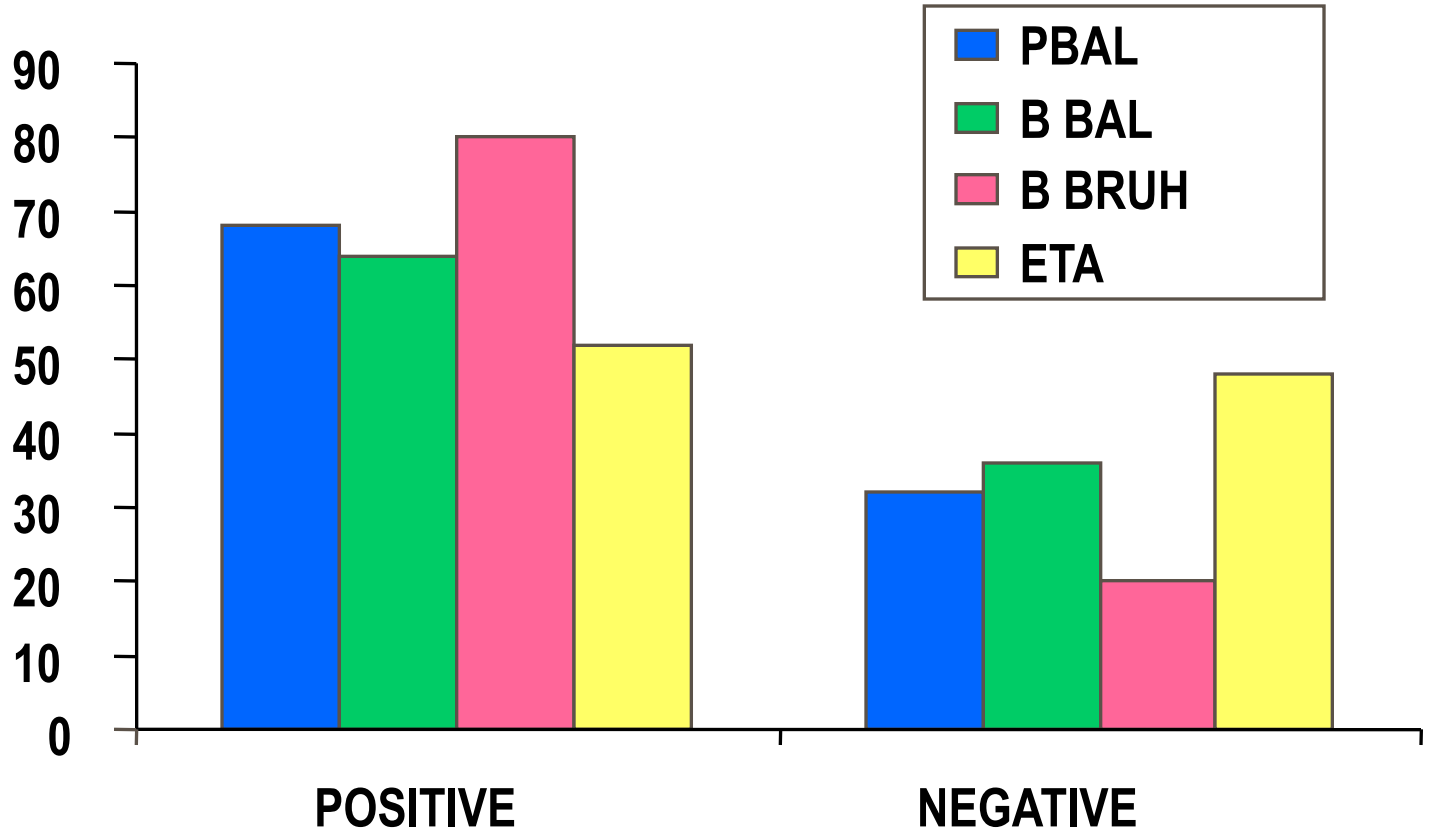
[2] Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India

**Background:** The diagnosis of ventilator associated pneumonia (VAP) remains a challenge because the clinical signs and symptoms lack both sensitivity and specificity and the selection of microbiologic diagnostic procedure is still a matter of debate. **Aims and Objective:** To study the role of various bronchoscopic and non-bronchoscopic diagnostic techniques for diagnosis of VAP. **Settings and Design:** This prospective comparative study was conducted in a medical ICU of a tertiary care center. **Materials and Methods:** Twenty-five patients, clinically diagnosed with VAP, were evaluated by bronchoscopic and non-bronchoscopic procedures for diagnosis. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of various bronchoscopic and non-bronchoscopic techniques were calculated, taking clinical pulmonary infection score (CPIS) of ≥6 as reference standard. **Results:** Our study has shown that for the diagnosis of VAP, bronchoscopic brush had a sensitivity, specificity, PPV and NPV of 94.9% [confidence interval (CI): 70.6-99.7], 57.1% (CI: 13.4-86.1), 85% (CI: 61.1-96) and 80% (CI: 21.9-98.7), respectively. Bronchoscopic bronchoalveolar lavage (BAL) had a sensitivity, specificity, PPV and NPV of 77.8% (CI: 51.9-92.6), 71.8% (CI: 24.1-94), 87.3% (CI: 60.4-97.8) and 55.5% (CI: 17.4-82.6), respectively. Sensitivity, specificity, PPV and NPV for non-bronchoscopic BAL (NBAL) were 83.3% (CI: 57.7-95.6), 71.43% (CI: 24.1-94), 88.2% (CI: 62.3-97.4) and 62.5% (CI: 20.2-88.2), respectively. Endotracheal aspirate (ETA) yield was only 52% and showed poor concordance with BAL (k-0.351; P-0.064) and NBAL (k-0.272; P-0.161). There was a good microbiologic concordance among different bronchoscopic and non-bronchoscopic distal airway sampling techniques. **Conclusion:** NBAL is an inexpensive, easy, and useful technique for microbiologic diagnosis of VAP. Our findings, if verified, might simplify the approach for the diagnosis of VAP.

# Mini BAL



# Results of P BAL, B BAL, B Brush and ETA cultures




Khilnani GC et al Am J Respir Crit Care Med 2007

Indian J Crit Care Med, 2011

## Comparison of bronchoscopic and non-bronchoscopic techniques for diagnosis of ventilator associated pneumonia

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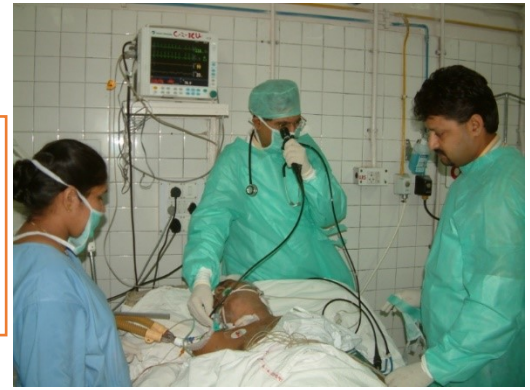


| Methods | Sensitivity | Specificity | PPV | NPV | Yield |
|---|---|---|---|---|---|
| Endotracheal aspirate | 55.6% | 71.4% | 83.3 | 38.5 | 52 |
| NBAL | 83.3% | 71.4% | 88.2 | 62.5 | 68 |
| Bronchoscopic BAL | 77.8% | 71.8% | 87.3 | 55.5 | 64 |
| Bronchoscopic PSB | 94.9% | 57.1% | 85 | 80 | 80 |

**N= 25**

Indian Journal of Critical Care Medicine 2011

| Procedure | Threshold | Sensitivity (%) | | Specificity (%) | |
|---|---|---|---|---|---|
| | | Range | Mean | Range | Mean |
| Tracheal Aspirate | $10^6$ cfu/ml | 33-82 | 76±9 | 72-85 | 75±28 |
| BAL | $10^4$-$10^5$cfu/ml | 42-93 | 73±18 | 45-100 | 82±19 |
| BAL Intracellular organism | | | 69±20 | | 75±28 |
| PSB | $10^3$ | 33-100 | 66±19 | 50-100 | 90±15 |
| Non-bronchoscopic BAL | | 64-97 | | 74-100 | |
| Mini BAL | | 63-100 | | 66-96 | |
| Blind PSB | | 58-86 | | 71-100 | |
| AIIMS Study Khilnani GC et al Am J Respir Crit Care Med 2007 | | | | | |
| Tracheal aspirate | Qualitative | | 75 | | 55 |
| BAL | $10^4$cfu/ml | | 77.85 | | 71.83 |
| Bronchoscopic Brush | $10^3$ | | 94.9 | | 57.14 |
| Non-bronchoscopic BAL | $10^4$ | | 83.3 | | 71.43 |

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

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 21, 2006 VOL. 355 NO. 25

# A Randomized Trial of Diagnostic Techniques for Ventilator-Associated Pneumonia

**METHODS**

In a multicenter trial, we randomly assigned immunocompetent adults who were receiving mechanical ventilation and who had suspected ventilator-associated pneumonia after 4 days in the intensive care unit (ICU) to undergo either bronchoalveolar lavage with quantitative culture of the bronchoalveolar-lavage fluid or endotracheal aspiration with nonquantitative culture of the aspirate. Patients known to be colonized or infected with pseudomonas species or methicillin-resistant *Staphylococcus aureus* were excluded. Empirical antibiotic therapy was initiated in all patients until culture results were available, at which point a protocol of targeted therapy was used for discontinuing or reducing the dose or number of antibiotics, or for resuming antibiotic therapy to treat a preenrollment condition if the culture was negative.

**RESULTS**

We enrolled 740 patients in 28 ICUs in Canada and the United States. There was no significant difference in the primary outcome (28-day mortality rate) between the bronchoalveolar-lavage group and the endotracheal-aspiration group (18.9% and 18.4%, respectively; P=0.94). The bronchoalveolar-lavage group and the endotracheal-aspiration group also had similar rates of targeted therapy (74.2% and 74.6%, respectively; P=0.90), days alive without antibiotics (10.4±7.5 and 10.6±7.9, P=0.86), and maximum organ-dysfunction scores (mean [±SD], 8.3±3.6 and 8.6±4.0; P=0.26). The two groups did not differ significantly in the length of stay in the ICU or hospital.

**CONCLUSIONS**

Two diagnostic strategies for ventilator-associated pneumonia — bronchoalveolar lavage with quantitative culture of the bronchoalveolar-lavage fluid and endotracheal aspiration with nonquantitative culture of the aspirate — are associated with similar clinical outcomes and similar overall use of antibiotics. (Current Controlled Trials number, ISRCTN51767272.)

# Approach to diagnosis: Recommendations

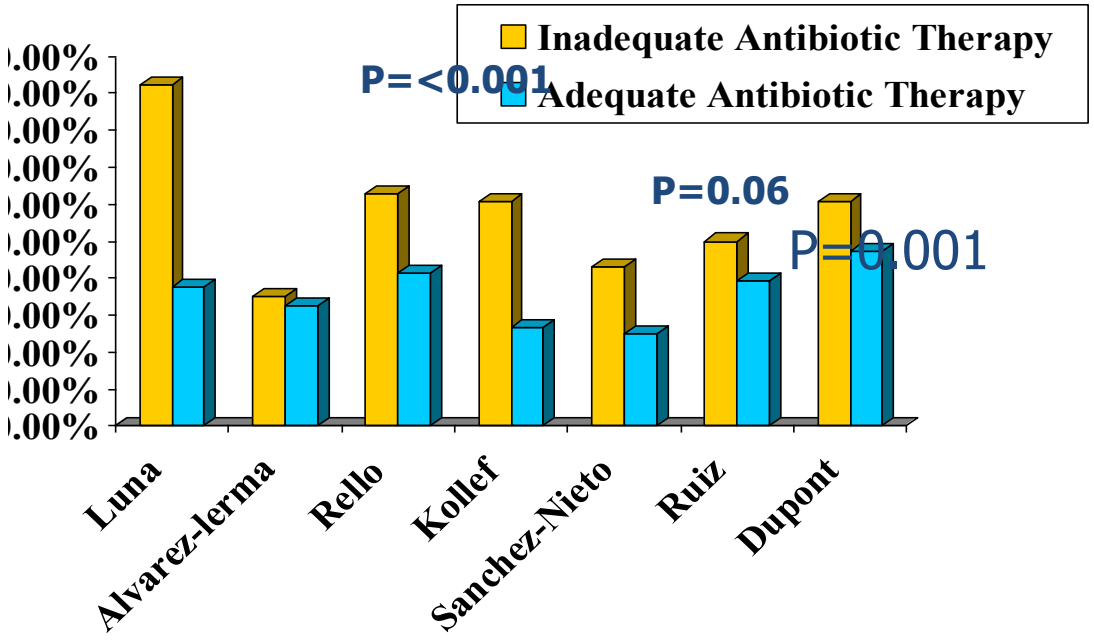
- HAP/VAP can be clinically defined by modified CDC criteria (2A)
- Send lower respiratory tract samples and blood for cultures prior to antibiotics (1A)
- **Weak Recommendation, Low-quality Evidence!!**
- "For patients with suspected HAP/VAP, **we suggest using clinical criteria alone**, rather than using CPIS, CRP or PCT, to decide whether or not to initiate antibiotic therapy"

IDSA, 2016

Gupta et al. Indian J Chest Dis Allied Sci 2012

# Treatment

# MORTALITY RATES ACCORDING TO INITIAL EMPIRIC ANTIBIOTIC THERAPY (*AJRCCM 2002;165:880*)



# Procalcitonin in HAP/VAP

Questions

Evidence Statement or Recommendations

**Should procalcitonin levels be used to decide antibiotic initiation in HAP/VAP?**

| | |
|---|---|
| **Statement** | Procalcitonin alone has limited utility for diagnosing or predicting outcome of hospital-acquired or ventilator-associated pneumonia. Baseline procalcitonin values may be used to aid clinical parameters for decision-making. |
| **Recommendation** | Baseline procalcitonin levels alone should not be used to make the clinical decision regarding antibiotic initiation in patients with VAP and HAP (1A) |

**How often should procalcitonin level be repeated after baseline in VAP and HAP?**

| | |
|---|---|
| **Statement** | Serial procalcitonin levels have been used in antibiotic de-escalation and antibiotic stewardship studies. Most studies have measured procalcitonin daily in critically ill and every 48 to 72 hours in stable patients. Most studies on VAP have done daily PCT. |
| **Recommendation** | Serial serum procalcitonin level measurement, preferably every 48 hours, should be used in antibiotic de-escalation. (UPP) |

Khilnani GC et al. Guidelines for the use of Procalcitonin for Rational Use of Antibiotics. IJCCM 2022 (Accepted for publication)

What are the common organisms causing VAP?

What are risk factors for infection with MDR pathogens?

# Indian Guidelines for Antibiotics in ICU

Questions

## What are the common organisms causing VAP?

Statement

Globally m/c aerobic GNB, such as Acinetobacter, K. pneumoniae, P. aeruginosa, or GPC (e.g., S. aureus).
India: GNBs (most common Acinetobacter, Klebsiella, Pseudomonas spp.)
Mostly MDROs
Microbiology and resistance varies by hospital, patient population, type

## What are risk factors for VAP due to MDR pathogens?

Statement

Age > 60 years
MV ≥ 7 days
Prior antibiotic use within 3 months
Severe sepsis/septic shock at time of VAP
ARDS preceding VAP
RRT prior to VAP
Systemic corticosteroid therapy

Evidence Statement or Recommendations

What should be the initial empirical antimicrobial therapy in this case?

# Indian Guidelines for Antibiotics in ICU

| Recommendation | |
|---|---|
| ▪Among patients with VAP who are not at high risk of MDR pathogens and are in ICU with low prevalence of MRSA(<15%) and resistant gram negatives (<10%)<br>➢Single antibiotic active against both MSSA and pseudomonas is preferred over combination antibiotic | [1A] |
| **▪Among patients with VAP who are not at high risk of MDR pathogens and are in ICU with high prevalence of resistant gram negatives (>15%) but low prevalence of MRSA(<10%)**<br>**➢Two agents active against gram negative organism including pseudomonas aeruginosa is recommended** | [3A] |
| ➢Fluroquinolones and aminoglycoside should be cautiously used as monotherapy in VAP in our country or areas with high endemicity of tuberculosis | [UPP] |

Khilnani GC et al. Indian Journal of Critical Care Medicine 2019;23(Suppl 1): S1-S63

# Is there a role for upfront colistin in patients with VAP?

# Role of Colistin

## Role of Colistin as Empiric Therapy?

Recommendation

- Colistin is not recommended for **routine use** as empirical agent in VAP however it may be used upfront in the ICUs if there is high prevalence of Carbapenem-resistant Enterobacteriaceae(>20%) [UPP]

Antibiotics changed to cefoperazone sulbactam, levofloxacin

# *Current Scenario in Indian ICUs*

MiniBAL AST report

| Antibiotics | Klebiella pneumoniae |
|---|---|
| Amikacin | R |
| Cefotaxime | R |
| Ceftazidime | R |
| C | |
| C | |
| Imipenem | R |
| M | |
| P | |
| Colistin | S |
| Tigecycline | S |

How often you see resistant Klebsiella in your recent practice?

Antibiotics modified; colistin added, levofloxacin stopped

# *Case scenario 2*

- Day 9: Patient afebrile,
- Fit for extubation
- TLC 10000


What should be the optimal duration of treatment ?

# Indian Guidelines for Antibiotics in ICU

Recommendation

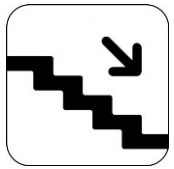
## Duration of Antibiotic therapy?

- **Short course ( 7-8 days) of antibiotic therapy should be used, i**n case of VAP with *good clinical response to therapy.[1A]*

- Longer duration (14 days) of antibiotic therapy should be considered*, in case of VAP caused by NF-GNBs or is associated with severe immunodeficiency , structural lung disease (COPD, Bronchiectasis, ILD) , empyema, lung abcess, necrotizing pneumonia and inappropriate initial antimicrobial therapy.[3A]*

Khilnani GC et al. Indian Journal of Critical Care Medicine 2019;23(Suppl 1): S1-S63

# Antibiotic de-escalation



- Broad spectrum → Narrow spectrum
  - According to sensitivity pattern
- Combination therapy → Monotherapy
- Judicious de-escalation of antibiotics:
  - **Improved or unaltered treatment outcomes**
  - Decreased antimicrobial resistance
  - Decreased side effects
  - Reduced overall costs

Clin Chest Med 2011; 32: 517-34
Crit Care Med 2007; 35:379-85

# Role of biomarkers (Procalcitonin for de-escalation)

# Procalcitonin in HAP/VAP

Questions

Evidence Statement or Recommendations

**Should procalcitonin be used for the de-escalation of antibiotics in patients with VAP/HAP?**

| | |
|---|---|
| **Statement** | Procalcitonin-based antibiotic de-escalation has been associated with decreased antibiotic exposure and better outcomes without any significant increase in treatment failure. |
| **Recommendation** | Procalcitonin should be used as a part of an antibiotic stewardship program for antibiotic de-escalation in patients with VAP on antibiotics beyond 7 days (1A). |

**What cutoff value of procalcitonin should be used to consider de-escalation of antibiotic therapy in VAP?**

| | |
|---|---|
| **Statement** | For procalcitonin, various studies have used absolute cutoffs of 0.5. Also, a decline of 80 to 90% from baseline has been. In CKD, cutoff of 0.5 has been proposed. |
| **Recommendation** | PCT< 0.5 ng/ml or a decline of 80% from baseline along with clinical criteria should be used for de-escalation in VAP and HAP (3A<br>Decline of ≥80% from baseline and clinical criteria can be used for de-escalation if baseline values are available. (UPP) |

Khilnani GC et al. Guidelines for the use of Procalcitonin for Rational Use of Antibiotics. IJCCM 2022 (Accepted for publication)

# Aerosolized antibiotics

- Colistin and tobramycin nebulisation may be used as adjunct to intravenous antibiotics(2A)
    - For MDR pathogens where toxicity is a concern
    - Acinetobacter and pseudomonas
- Should not be used as monotherapy (2A)
- Should be used concomitantly with IV antibiotics (2A)

Gupta et al. Indian J Chest Dis Allied Sci 2012

# Aerosolized antibiotics

**PRO**

- Antimicrobial agent quickly reach the infected location
- Bind to a target site
- Lesser systemic side effects
- Determining factors
  - Particle size (1-3 µm)
  - Delivery system

**CONS**

- Very limited data
- High deposition in trachea, lesser in dense consolidation
- Mucus plug, secretions, bronchospasm, ventilator asynchrony all can hinder the deposition of inhaled antibiotics
- Mismatch between clinical and microbiological improvement

Respir Care 2016;61(6):737–748

Zampieri *et al. Critical Care* (2015) 19:150
DOI 10.1186/s13054-015-0868-y

CRITICAL CARE

RESEARCH Open Access

# Nebulized antibiotics for ventilator-associated pneumonia: a systematic review and meta-analysis

Fernando G Zampieri[1,2,3*†], Antonio P Nassar Jr[1,2,4†], Dimitri Gusmao-Flores[1,5,6], Leandro U Taniguchi[2,7], Antoni Torres[8] and Otavio T Ranzani[1,8,9,10]

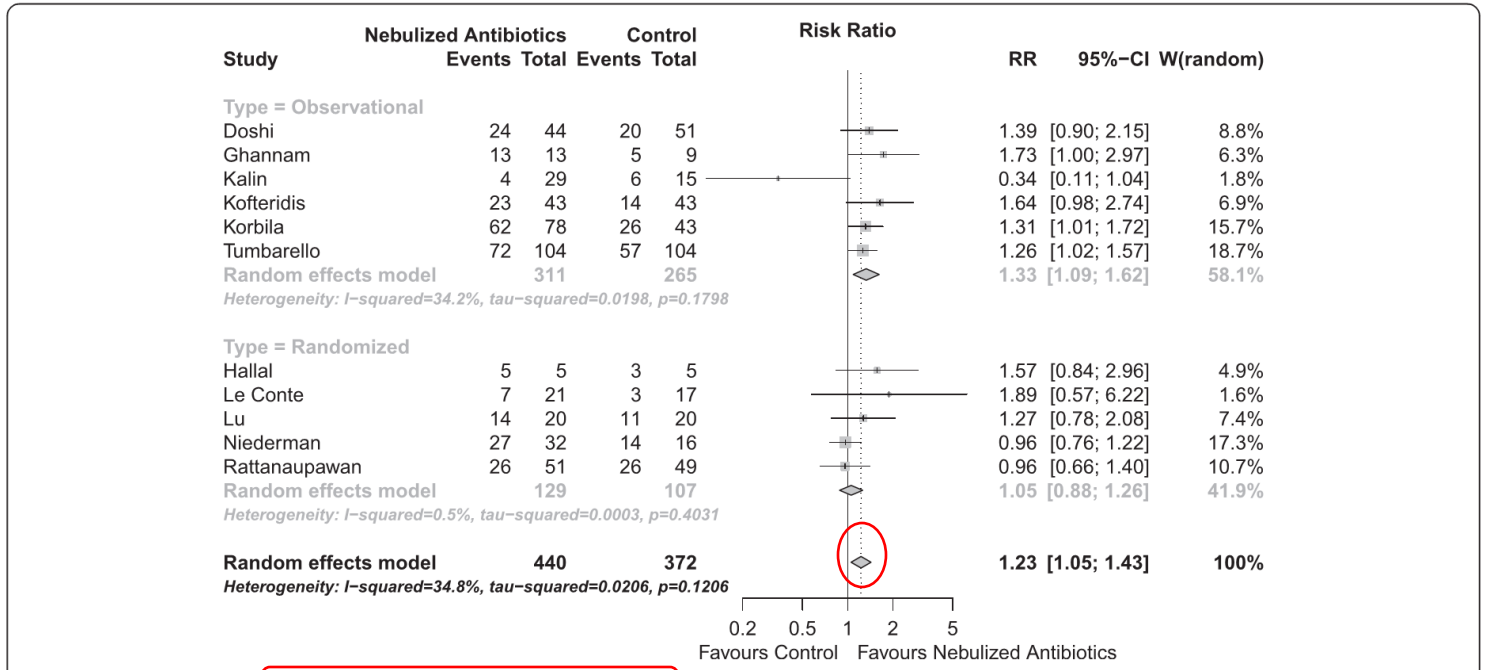



**Figure 3 Forest plot for clinical cure.** *P* for overall effect = 0.009. CI, confidence interval; RR, relative risk.

# ROLE OF INHALED ANTIBIOTIC THERAPY

For patients with VAP due to gram-negative bacilli that are susceptible to only aminoglycosides or polymyxins (Colistin or polymyxin B), we suggest both inhaled and systemic antibiotics, rather than systemic antibiotics alone

*(weak recommendation, very low-quality evidence) !!!!*

IDSA GUIDELINE

# PREVENTION OF VAP

# VAP BUNDLES

- **8 practices**:
  - ✓ Hand hygiene
  - ✓ Glove and gown compliance
  - ✓ Elevation of the head of the bed
  - ✓ Oral care with chlorhexidine
  - ✓ Maintaining an ET cuff pressure >20 cm H20
  - ✓ Orogastric rather than nasogastric feeding tubes
  - ✓ Avoiding gastric over distention
  - ✓ Eliminating nonessential tracheal suctioning


- **Rate of VAP decreased from 23 to 13 VAP episodes per 1000 ventilator-days**
- **No differences in total duration of mechanical ventilation or the ICU and hospital death rates**

**Bouadma L, et al. Long-term impact of a multifaceted prevention program on ventilator-associated pneumonia in a medical intensive care unit. Clin Infect Dis. 2010;51(10):1115**

- **5 interventions**:
  - ✓Semirecumbent position
  - ✓Stress ulcer prophylaxis
  - ✓DVT prophylaxis
  - ✓Adjustment of sedation
  - ✓Daily assessment for extubation


- Tested in 112 ICUs with 550,800 ventilator-days
- VAP rate declined from a median of 5.5 cases per 1000 ventilator-days at baseline to a median of 0 cases at 16 to 18 months after implementation

BerenholtzSM et al. Infect Control Hosp Epidemiol. 2011;32(4):305

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