307. Hot topics in respiratory infections

2811 Multidimensional approach to non-cystic fibrosis bronchiectasis. The FACED score
Miguel Angel Martínez-García1, Javier De Gracia-Roldán2, Montserrat Vendrell-Relat3, Rosa Girón4, Luis Maiz5, David de la Rosa6, Casilda Olivera7. 1Pneumology Service, La Fe University Hospital, Valencia, Spain; 2Pneumology Service, Vall Hebron University Hospital, Barcelona, Spain; 3Pneumology Service, Josep Trueta University Hospital, Girona, Spain; 4Pneumology Service, La Princesa University Hospital, Madrid, Spain; 5Pneumology Service, Ramón y Cajal University Hospital, Madrid, Spain; 6Pneumology Unit, Hospital Platón, Barcelona, Spain; 7Pneumology Service, Carlos Haya University Hospital, Málaga, Spain

Background: The severity of non-cystic fibrosis (NCF) bronchiectasis cannot be adequately quantified by analyzing one single variable.

Objective: To develop and validate an easy-to-use multidimensional score that classifies the severity of bronchiectasis according to its prognosis.

Methods: Multicenter study in an initial cohort of 819 patients diagnosed with NCF bronchiectasis by HRCT scan. 397 subjects were selected at random (construction cohort) and 422 were the validation cohort. Outcome: 5-year all-cause mortality after diagnosis. From an initial set of 30 variables, those included in the final score were selected using a logistic regression analysis and dichotomized to facilitate the score’s interpretation.

Results: Mean age: 58.7 yrs (56% women), 154 deaths during follow-up. The final 7-point calculated score (FACED score) incorporated 5 dichotomized variables (OR [95%IC]): FEV1 predicted % (F, cut-off point 50%; OR: 5.2 [2.8-9.8]; maximum value: 2 points); age (a, cut-off point: 70 yrs; OR: 4.9 [2.7-9.3]; maximum value: 2); chronic colonization by P. aeruginosa (C, OR: 2.4 [1.3-4.6]; maximum value: 1); radiological extension (E, number of lobes affected: cut-off point at 2 lobes; OR: 1.9 [1.1-3.5]; maximum value: 1) and dyspnea (D, cut-off point at grade II on the MRC scale; OR: 5.8 [1.5-2.2]; maximum value: 1). No differences were found between the ABC-ROC (prognostic value) of the construction cohort 0.87 [0.82-0.91] and validation cohort 0.83 [0.78-0.89]. All centers had an ABC-ROC > 0.8.

Conclusions: This easy-to-use multidimensional grading system proved capable of accurately classifying the severity of bronchiectasis according to its prognosis.

2812 Clostridium difficile infection (CDI): Are junior doctors aware of risk factors and markers of severity?
Clara Addison, Toni Jordan. Respiratory Medicine, University Hospital North Staffordshire, Stoke-on-Trent, Staffordshire, United Kingdom

Introduction: There are approximately 20,000 cases of CDI in England per annum. 1 Lower Respiratory Tract Infections are the main indication for antibiotic prescription in hospitals. 2 In order to reduce CDI, it is essential that doctors are able to identify patients at risk of CDI to facilitate appropriate antibiotic prescribing. 3 Trust’s clinical guidance on CDI informs on markers of severity but not risk factors. We sought to determine the level of knowledge of both among doctors based on a Respiratory ward including clinical guidelines as a conduit of knowledge.

Methods and results: Using a questionnaire 19 doctors and 5 fourth and fifth year medical students were asked to identify risk factors and markers of severity for CDI. 1st year doctors identified 36% of risk factors, 28% of severity markers; senior house officers 38% and 24%; registrars 47% and 21%; medical students 41% and 21%.

Conclusions: Knowledge of risk factors and severity markers for CDI amongst doctors and medical students on the Respiratory ward is poor. Clinical guidance is not a reliable conduit of knowledge. To raise awareness, information should be relayed more directly e.g. at induction.

References:

2813 The respiratory microbiome in chronic obstructive pulmonary disease (COPD) exacerbations: Relationships with clinical characteristics
Bethan Barker, Mona Bafadhel, Koorihi Haldar, Ian Pavord, Mike Barer, Chris Brightling. Institute for Lung Health, Department of Infection, Immunity and Inflammation, The University of Leicester, United Kingdom

Background: There has been recent interest in the significance of the respiratory microbiome in COPD.

Methods: Within an observational COPD study, spontaneous and/or induced sput-
Admission serum glucose levels are a risk factor predicting short- and long-term mortality in community acquired pneumonia

Participants: 6,891 CAP patients with community acquired pneumonia included in the prospective German CAP Competence Network (CAPNETZ) study between 2003 and 2009.

Main outcome measures: Uni- and multivariable hazard ratios (HR) adjusted for gender, age, body mass index (BMI), current smoking status, CRB-65 and various co-morbidities for 28-, 90-, and 180-day mortality of CAP were calculated according to serum glucose levels on admission.

Results: In patients without known diabetes, an elevated glucose level at admission was an independent predictor of 28-, 90-, and 180-day mortality of CAP. As compared to individuals with normal glucose levels on admission, subjects with mild acute hyperglycemia (glucose on admission 6–11 mmol/L) had a significantly increasedHRfor death at 90 days (1.55; 95% CI: 1.18 to 2.04; P < 0.001), which increased to 6.04 (95% CI: 4.18–8.74; P < 0.001) if admission glucose levels were >14 mmol/L. In sensitivity analyses the predictive value of admission glucose levels was confirmed for short- (28 days) and long-term mortality (180 days).

Conclusions: Admission glucose levels predict an adverse outcome in CAP in patients without known diabetes. Hence, acute hyperglycemia may identify patients in particular need of intensified care to reduce mortality in CAP.

Long-term use of inhaled corticosteroids on the development of pleural effusion in community-acquired pneumonia

Introduction: Long-term use of inhaled corticosteroids (ICS) in patients with Chronic Obstructive Pulmonary Disease (COPD) has been associated with increased risk of CAP. Most recently, ICS have been associated with less severity of CAP and decreased risk of pneumonia-related mortality. Pleural infection is a frequent complication of CAP that may increase mortality. The aim of this study was to assess the influence of long-term use of ICS on the incidence and severity of parapneumonic effusion and empyema in patients with different baseline respiratory diseases.

Methods: We conducted a single centre cohort study of 3602 patients consecutively collected with CAP. We assessed clinical, radiographic and pleural fluid chemistry and microbiological variables. Patients were classified whether they received prior long term ICS treatment or not.

Results: 659 patients (18%) were treated with ICS before diagnosis of CAP (COPD: 56%). Long-term use of ICS was significantly associated with less incidence of parapneumonic effusion compared to those without prior ICS treatment 5% vs. 12%, p < 0.001. Multivariate analysis adjusted by sex, age, comorbidities and CAP severity showed a significant association between ICS treatment and lower incidence of pleural effusion (OR 0.42; 95% CI: 0.28-0.64; P < 0.001). Prior treatment with ICS was significantly associated with lower incidence of empyema compared to those without treatment (3% vs. 16%; p < 0.001).

Conclusions: Long-term use of ICS in patients who develop CAP is associated with lower incidence and less severity of parapneumonic effusion regardless of the baseline chronic respiratory condition.

Pulmonary immunostimulation with macrophage-activating lipopeptide-2 in influenza-A-virus infected mice increased survival of subsequent pneumococcal pneumonia

Methods: Influenza-A/H1N1/PR/834-virus infected female C57Bl/6 mice received the TLR-2 ligand macrophage-activating lipopeptide-2 (MALP-2) intra-nasally 24h prior to transnasal infection with S. pneumoniae.

Results: Intranasal application of MALP-2 increased pro-inflammatory cytokine and chemokine release and enhanced recruitment of leukocytes, mainly neutrophils in the alveolar space of influenza virus infected mice. After secondary pneumococcal infection, Influenza-A-virus infected mice pretreated with MALP-2 showed increased survival rates compared with untreated influenza infected mice. Notably, levels of pro-inflammatory cytokines and leukocytes were comparable in bronchoalveolar lavages of virus infected mice treated with MALP-2 and untreated infected controls. Further, MALP-2 significantly reduced bacterial numbers in the lung tissue without changing pulmonary viral load.

Conclusion: Local immunostimulation with MALP-2 in influenza virus infected mice improved pulmonary bacterial elimination and increased survival in secondary pneumococcal pneumonia.

Safety and pharmacokinetics of two dose strengths of ciprofloxacin dry powder for inhalation (DPI) in patients with moderate to severe COPD

Methods: In a randomized, phase I, double-blind, crossover study, 12 (8m/4f) adults with GOLD stage II or III COPD received a single dose of 32.5 mg and 48.75 mg ciprofloxacin DPI (corresponding to 50 mg and 75 mg dry powder, respectively). The washout period was 7–14 days between doses.

Results: There were no serious or severe AEs nor clinically relevant differences in incidence or severity of AEs between the doses, most being mild. Drug-related AEs (bitter taste) occurred in 7 and 6 patients after 32.5 mg and 47.85 mg ciprofloxacin DPI, respectively. The PK (Table) was similar to previous studies, showing high and variable lung exposure at low systemic exposure.

Conclusion: Ciprofloxacin DPI was well tolerated in patients with moderate to severe COPD.
to severe COPD with no clinically relevant differences between the two dose strengths. Increased systemic exposure from the 48.75 mg dose was not matched by increased lung exposure. PK data indicate that the lower dose produced similar drug concentrations in the lung, with less powder inhaled.

2818  
**T cells in peripheral blood during viral acute exacerbation of COPD**  
María Inés Vargas-Rojas¹, Alejandra Ramírez-Venegas¹,  
Leonardo Limón-Camacho², Oliver Pérez-Bautista¹,  
Helena Solleiro-Villavicencio¹, Raúl H. Sansores¹. ¹Department of Research in Smoking and COPD, Instituto Nacional de Enfermedades Respiratorias “Ismael Cosio Villegas”, México, D.F., México; ²Rheumatology, Hospital Central Norte PEMEX, México, D.F., México  

**Introduction:** Exacerbations in COPD patients increase premature mortality. The main cause of AECOPD are viral infections however, the type of predominant cellular immune response is unknown.  
**Objective:** To quantify the T cell subpopulations in peripheral blood of patients with viral AECOPD and compare them with patients in a stable disease (COPD) and healthy controls (HC).  
**Methods:** We included 82 patients from the Cohort of COPD Clinic, between May 2009 and December 2011, 49 of them were exacerbated and we included 19 HC. Viral diagnosis was performed by using real-time PCR and we used flow cytometry to determine T-cell subpopulations. Differences between groups were evaluated by Kruskal-Wallis and we performed a post-hoc U-Mann-Whitney test.  
**Results:** 26 patients (53%) had a viral exacerbation (Influenza A 54%, Coronavirus 14%, Influenza B 7%, RSV 7%, H1N1 7%, MPV 4%). In these patients predominated the Th1 response 8.6 (6.2-11) versus COPD 2.5 (1.3-4.29) and HC 1.1 (0.8-1.4) p < 0.0001. The TCD8 response has a predominance of Tc17 AECOPD 11.2 (7.1-13), COPD 2.8 (1.9-4.2) and HC 1.0 (0.5-2.2) p < 0.0001 and Tc1 AECOPD 7.6 (4.1-10), COPD 1.7 (1.1-2.8), HC 1.1 (0.8-1.2) p < 0.0001.  

**Conclusions:** Our data show a polarization Th1, Tc1, Tc2 and Tc17 in AECOPD patients suggesting the involvement of these populations in the cellular immune response during viral infections. We did not find a higher prevalence of H1N1 infections in patients in the cohort.