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ABSTRACTS 15th ERS Annual Congress

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28. Diagnosis and prognosis of ventilator associated pneumonia: the clinical track

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Automatic control of the tracheal cuff pressure does not prevent ventilator-associated pneumonia (VAP)

M. Valencia¹, M. Ferrer¹, R. Farre², D. Navajas², R. Badia¹, M. Nicolas³, A. Torres¹. ¹S Pneumologia, H Clinic, Barcelona, Spain; ²Biofisica Bioenginyeria, U Barcelona, Barcelona, Spain; ³AVI, H Clinic, Barcelona, Spain

Background: The aspiration of subglottic secretions colonized by bacteria around the tracheal tube cuff due to inadvertent deflation of the cuff plays a pivotal role in the pathogenesis of VAP. We assessed the efficacy of an automatic device for the continuous control of the cuff pressure in preventing VAP.

Methods: We prospectively randomised ventilated patients to receive either the automatic device or routine cuff pressure care (control group). Patients with pneumonia or tracheotomy were excluded.

Results: We included 124 patients, 60 in the automatic and 64 in the control group, age 64±17 yr, APACHE-II 18±5. The main causes for intubation were decreased consciousness (38, 30%) and exacerbation of chronic lung diseases (30, 24%). Both groups were similar at baseline. The VAP rate was similar between groups (12, 21% in the automatic group vs 18, 29% in the control group, p=0.40). Similarly, the rates of tracheotomy (15, 25% vs 10, 15%), mortality in the ICU (17, 28% vs 14, 22%) and in the hospital (26, 43% vs 20, 31%), as well as the ICU (13±15 vs 13±13 days) and hospital stay (27±24 vs 25±20 days) were similar among the automatic and the control groups, respectively.

Conclusions: The use of an automatic device for the continuous regulation of tracheal cuff pressure does not prevent VAP and mortality.

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Non-invasive assessment of alveolar infection using HME filter elution

Nazim Nathani¹, Nick Murphy¹, Bill Tunnicliffe¹, Mav Manji¹, David Thickett². ¹Critical Care, University Hospital Birmingham, Birmingham, United Kingdom; ²Respiratory Medicine, University Hospital Birmingham, Birmingham, United Kingdom

VAP is the leading cause of death in intensive care units. In ARDS the diagnosis of pneumonia is difficult with similar clinical manifestations and lack of predictability of the clinical markers. Tracheal aspirate is unreliable source of bacteriological sampling, whereas bronchoalveolar lavage (BAL) is the gold standard. We investigated whether the HME filter used as part of the ventilator circuit could be utilised to sample clinically relevant alveolar infection. A hydrophobic pleated HME filter is placed at the junction of the endotracheal tube and ventilator circuit. This ensures humidification of the inspiratory air by evaporation on a warm filter and water retention from the warm expiratory air by condensation.

Method: Filter elution (FE) was obtained by introducing 20 ml of sterile 0.9% saline into the foam side of the filter before aspirating back the saline. The FE that is obtained is then centrifuged at 1100rpm for 10 minutes and residue was cultured for bacterial growth. Microbiology from FE was compared to tracheal aspirates (TA) and BAL from 27 patients with ARDS. Where there was significant BAL growth, FE grew significantly more bacterial pathogens compared to TA (p=0.02).

Results:

Samples, n=27	BAL	FE	TA	Matched Growth	
				BAL - FE	BAL - Sputum
Positive Growth	20	14	5	12	3
No Growth	7	13	22		

These results suggest that FE may represent an improved method of non-invasive assessment of alveolar infection in patients with ARDS.

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Clinical pulmonary infection score (CPIS) and inflammatory response in patients with new pulmonary infiltrates and suspected ventilator acquired pneumonia (VAP)

R. Badia¹, M. Cavalcanti¹, X. Filella², M. Ferrer¹, I. Aldabo¹, A. Torres¹. ¹Servei Pneumologia, Hosp. Clinic, Barcelona, Spain; ²S. Bioquímica, Hosp. Clinic, Barcelona, Spain

VAP bears a high morbi-mortality and is a complex diagnosis.

Aim: assess the relation between the clinical pulmonary infection score (CPIS) and the inflammatory response in ventilated patients with suspected VAP.

Methods: We included 32 ICU patients ventilated for >48h with new pulmonary infiltrates and suspected VAP and 12 ventilated controls without infiltrates. CPIS

was measured and systemic and local inflammatory response was assessed in plasma and BAL fluid respectively at day 1 and day 3 (TNF-alpha and soluble receptors, IL1b, IL6, IL8, IL10, PCR and procalcitonine). A standard microbiological work-up was carried out.

Results: IL6 was increased in patients with infiltrates compared to controls both in plasma (515±614 vs 46±2 pg/ml: p<0.05) and BAL (1756±659 vs 132±200: p<0.05). PCR was also higher those with suspected VAP (79±72 vs 39±29: p<0.04). 17 patients had CPIS ≤ 6 (64±14yr; APSII:21+4) and 15 (53±14yr; APSII:20+7) had CPIS>6. We did not find significant differences in inflammatory markers between these two groups with this cut-off point usually considered in clinical decision making.

Conclusion: Ventilated patients with suspected VAP have an increased inflammatory response compared to controls. Supported by FIS 02/0632, Red GIRA and Red Respira.

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Evaluation of severe pneumonias in the ICU of a tertiary center in Southern India

Saicharan G. Bodi, Sarada, Ramulu, Bharati, Alok Ranjan. Pulmonary & Critical Care, Apollo Hospitals, Secunderabad, AP, India

Introduction: Severe pneumonias are frequently encountered in the ICU setting, contributing to high mortality. They include ventilator associated pneumonias (VAP), Aspiration pneumonias, severe Community Acquired Pneumonias.

Objective: To systematically evaluate the incidence of severe pneumonias, their major risk factors, causative organisms & their drug resistance patterns and the treatment outcomes which may serve as basis for a multidisciplinary approach to reduce their incidence.

Design: Retrospective study

Setting: 18 bedded tertiary care ICU (Apollo Hospitals, India)

Subjects: 124 patients (Jan 2002 - Dec 2004) met the study criteria.

Results: APACHE II scores ranged from 14 to 49. VAP observed in 54 patients. Commonest organisms were Gram negative bacteria - Pseudomonas 36%, Klebsiella 24%, Staph aureus 12%. Resistance also observed to anti-pseudomonas penicillins. Carbapenems were very effective in resistant cases. Overall mortality was higher in elderly with serious Comorbid conditions and Polytrauma patients.

Conclusions: VAP is seen in more than 40% patients. There is increasing incidence of ESBLs producing organisms leading to increased resistance. Judicious use of Beta-lactam antibiotics like Carbapenems with Aminoglycosides and newer Quinolones is very essential in reducing the mortality.

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The risk of bronchoalveolar fluid (BAF) contamination in ICU patients with infectious pulmonary complications

Jana Skrickova, Anna Hrazdova. Department of Respiratory Disease and TB, University Hospital Brno, Brno, Czech Republic

We compared the results of bacteriological examination and examination for the presence of fungi in mouth washing, in the sample from large airways, in the bronchial sample and in BAF sample in 151 ICU patients.

Mouth washings were made prior BAL in 93 and lavage from main and lobar bronchi in 121 patients. Negative bacterial findings in mouth and BAF were in 35 (38%), positive findings in mouth and BAF in 4 (4%), positive but differing findings in mouth and BAF in 16 (17%), positive in the mouth but negative in BAF was in 17 (18%), and negative bacterial finding in the mouth but positive in BAF in 21 (23%) patients. Negative bacterial findings in bronchial samples and in BAF were observed in 78 (65%), identical findings in large airways and BAF in 8 (6%), and differing findings in large airways and BAF in 6 (5%) patients. A positive finding in the large airways and negative in BAF was seen in 5 (4.1%) patients, whereas in 24 (20%) patients there were negative findings in large airways and positive in BAF. In 63 (68%) no fungal microorganisms were found either in mouth washings or in BAF. In 2 (2%) identical findings of fungal microorganisms were present in mouth washing and BAF, in 4 (4%) different organisms were in mouth washing and BAF. In 14 (15%) patients there was a positive finding in the mouth but negative in BAF, and in 10 (11%), a positive finding in BAF but negative in the mouth.

The risk of BAF contamination by bacteria and fungi from either large airways or mouth is unlikely if the methodology of BAL is strictly adhered to.

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Late-onset ventilator-associated pneumonia in patients with acute nervous system infections

Olga M. Gajovic, Predrag S. Canovic, Zeljko D. Mijailovic, Zorica M. Lazic. Department of Infection Disease, Clinical Center Kragujevac, Kragujevac, Serbia & Montenegro

Late-onset Ventilator-associated pneumonia (VAP) in patients with acute nervous system infections which treated at the Intensive Care Unit (ICU) is a major cause of mortality. The objective of this paper was to establish the type of nervous system infections, etiology, disposition and risk factors for the development VAP.

Method: 180 patients with bacterial meningoencephalitis and cerebritis, were ad-

mitted to the ICU; 108 patients required mechanical ventilation, while 35 patients developed late-onset VAP (19 males, 16 females, average 58 years). Risk factors for VAP were: chronic respiratory diseases (58.9%), depressed consciousness or coma (66.1%), infections diseases and previous antibiotic exposure (third generation cephalosporins and metronidazole 88.2%), duration of mechanical ventilation (>23 days). The most common pathogens isolated were: *Pseudomonas aeruginosa* (56.1%), *Acinetobacter* spp. (19.8%) *Staphylococcus aureus* (21.7%). The sensitivity to antibiotics were investigated by Sceptor system of Bacton Dickinson (USA). We found that *Pseudomonas aeruginosa* showed a high degree of resistance to a large number of examined antibiotics: piperacilin-tazobactam (53%), amynoglycoside (92%), levofloxacin (66.7%), ceftriaxone (88%), ceftazidime (67%), cefotaxim (80%) while sensitivity was to imipenem (100%) and aztreonam (96%). Total mortality was 24/35 (71.4%). We conclude that prolonged mechanical ventilation was associated to higher percentage of multiresistant *Pseudomonas aeruginosa* (statistic significance).

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Predictors of early mortality after ICU discharge

Tansu Ulukavak Ciftci, Elif Han, Gul Gursel. *Pulmonary Disease, Gazi University, Ankara, Turkey*

The aim of the study is to evaluate possible predictors of early mortality after ICU discharge. Sixty-four consecutive patients discharged alive from ICU and were followed up 1 year. The patients were divided into two groups: Patients who had died in 1 month after discharge (group I) and patients who were still living 1 month later after discharge (group II). The age, diagnosis, comorbidity, home oxygen and mechanical ventilation therapies, duration of mechanical ventilation, duration of stay in the ICU, APACHE II score (in admission and discharge), sequential organ failure assessment (SOFA), logistic organ dysfunction score (LODS) and therapeutic intervention scoring system (TISS) (discharge), several laboratories and mechanical ventilation data (admission) were compared between two groups. The early mortality was 25%. Reasons for ICU admission in group I were acute exacerbation of COPD (43.75%), asthma (6.25%), pulmonary embolism (6.25%), pneumonia (18.75%), restrictive lung disease (12.5%) and acute renal failure (12.5%). Univariate analysis indicated a statistically significant difference between the group I and II in the following variables respectively: age (69.44 ± 12.82 ; 59.05 ± 15.49) APACHE II score (11.43 ± 2.5 ; 9.65 ± 2.43), LODS (6.07 ± 2.46 ; 4.42 ± 2.44) and hemoglobin levels (12.01 ± 1.84 ; 13.38 ± 2.21). The early mortality was independently associated in the multivariable analysis with only age (OR=1.08 CI 95%: 1.01-1.14 $p=0.021$). In conclusion, early mortality after ICU discharge is very high and according to our results most of the clinical variables except age may not predict early mortality after discharge.

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Risk factors, etiology, and clinical outcomes of ventilator-associated pneumonia

Emad Ibrahim¹, Taysier Zytoon². ¹Chest Department, Alexandria Faculty of Medicine, Alexandria, Egypt; ²Critical Care Medicine, Alexandria Faculty of Medicine, Alexandria, Egypt

Introduction: Ventilator-associated pneumonia (VAP) is a frequent ICU problem. **Aim:** To update our data of risk factors, etiological agents, and clinical outcomes of VAP.

Method: We included 70 mechanically-ventilated patients admitted to respiratory and critical care ICUs from June 2003 to June 2005 in Alexandria Main University Hospital, Egypt. Data was gathered and tracheal aspirates was used for cultures.

Results: Ventilator-associated pneumonia occurred in 55.7% of mechanically ventilated patients. The most common causative pathogens were *Pseudomonas* (23.9%), *Klebsilla* (14.1%), *Proteus* (8.5%), *MSSA* (5.6%), and *Mycoblasma* (5.6%).

Table 1. Risk Factors and Outcomes of VAP

Variable	Non-VAP Patients (31)	VAP Patients (39)	P Value
Age	47.2±12.4	42.9±9.7	0.120
APACHE II Score	31.6±5.7	30.7±5.7	0.543
Supine Position	16 (51.6%)	33 (84.6%)	0.003
Early feeding	13 (42%)	34 (87.2%)	<0.001
Mechanical days	14.2±9.3	20.7±6.7	0.002
Mortality	8 (25.8%)	10 (25.6%)	0.600

Conclusion: Supine position, tracheostomy, early enteral feeding, prolonged enteral feeding, and lower albumin serum level were most common risk factors to develop VAP. *Pseudomonas aeruginosa* and *Klebsilla pneumoniae* were the most common causative pathogens of VAP. Mechanical ventilation, ICU stay, and hospitalization days were prolonged for patients with VAP. Patients with VAP had longer duration of antibiotic therapy. Prevention of VAP would help improving clinical outcomes of ICU patients.

29. Basic mechanisms in asthma and COPD – new insights

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Interleukin-13 receptor alpha 2: a regulator of IL-13 and IL-4 signal transduction

Allison-Lynn Andrews¹, John W. Holloway², Stephen T. Holgate¹, Donna E. Davies¹. ¹Infection, Inflammation and Repair, University of Southampton, Southampton, Hampshire, United Kingdom; ²Human Genetics, University of Southampton, Southampton, Hampshire, United Kingdom

Introduction: IL-13 and IL-4 are pleiotropic cytokines with roles in asthma and allergic disease. IL-13 shares many functional properties with IL-4 as a result of the common IL-4R α component in their receptors. IL-13 signals via its cognate receptor, a complex of IL-13R α 1 with IL-4R α . A second IL-13 binding protein, IL-13R α 2, binds IL-13 with high affinity. Despite this increased binding affinity, it appears unable to initiate the IL-13 downstream signalling pathway and may act as a “decoy” receptor. We have examined the regulation of IL-13 and IL-4 by IL-13R α 2.

Methods: Expression of IL-13R α 2 in primary human airways cells was confirmed by FACS analysis. Immunoprecipitation of receptor chains was followed by SDS-PAGE and Western Blotting. Eotaxin and IL-8 release was measured by ELISA.

Results: A soluble form of IL-13R α 2 was able to block the effects of IL-13 on primary epithelial cells and fibroblasts *in vitro*. Cells with high surface levels of IL-13R α 2 failed to respond to IL-13 or IL-4, even though they responded to TNF α . In the presence of IL-4, IL-13R α 2 associated with IL-4R α and inhibited signal transduction. The addition of an IL-13R α 2 blocking antibody restored IL-4 signalling.

Discussion: Our data suggests that IL-13R α 2 may act as a “decoy” receptor for IL-13 and IL-4 or maybe an autoregulatory mechanism to attenuate the effects of IL-13 and IL-4 in primary bronchial epithelial cells and fibroblasts.

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Role of I κ B kinases (IKKs) α and β in severe asthma and COPD

Rosalia Gagliardo¹, Flora Pompeo¹, Anna M. Merendino², Mark Gjornmarkaj, Isabelle Vachier³, Jean Bousquet³, Giovanni Bonsignore¹, Pascal Chanez³.

¹IBIM, CNR, Palermo, Italy; ²Istituto di Medicina e Pneumologia, Università di Palermo, Italy; ³U454, INSERM, France

IKK α and IKK β , highly homologous catalytic kinases, phosphorylate I κ B inhibitory proteins, causing their degradation and NF- κ B activation. IKK α is involved in morphogenesis, prevention of cell death and functional development of mature B cells; IKK β is essential for cytokine signalling. To better characterize the NF- κ B activation pathway we evaluated, by immunoprecipitation and Western Blot, the levels of the upstream regulators IKK α and IKK β , and the phosphorylated form of both kinases (p-IKK α and p-IKK β), in PBMC from controls (C), mild to moderate asthmatics (MMA), severe asthmatics (SA), healthy smokers (HS) and COPDs. By Luminescent Kinase Assay we analyzed the IKKs activity. p-IKK α was not expressed in C and in MMA while it was expressed in 2 of 8 SA, 3 of 6 healthy smokers and 10 of 10 COPDs. p-IKK β was expressed in MMA, SA, HS and COPD. Functional activation analyses showed that IKK α activity was similar in HS and COPDs and higher than in C, MMA and SA. IKK β activity was similar in HS, SA and COPDs and higher than in C and MMA. These results suggest a different NF- κ B regulation in SA and COPDs due to distinct kinase activation. IKK β activation in COPD, other than in severe asthma, suggests an important role of inflammatory processes also in COPD. The exclusive IKK α activation in HS and in COPDs suggests the presence of an altered cell differentiation and/or cell apoptosis control.

Dedicated to the memory of Maurizio Vignola.

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Human myeloid lung dendritic cells are strong inducers of T cell proliferation compared to plasmacytoid lung dendritic cells

Ingel K. Demedts, Guy F. Joos, Guy G. Brusselle. *Department of Respiratory Diseases, Ghent University Hospital, Ghent, Belgium*

Dendritic Cells (DC) are a subtype of leukocytes that play a central role in the development of asthma. They present antigen to T-cells and induce and modulate a T helper response.

Previously, we identified three different DC subtypes in human lung: myeloid DC type 1 (mDC1), plasmacytoid DC (pDC) and myeloid DC type 2 (mDC2). mDC are more mature than pDC: they express higher levels of costimulatory molecules (Demedts, I. *et al.* Am J Respir Cell Mol Biol 2005; 32: 177-184)

This raises the question if myeloid DC are stronger inducers of T cell proliferation compared to plasmacytoid DC. To evaluate this, we purified the three different lung DC subsets from surgical resection specimens and cocultured them with allogeneic T cells. The amount of T cell proliferation was measured by ³H thymidine incorporation.