389. Phenotyping and monitoring of airway diseases

P3508

Bronchoprovocation challenge testing – The estimation of FEV1 decline

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Background: Methacholine and histamine bronchoprovocation challenge (BPC) is an important tool in the diagnosis of bronchial hyperreactivity (BHR). Some patients respond to BPC by a significant and fast drop in forced expiratory volume in one second (FEV1). The aim of the study was to evaluate which baseline anamnestic data correlates with a fast and severe drop in FEV1.
Methods: BPC was performed in each of 1375 patients presenting with suspected bronchial asthma (BA) of either occupational (OA) - 207 patients (15%) or non-occupational origin (1168 patients - 85%). The consequential impact of

the following parameters on FEV1 drop was also checked: age, sex, respiratory difficulties (dyspnoea, irritating cough, wheezing and allergic rhinitis symptoms), atopy, past medical history (PMH) of respiratory infection, smoking, chronic bronchitis. A 30% or higher FEV1 drop at bronchoprovocant dosages or concentrations lower than the planned cumulative dose or a 40% or higher FEV1 drop after inhalation of the whole bronchoprovocant dose was considered as severe.
Results: A severe FEV1 drop was found in 248 persons (18%), of which 201 patients (14.6%) were finally diagnosed with BA (52 patients with OA, 149 with non OA origin). Statistically significant FEV1 drop was found in both subgroups among patients with a PMH of whistling, among patients with atopy and smokers.
Conclusion: Caution is recommended when performing BPC in some patients, particularly in those with suspected asthma who are smokers, diagnosed with atopy and those with a PMH of wheezing. These patients may experience greater discomfort from bronchial obstruction and therefore, the provocational dose may need to be increased at a slower rate.

P3509
Small airways function in allogeneic hematopoietic stem cell transplant recipients worsens over time and is correlated with change in chronic GVHD grade
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Bronchiolitis obliterans (BO) following allogeneic hematopoietic stem cell transplantation (HSCT) is believed to be related to chronic graft-versus-host disease (cGVHD). Detection of BO is presently delayed by the low sensitivity of spirometry.
We examined the changes in small airways function and spirometry during 2 separate visits following allogeneic HSCT in 22 clinically stable recipients. Measurements of lung function, exhaled NO, forced oscillatory respiratory system resistance and reactance, acinar (Sacin) and conductive airways (Scond) ventilation heterogeneiy and lung clearance index (LCI) measured by multiple breath nitrogen washout were performed. These functional measurements were then compared with changes in cGVHD grade and respiratory quality of life (RQOL). Patients were tested 12±9 months after HSCT and repeat visits were performed 10±6 months later. Sacin and LCI were the only measures to change significantly between 2 visits, with both worsening. Changes in Sacin and LCI were not correlated with change in FEV1%predicted, change in RV/TLC% predicted, nor with change in any other measured parameters. Change in Sacin was the only parameter to correlate with change in cGVHD grade (r=0.63, p=0.003). Change in RQOL was not correlated with change in any physiological measurement.
This study shows that change in small airways function in HSCT recipients can be detected without change in spirometry or in RQOL. The correlation between change in Sacin and change in cGVHD grade suggests that Sacin may be more sensitive than spirometry in detecting BO at an early stage, which needs confirmation in a prospective study.

P3510
Cough reflex sensitivity during acute viral upper respiratory tract infection (common cold)
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One previous study has demonstrated that cough reflex sensitivity to inhaled capsaicin is transiently enhanced during acute viral respiratory tract infection (URI) by comparing single cough reflex sensitivity measurements at baseline and during URI (O'Connell F, et al. Respir Med 1996;90:279-286). To our knowledge, no one has performed multiple measurements of cough reflex sensitivity during acute URI to evaluate presence or absence of stability during the acute viral illness. To date, we have evaluated 37 otherwise healthy adult nonsmokers with acute URI. Subjects underwent capsaicin cough challenge testing, as previously described in the ERS guidelines (Morice et al. Eur Respir J 2007;29:1256-1276), on 2 consecutive days within the first 8 days of their illness, and again after 4-8 weeks (post-recovery). Briefly, subjects inhaled single, vital-capacity breaths of nebulized capsaicin, administered in incremental doubling concentrations, until the concentration inducing 5 or more coughs (C5) was attained. All 37 subjects had serial C5 measurements within 1 doubling concentration during the acute illness. Post-recovery mean log C5 was significantly higher than during illness (0.84±0.08 [SEM] vs. 0.50±0.08; p=0.000004). Our results demonstrate that cough reflex sensitivity remains stable in the acute phase of URI, and confirm previous findings of a transient increase of cough reflex sensitivity during URI compared to healthy baseline levels. The demonstration of stability of cough reflex sensitivity during the early stages of URI is relevant to potential investigators planning to evaluate the effect of a pharmacological intervention on cough reflex sensitivity during URI.

P3511
Gastro-oesophageal reflux disease, upper gastro-intestinal motility and autonomic function in adult asthmatics
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Introduction: Asthmatics have increased prevalence of gastro-oesophageal reflux disease (GORD). Oesophageal hypomotility, delayed gastric emptying (GE) and autonomic hypofunction increase GOR. Our aim was to study the relationship of GOR with autonomic function, oesophageal motility and GE in adult asthmatics.
Methods: Thirty consecutive mild, stable asthmatics (American Thoracic Society criteria) and 30 healthy volunteers underwent stationary oesophageal manometry, GE by real-time ultrasonography and autonomic function testing (cardiovascular reflex tests). GORD was assessed by symptom assessment and 24-hour pH monitoring.
Results: The asthmatics (40% male; mean age 34.8 years (SD 8.4)) and controls (50% male; mean age 30.9 years (SD 7.7)) were comparable. Twenty two (73.3%) asthmatics had increased reflux on pH monitoring. Asthmatics with higher GOR symptom scores had lesser peristaltic contractions (p=0.032), prolonged acid contact times (p<0.001), delayed GE (p=0.097) and decreased antral motility (p<0.001) than those with lower scores and controls. 69% of asthmatics showed hypervagal activity, rest had normal autonomic function, none had a hyperadrenergic response. There was no association between vagal function, oesophageal or gastric motility parameters in asthmatics.
Conclusions: A cohort of mild, stable adult asthmatics had increased GOR, decreased oesophageal motility and delayed GE. This was not associated with autonomic hypofunction, but with a hypervagal response. Our findings support the hypothesis that vagal hyperreactivity induced acid secretion leads to a reflex decrease in gastric motility, inducing GOR and secondary reduction in oesophageal motility.

P3512
Can asthma control test (ACT) replace a global assessment of asthma control according to GINA guidelines?
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Background: Asthma Control test (ACT) has been proposed as a surrogate of the assessment of asthma control, but there is controversy if it corresponds to GINA criteria (O'Byrne, ERJ 2010).
Aim: To compare GINA assessment of asthma control and ACT score
Patients and methods: We evaluate 68 outpatients (33 in inhaled corticoseroids, ICS, treatment, and 35 ICS-naïve), with mild-to-moderate asthma. Assessment of asthma was based on symptom score (SS), rescue salbutamol (RS), PEF (MA%), pulmonary function, and asthma exacerbations in the last year (GINA guidelines).
Results: ACT score significantly correlated with SS (r= 0.49), RS (r= 0.46) and MA% (r= 0.45), not with FEV1. ACT score only partially correlated with GINA categories of well (WC), partly (PC) and uncontrolled (UC) patients.

Contingency table between asthma control level (according to GINA Guidelines, gold standard) and ACT categories

	ACT: 25	ACT: 24–20	ACT: < 19	p
No.	9	28	31	
Symptom Score 14 days, mean (SD)	5.7 (9.5)	3.6 (7.4)	13.8 (16.3)	0.018
SABA Use days , mean (SD)	0.5 (1.3)	0.5 (2.1)	5.1 (5.7)	0.0005
No. days with MAPEF >10%, mean (SD)	1.3 (1.7)	2.2 (3.1)	3.8 (3.7)	0.076
FEV1, % pred, mean (SD)	96.4 (14.9)	92.4 (21.8)	98.2 (14.7)	ns
GINA control categories WC / PC / UC	3 / 4 / 2	9 / 9 / 5	3 / 8 / 18	0.022

ACT ≥ 20 had high Positive Predictive Value for WC+PC (PPV: 78%), while ACT ≤ 19 had high Negative Predictive Value for UC (NPV: 89%).
Conclusion: Cut-of value of ACT has a good accuracy for detecting uncontrolled asthmatics, but not for distinguish well from partly controlled asthmatics. The high correlations with data derived from 2-week diary card recording support ACT as a simple tool for the quantification of symptomatic asthma control.

P3513
Utility of the Hull airways reflux questionnaire in the assessment of patients in the acute admissions unit
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Airway reflux and aspiration are thought to be common precipitants of acute exacerbations of COPD. A validated instrument, the Hull Airway Reflux Questionnaire

(HARQ) has been developed to assess symptoms associated with airway reflux. The Acute Respiratory Assessment Service team are asked to review all respiratory admissions to the Acute Assessment Unit based in Hull Royal Infirmary. 55 patients, 22 male, mean age 67 were assessed over the winter of 2010/11. The admitting physician's diagnosis was an acute exacerbation of COPD in 72% of patients, with other diagnoses including acute asthma, reflux and aspiration and lower respiratory tract infection. Mean HARQ score was 28 (mean score for normal subjects 4, with an upper limit of normal of 13). Just over half of the subjects scored in excess of 30 on the questionnaire giving a very high likelihood of the exacerbation being associated with an episode of airway reflux. There was an average of 2.1 previous admissions in the last two years. Surprisingly, there was no strong correlation between the number of previous exacerbations and the HARQ score.
Airway reflux and aspiration, unlike the liquid acid reflux of heartburn, can present without obvious classic symptoms. The HARQ questionnaire enables the clinician to diagnose non acid gaseous reflux impacting on the airway leading to bronchospasm and shortness of breath. This study suggests that the majority of patients presenting with acute exacerbations of COPD are in fact suffering from aspiration events which have previously been overlooked.

P3514
Investigating change in the COPD assessment test (CAT) within α-1 antitrypsin deficiency (A1ATD)
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Introduction: The COPD Assessment Test (CAT) has been validated in COPD as a health status questionnaire (HSQ). Our group has validated the CAT in A1ATD, with correlations between CAT score and total St Georges Respiratory Questionnaire score (SGRQ) (R^2=0.81, p<0.001, n=320). Associations between CAT scores and lung function mirrored those seen with the SGRQ. We wished to determine if CAT could identify changes in health status over time and whether this correlated with differences in total SGRQ scores and its domains.
Method: 34 clinically stable patients with A1ATD attending the ADAPT centre annually completed both SGRQ and CAT prior to lung function and medical review. Demographics: 21 male (62%), mean age 54yrs (range 25-82), mean FEV_1% pred 57 (range 23-123), mean KCO% pred 58 (range 29-95).
Result: Over the two time points, there was a significant change in CAT score compatible with a worsening of health status (mean difference 1.65 (SEM 0.83) p=0.03) and a significant change in mean total SGRQ score (mean difference 2.91 (SEM 1.7) p=0.04). There were no changes in mean domain scores.
A significant correlation between the change in total SGRQ and CAT scores over 1 year (p=0.002) was observed. There were no difference in sensitivity of change indices, SGRQ 1.71 and CAT 1.99 and no differences in clinical or physiological parameters over the 2 time points.
Conclusion: Both CAT and total SGRQ scores increased within our patient group over one year. Changes in total SGRQ and CAT scores correlated significantly suggesting that the CAT can be used as an HSQ to track change over time in A1ATD. Further recruitment will allow us to correlate CAT scores with decline.

P3515
Associations between BODE index and systemic inflammatory biomarkers in COPD
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Background: COPD is a multi-component disease and systemic inflammation represents one of the key mechanisms responsible for the systemic manifestations of this disorder, including skeletal muscle weakness and cachexia. Fat-free mass index (FFMI) which reflects better the skeletal muscle mass, has been shown to relate to both dyspnoea and exercise capacity. We hypothesized that the multidimensional BODE index, that reflects the multi-component nature of COPD, might be related to biomarkers of systemic inflammation. We further evaluated associations between FFMI and systemic inflammation.
Methods: BODE index and FFMI were calculated in 222 stable COPD patients and 132 smokers without from COPD. Systemic inflammation was evaluated with the measurement of leptin, adiponectin, CRP, IL-6, and TNF-α in serum samples of COPD patients.
Results: In patients with COPD, both BODE index and FFMI presented significant associations with leptin levels (R2 0.66 and 0.71, respectively), whereas FFMI presented an additional association with the levels of TNF-α (R2 0.37). No significant associations were observed in normal smokers.
Conclusions: Both BODE index and FFMI, are related to the circulating levels of leptin in patients with COPD, a fact that strengthens a possible role for leptin in the systemic inflammatory process of COPD. The additional association of FFMI with TNF-α further supports the closer association of FFMI with muscle wasting in COPD.

P3516
Different trends of health-related quality of life in asthma and COPD
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Background: The prognosis of COPD and asthma, even though frequently overlapping, differ markedly in adult population. In general COPD is progressive, the major contributors include ongoing smoking combined with dyspnoea and disease exacerbations. In the management of COPD and asthma, monitoring of FEV1 alone does not adequately identify the high-risk patients. In this study we aimed to define the potential value of repeated measures of Health-Related Quality of Life (HRQoL) in these two diseases.
Materials and methods: Patients with asthma (N=1198) or COPD (N=601) had been recruited from two University Hospitals in Finland. Since year 2005 their HRQoL had been assessed at time points 0, 1, 2 and 4 years from the recruitment by using the 15D questionnaire validated in several chronic diseases. The variation of HRQoL between the patient groups was modelled by using mixed effects models.
Results: The average trend of HRQoL separated the groups (p = 0.00003) from each other (-0.005/year for COPD, -0.001/year for asthmatics). The measures of the asthma patients developed positively or negatively regardless of their baseline 15D score, whereas those of the COPD patients tended to develop only negatively when their baseline 15D score was harmed to the level of < 0.75 (full HRQoL = 1.0). The 15D score declined more significantly in patients who died during the follow-up period (p = 0.007). The average trends in HRQoL were not different between males and females neither for the asthmatics (p = 0.8) nor for the COPD-patients (p = 0.4).
Conclusions: HRQoL trend could serve as a valid and cost-efficient tool to identify patients who display deviant development of the disease and needs to be further investigated.

P3517
Validity of an automated telephonic system to assess exacerbation rates in prospective clinical COPD studies
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Background: Current methods for measuring COPD exacerbation rates in prospective studies are limited and often lack validity testing. We assessed the validity of an automated telephonic exacerbation assessment system (TEXAS) as a novel tool to measure COPD exacerbation rates.
Methods: In a 1-yr prospective cohort study COPD patients were called bi-weekly by TEXAS to record respiratory symptom changes, unscheduled healthcare utilization, and use of respiratory medication. Home visit observations within 3 days after a call were used to verify the responses of the patients to TEXAS. Diagnostic test characteristics were assessed using 4 common definitions of exacerbation. Detection rates, compliance, and patient preference were compared with the results of conventional methods, i.e. paper diary cards and medical record review.
Results: During follow-up 1,824 successful TEXAS calls were recorded in 86 COPD patients (22.1% female, mean age 66.5 years, mean post bronchodilator FEV1 53.4% predicted). 292 home visits were performed (median: 4 per patient, interquartile range: 3 to 5). Overall, validity of TEXAS was high with sensitivities and specificities between 66% and 98%, but differed between the four exacerbation definitions. Detection rates were higher with TEXAS than with the conventional methods. Compliance was higher with TEXAS than with diary cards, but patient preferences did not differ.
Conclusions: TEXAS appears to be a valid tool to measure COPD exacerbation rates and it may be used with various exacerbation definitions. In the interpretation of studies on exacerbation outcomes it should be realized that the exacerbation rate much depend on the detection method used.

P3518
Association of the transfer coefficient (Kco) with emphysema progression in heavy smokers
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Background: The transfer coefficient Kco is a measurement of the ability of the lungs to transfer gas from air to the pulmonary capillaries. A decrease in Kco is associated with emphysema.
Aim: To evaluate whether the Kco was associated with the progression of CT-detected emphysema and decline of lung function.

Methods: 522 heavy smokers, mean (SD) 41.3 (18.7) pack years, participating in a lung cancer screening trial underwent diffusion testing and CT-scanning of the lungs. CT-scanning was repeated after median (interquartile range) 2.8 (2.7-3.0) years and emphysema was assessed by lung densitometry using the 15th percentile (Perc15, point below which 15% of the low attenuation areas voxels are distributed). The association between Kco at baseline with progression of emphysema and lung function decline was assessed by multiple linear regression, correcting for baseline CT-quantified emphysema severity and FEV_1/FVC, age, height, BMI, pack years and smoking status.
Results: Mean (SD) age was 60.1 (5.4) years, Perc15 was -938 (19), FEV_1/FVC was 71.6% (9) and Kco was 1.23 (0.25), which is 81.8% (16.5) of predicted. A lower baseline Kco was significantly related to an increased progression of CT-quantified emphysema and a more rapid decline in FEV_1/FVC. A one standard deviation (0.25) lower Kco value at baseline, predicted a 1.6 HU lower Perc15 and a 0.78% lower FEV_1/FVC after follow-up ($p<0.001$).
Conclusion: A lower baseline Kco value is independently associated with a more rapid progression of emphysema and lung function decline in heavy smokers.

P3519
Abnormal heart rate recovery and chronotropic incompetence on submaximal exercise in COPD
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Background: A delayed heart rate recovery (HRR) after graded and an attenuated heart rate response (chronotropic incompetence, CI) are markers of cardiac autonomic dysfunction and predict cardiovascular mortality. The latter also characterize COPD. Therefore we hypothesized that decreased HRR and CI should coexist in COPD.
Methods: After lung function evaluation, 39 stable COPD patients and 11 healthy controls underwent submaximal cycle ergometry. Heart rate was measured at peak exercise and at 1-min recovery. Abnormal HRR was defined as a recovery of ≤12 beats in the first minute post-exercise. Chronotropic incompetence was evaluated by measuring the Chronotropic Response Index (CRI = [(peak heart rate - resting heart rate)/] [(220 - age) – (resting heart rate)].
Results: The HRR was 13±9.1 beats and 23.9±5.9 beats in patients and controls ($p<0.001$) while CRI was 44.59±13.9 and 61.2±5.1 ($p<0.01$) in these groups, respectively. An abnormal HRR was observed in 29 (74.4%) of the patients. The HRR and CRI were significantly correlated. Both HRR and CRI showed a decreasing trend with increasing GOLD severity and BODE index. On univariate analysis, HRR was negatively associated with age, pack-years of smoking and diffusion capacity/alveolar volume (DLCO/VA). On multiple logistic regression, after adjusting for other variables, a reduced DLCO/VA was the only significant, though weak, determinant of reduced HRR.
Conclusions: Patients with COPD have a decreased HRR and CI on exercise indicating autonomic dysfunction. These well-established markers of cardiovascular morbidity and mortality should be clinically useful tools for risk stratification and prognostication in patients with COPD.

P3520
Association of systemic inflammation with clinical recovery in patients with acute exacerbation of COPD
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Background: The association between changes in inflammatory markers and clinical response in acute exacerbations of COPD (AECOPD) is poorly defined.
Methods: Serum levels of Interleukin-6 (IL-6), High sensitivity C-reactive protein (Hs-CRP), and Fibrinogen were measured in patients with AECOPD at the time of admission and one month after discharge (stable state) and correlated with mortality and indices of disease severity.
Results: Out of 53 patients admitted with AECOPD during the study period, mortality was 28.4%. Patients who died were older, had significantly higher baseline serum IL-6, Hs-CRP, and Fibrinogen, higher smoking index, APACHE-II and SAPS-II scores. The 38 survivors were mostly males (82%), with mean (SD) age 63(8) years, mean (SD) duration of COPD of 11 (5) years, and mean (SD) smoking index of 288 (75). Majority (29/38) had type I exacerbation. Of these, 33 patients completed one month follow up assessment and demonstrated normalization of arterial blood gases, leucocyte counts and acute symptoms. They had a significant decline in serum IL-6 (152.5 and 14.05 pg/ml, p=0.001), Hs-CRP (18.2 and 3.5 mg/L, p=0.001), and Fibrinogen (46.3 and10.4 g/L, p=0.001) respectively from baseline till the stable state though the levels remained above the normal cutoffs. However, there was no statistically significant correlation between the change in the inflammatory markers with various indices of clinical and laboratory recovery from acute episode.
Conclusion: Although the initial surge in systemic inflammatory activity in AECOPD declines with recovery, the rate of normalization seems to lag behind the other conventional indices of disease activity and severity.

P3521
Bacterial profile of acute infectious exacerbations of chronic obstructive pulmonary disease requiring hospitalization in Greece
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Bacterial infections are a major cause of acute exacerbations of chronic obstructive pulmonary disease (AECOPD) resulting in significant mortality and morbidity. This study was undertaken to investigate the bacterial spectrum of AECOPD requiring hospitalization.
We examined 40 patients with COPD hospitalized for infectious AECOPD according to Anthonisen's criteria. We measured lung function, and assessed sputum for inflammation and for bacterial infection using PCR. All patients had no previous intubation and none was diagnosed with pneumonia.
Patients were hospitalized for 9±3 (mean ± SD) days. AECOPD were associated with impaired lung function (FEV_1: 42±20, FVC: 69±11, FEV1/FVC: 52±16), respiratory failure and increased sputum neutrophilia (mean ± SD, 72±26). PCR revealed pathogens in 88% of the sputum samples analyzed. The most commonly isolated pathogens were *S. pneumonia (65%), Haemophilus influenzae* (45%), *Ps. aeruginosa (33%), Klebsiella (7.5%),* and *Mycoplasma Hominis (7.5%).*
A mixed flora was revealed in 52.5% of sputum samples. The most common co-infection identified was by *S. pneumonia* and *Haemophilus influenzae* (35%), followed by *S. pneumonia* and *Ps. aeruginosa* (25%). In 12.5% there was a co-infection by three bacterial strains (*S. pneumonia, Haemophilus influenzae,* and *Ps. aeruginosa).*
S. pneumonia and *Haemophilus influenzae* were the commonest sputum pathogens isolated in hospitalized patients with infectious AECOPD. Interestingly, in more than 50% of the cases a co-infection by 2 or three different strains was revealed. These results should be considered when deciding the initial antibiotic treatment in Greek patients with AECOPD.

P3522
Chronic obstructive pulmonary disease at the cleanup workers at Chernobyl accident per clinical and instrumental indicators at the remote period after low-dose radiation exposure
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The aim of this study was to define the clinic and the pulmonary function (PFT) in patients with COPD at the remote period after low-dose ionizing radiation exposure and inhalation of radionuclides emergency descent.
Methods: Group1-57 COPD cleanup workers (individual documented dose of irradiation: 0,01 to 0,5 sZv) exposed to external and internal irradiation (mean age 62,1±1,4 yrs), group2 - 20 COPD patients who were not exposed to radiation (mean age 63,2±2,9 yrs). Clinical examination included-questioning, physical examination, MRC scale, BODE index. PFT was measured using spirometry, bodypletismography and DLCO.
Results: It was found out the significant reduction of lung capacity, a clear violation of the ratio of lung volume, due to certain growth of residual volume and total lung capacity, and reduction of diffuse capasity in a group of clean-up workers COPD patients in compareson with nosological control.Complaints of breathlessness varying degrees of intensity significantly more often expressed by patients with COPD who suffered from Chernobyl compared with control group.
Conclusion: Analysis pathognomonic symptoms for bronchopulmonary disease showed the presence of cough, sputum selection, shortness of breath, in most patients, but complaints of breathlessness varying degrees of intensity significantly more often expressed by patients with COPD who suffered from Chernobyl compared with control group, indicating worse quality of life. Also we indicate the presence of distinct pulmonary hyperinflation, emphysema, and diffuse lung function in a group 1 compared with control.

P3523
Genetic association analysis of functional impairment of chronic obstructive pulmonary disease in a north Chinese Han population
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Objectives: To determine the association of polymorphisms in serine protease inhibitor E2 (SERPINE2), microsomal epoxide hydrolase (EPHX1), transforming growth factor-β1 (TGF-β1) and glutathione S-transferase P1 (GSTP1) with the functional impairment in COPD in Chinese Hans.
Methods: Three hundreds and ten patients with COPD from North China performed pulmonary function test and six-minute walk test. Dyspnea was measured with Medical Research Council (MRC) dyspnea scale, Anxiety and Depression were measured using the Hospital Anxiety and Depression scale (HADS). Forty-two SNPs from the four genes were genotyped using Allele-specific hybridization.

Logistic regression and linear regression were used to test for association between these SNPs and the COPD-related traits, assuming dominant (D), recessive (R) and additive (A) genetic model.
Results: Only one SNP (rs3766934) from EPHX1 showed significant association with the six-minute walking distances after Bonferroni correction (A:β=-40.88, *P*=0.039)One SNP (rs3738040) from EHPX1 showed significant association with anxiety in COPD patients (A: OR=5, *P*=0.0292). Another SNP (Ile105Val) from GSTP1 showed borderline significance with anxiety symptom (D: OR=2.94, *P*=0.0545). The haplotype analyses validated the results from the single SNP analyses.
Conclusions: This study provides evidences that genetic variants on EPHX1 and GSTP1, two genes encoding xenobiotic metabolizing enzymes, contribute to the functional impairment of COPD in northern Chinese Hans.

P3524
Validation of a (semi)-automatic measurement- and control platform for centralized, simultaneous electronic nose (eNose) analyses in multi-centre trials
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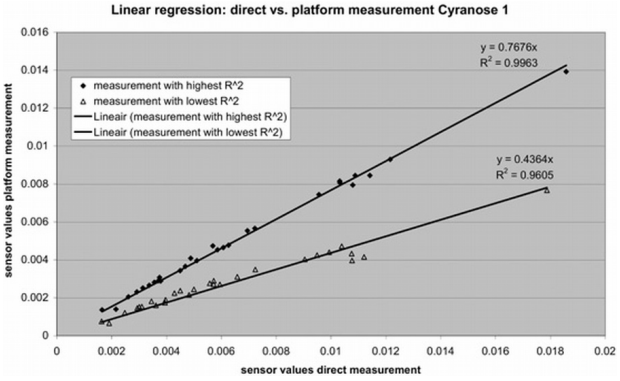
Rationale: Breath analysis by eNose technology represents a promising diagnostic tool in lung disease. Thet next step in making this technology suitable for multi-centre trials, such as the U-BIOPRED study, is to facilitate centralized (semi)-automatic measurements simultaneously.
Hypothesis: Incorporating multiple eNoses in a measurement- and control platform (integrated system of PC, mass flow controllers and valves) does not influence the sensor responses.
Methods: In this cross-sectional study on healthy volunteers (n = 12), exhaled breath was collected using a standardized method (Fens *et al*. AJRCCM 09). Two paired randomized measurements (standard configuration *vs*. platform) were done on two parallel eNoses (Cyranose C320). Analysis was done by linear regression. (see figure).
Results: There was a slight difference in sensor responses between paired measurements. However this was proportional for all sensors. (eNose 1: $0.961 \leq R^2 \leq 0.996$, eNose 2: $0.982 \leq R^2 \leq 0.998$). The slopes of the linear regression lines differed when changing the sampling flow.



Conclusion: The platform has a minimal, proportional influence on sensor responses, which can be adjusted for.
Implication: A parallel eNose platform can facilitate centralized, integrative analysis of different types of devices and thereby application of eNose technology on larger cohorts in a multi-centre setting.

P3525
Circadian rythm of circulating microparticles in patients with obstructive sleep apnea
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Obstructive sleep apnea syndrome (OSAS) is considered as a risk factor to develop cardiovascular diseases. Circulating cell-derived microparticles (MP) are involved in endothelial dysfunction and atherosclerosis; however, their role is not fully explored in the pathophysiology of OSAS. Eleven patients with untreated, moderate to severe OSAS (Pre-CPAP) and 7 healthy controls underwent overnight polysomnography (apnea-hypopnea index (AHI) 40.4±19.5 vs 2.4±2.2, respectively). Blood samples were collected at 11:00 AM, 5:00 PM and 9:00 PM, and then 1:30 AM and 6:00 AM on the following day. Absolute numbers of platelet-derived (CD41a+) and Annexin V+ MP were measured by flow cytometry. Nine OSA patients were re-studied after 2 months of CPAP treatment (Post-CPAP; AHI 1.9±1.7). Comparisons were made by repeated measures ANOVA, and independent and paired t-test, as appropriate. Untreated OSAS patients exhibited higher levels (at 5:00 PM and 9:00 PM time points) and daily variability than healthy controls both in CD41+ ($p<0.05$) and Annexin V+ ($p<0.01$) MP levels. In OSAS patients, interestingly, peak daily MP levels occurred at 5:00 PM. There was significant positive correlation between AHI and the circadian variability both of CD41+ ($p<0.01$, $r=0.70$) and Annexin V+ ($p<0.05$, $r=0.60$) MP levels. Annexin V+ and CD41a+ MP counts decreased after CPAP treatment at 5:00 PM and 9:00 PM time points ($p<0.01$ Post-CPAP vs Pre-CPAP). Our data demonstrate that increased MP levels can only be detected at certain time points of the day in OSAS patients. The elevation of MP counts is largely reversible by CPAP treatment. The influence of circadian rythm should be considered to assess MP levels in these patients.