

MONDAY, SEPTEMBER 17TH 2007

176. Advances in respiratory mechanics

E1627**The ability of fluctuation analysis of airway function and symptoms to assess asthma stability in different asthma phenotypes**

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Background: In order to achieve effective asthma control, an asthma phenotype-specific treatment is needed. However, to find an objective parameter which can distinguish between asthma phenotypes is difficult based on conventional clinical assays. Fluctuation analysis of airway function has been shown to provide a quantitative measure of asthma stability (α). This study aims to assess whether asthmatics with different phenotypes (cough and wheeze-variant asthma) show differences in stability of peak expiratory flows (PEF).

Methods: PEF and symptom time series of a subgroup of 99 non-smoking adults with persistent asthma in a long-range crossover clinical trial were analyzed (Thorax 1998;53:744–52). Subjects from the placebo arm were separated into four phenotypes, characterized by the presence of above-median or below-median cough and wheeze episodes during the placebo period, and analyzed with detrended fluctuation analysis.

Results: Of the 99 patients, 15 were characterized to have above-median cough and below-median wheeze and 19 had below-median cough but above-median wheeze. There was no difference in PEFs between the two groups (426 95% CI 340–500 l/min and 427 95% CI 350–515 l/min). However, the cough-variant group showed significantly higher long-range correlations (α), a measure of PEF stability than the wheeze-variant group (0.88 95% CI 0.7–1.0 and 0.70 95% CI 0.6–0.8, $p=0.012$).

Conclusions: α is a new objective parameter to distinguish between asthma phenotypes with similar PEF. We showed that cough-variant asthmatics have a more stable asthma control than other phenotypes, consistent with clinical experience.

E1628**Changes in airway responsiveness to methacholine following haematopoietic stem-cells transplantation**

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Background: Changes in lung function and respiratory symptoms may occur in 20–50% of patients undergoing haematopoietic stem-cell transplantation (HSCT). Lung volumes and DL_{CO} was often reduced. Airway responsiveness to methacholine (MCh) was only occasionally increased.

Aims: To study systematically the effects of MCh on airway narrowing and air trapping before and after HSCT.

Methods: Seventeen subjects were studied 1 wk before and 3 mo after HSCT performed for haematological malignancies. A standard inhalation protocol was used and the following parameters were sequentially measured at each step: sGaw, FRC, FEV₁, and FVC. Occurrence of air trapping was inferred from changes in RV and the linear regression of changes in FVC vs. FEV₁.

Results: Following HSCT, neither PD₂₀FEV₁ nor PD₃₅sGaw were significantly changed ($P=0.21$, and $P=0.13$, respectively). However, the slope of the regression of FVC vs. FEV₁ during MCh challenge was significantly less steep ($P=0.005$) and the Y-intercept higher ($P=0.046$) after than before HSCT, indicating less air trapping with airway narrowing. In addition, deep inflations to TLC performed during the FVC manoeuvre had a stronger bronchodilator effect after than before HSCT as suggested by the significant ($P < 0.0001$) reduction in slope of FEV₁ vs. sGaw.

Conclusions: These data suggest that during MCh-induced bronchoconstriction the response of peripheral airways and air trapping are significantly blunted following HSCT.

E1629**Low glucose level alters the electrochemical function of human parietal pleura**

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Aim of the study was to investigate if decreased glucose concentration can alter the electrochemical function of healthy human parietal pleura. Parietal pleural pieces

MONDAY, SEPTEMBER 17TH 2007

were stripped off from 30 patients during thoracic surgery and were mounted between Ussing chambers. Krebs solutions containing 100mg glucose, 40mg or no glucose were added towards the pleural space surface. Trans-mesothelial Potential Difference (PD_{TM}) was measured after 1, 5, 10, 30, 45 and 60 min. Trans-membrane Resistance (R_{TM}) was calculated from Ohm's law. R_{TM} remained unchanged over time, when normal glucose Krebs was used. R_{TM} decreased when 40mg glucose Krebs was used, from the 5th minute and statistically from the 45th minute ($p=0.020$). Addition of no glucose Krebs caused R_{TM} decrease from the 5th minute but statistically from the 10th minute ($p=0.034$). R_{TM} decrease at 30th minute was more intense when no glucose Krebs was added than 40mg glucose Krebs ($p=0.024$). Lower glucose concentration causes alteration of the electrochemical function of human parietal pleural membrane. Low glucose content itself could additionally lead to exudates progression.

E1630**The acute effect of loaded inspirations upon airway resistance in mild to moderate asthmatics**

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Inspiratory muscle training (IMT) improves symptoms, FEV₁, and reduces medication use in asthmatics (Weiner, P. *et al.* Chest. 1992; 102: 1357–1361). It is suggested that the airway smooth muscle of asthmatics becomes 'latched' (Fredberg, J.J. *et al.* Am. J. Resp. Crit. Care. Med. 1999; 159: 959–967) and this may account for their abnormal airway response to deep inspiration (DI). We hypothesised that the greater intrathoracic pressure associated with IMT may generate greater airway stretch than DI, thus relaxing the 'latched' smooth muscle and normalising the bronchodilatory response to stretch.

Seven mild/moderate asthmatics (FEV₁/FVC < 5th percentile), who demonstrated increased airway resistance (AWR) in response to DI, gave informed consent. Changes in AWR were assessed in response to 3 inspiratory manoeuvres, on separate days, using the forced oscillation technique (4–8 Hz; [1 – single unloaded DI; 2 – single inspiration at 25 cmH₂O; 3 – single inspiration at 50% maximum inspiratory mouth pressure]; [MIP; mean = 59±19 cmH₂O]).

AWR increased in response to DI (13.5±10.7%) and a single inspiration at 25 cmH₂O (21.6±18.8%). No such increase was observed in response to a single inspiration at 50% MIP (2.2±16.8%).

Our finding of increased AWR after DI agrees with previous studies. We propose that airway stretch induced by loaded inspirations at 50% MIP may be sufficient to 'unlatch' airway smooth muscle and normalise the bronchodilatory response to stretch. The influence of chronic IMT upon airway resistance warrants investigation, as it may explain the influence of IMT upon FEV₁.

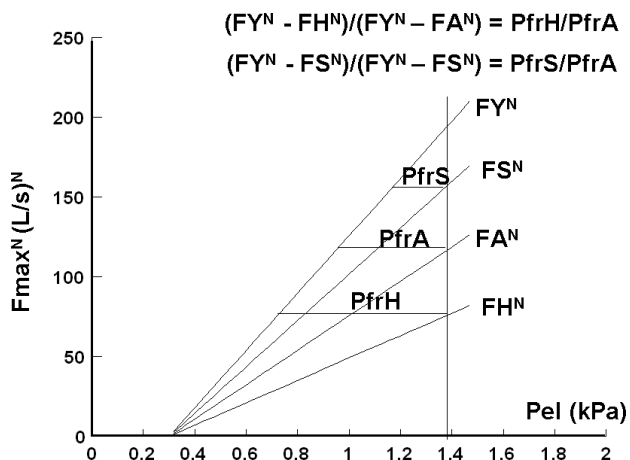
E1631**Determination of degree of turbulence and viscous resistance upstream to the choke point in a mechanical model using gases of different physical properties**

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Aim: To determine resistance and degree of turbulence upstream to CP.

Background: If maximum expiratory flow is corrected for density ($F_{max,corr} = F_{max,gas} (\rho_{air}/\rho_{gas})^{0.5}$ and plotted against elastic recoil pressure (Pel), these curves are superimposed, if the viscous loss is negligible ($Pfr=0$). If they are not, the ratio Pfr_{gas}/Pfr_{air} depends on $F_{max,gas}/F_{max,air}(DD)$, ρ_{gas} , ρ_{air} , μ_{gas} , μ_{air} and α , which is 1 for laminar flow and 2 for turbulent flow according to the equation $Pfr_{gas}/Pfr_{air} = (DD)^\alpha (\mu_{gas}/\mu_{air})^{\alpha-1} (\rho_{gas}/\rho_{air})^{2-\alpha}$, μ is viscosity.

Material and Method: A mechanical model with an elastic airway containing a Pitot-static probe was used for measurement of Pfr and other parameters. From maximum flows with air, He- and SF₆-mixtures MFSR-curves using $F_{max,corr}$ were constructed. The α and the extrapolated flow FY vs Pel were calculated from the equations in the figure and compared with measured α and $F_{max,air}$ vs Pel – Pfr.



Results: The non-invasively determined α was 1.24 ± 0.14 (mean \pm SD), compared with the measured α (1.38 ± 0.08). Non-invasive $R_{fr,air}$ was 0.44 ± 0.17 kPa/(L/s) compared with measured $R_{fr,air}$ (0.36 ± 0.06 kPa/(L/s)). The number of comparisons was 19, and in both cases the differences were significant ($p < 0.05$).

Discussion and Conclusion: Non invasive determination of α and FY is possible but small errors in flow cause large errors in α , FY and hence Pfr.

E1632**A new digital stethophone: bioacoustic analyses of breath sounds recorded from a simple mp3 player**

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Background: The detection, dissemination, and analysis of clinical sounds would be advanced if a cheap digital recorder and transmitter could be validated.

Aim: To show distinct spectral correlations and successful machine recognition of breath sounds recorded with a simple mp3 audio player (iriver model T30) using standard bioacoustic software (Raven, v. 1.3.1, Cornell Lab of Ornithology).

Methods: With IRB approval normal (right mid-4th clavicular interspace) and then bronchial (posterior T6 spinous process) breath sounds each with and without wheezing (inspiratory, expiratory, or both) were sequentially recorded by only applying the mp3 player microphone to the chest. mp3 files were transferred to a computer and converted to wav format. Pairwise time and short FFT transformed frequency spectrogram correlations were calculated. Breath sound recognition was attempted using the program's standard detection algorithms.

Results: Pairwise peak timing values were consistently best autocorrelated except between breath sounds with stridor. Bronchial breathing with wheeze had high absolute correlated lag times likely given its distinctly lower amplitude. Normalised peak short FFT spectrogram correlations sequentially diminished as breath sound abnormalities were added. The bioacoustics program's detectors could not recognize different breath sounds.

Conclusion: A simple mp3 recorder could collect and transmit spectrally discernible combinations of breath sounds. Further studies of custom machine recognition, correlation with human perception, Bluetooth (TM) transmission, other clinical sounds, and discrete wavelet transformations are underway.

E1633**Near-infrared high speed video microscopy is an effective tool for studying mucociliary transport in vitro**

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Visual and near-infrared (NIR) spectra of light have different rates of penetration through biological tissue, including airway mucous. We have designed a novel method of NIR video microscopy of airway epithelium *in vitro*.

Methods: Sheep trachea was cut lengthwise and mounted flat in a bath with the serosal surface perfused with gassed Krebs-Henseleit. The epithelial side was ventilated with 100% humidified air at 38°C. Mucus transport and ciliary activity were viewed through borosilicate glass using NIR corrected optics and a high speed monochrome NIR video camera. Coaxial illumination was achieved with a conventional halogen light source and visual and NIR light emitting diodes. A computer monitor was calibrated using a stage micrometer and mucus transport velocity (MTV) was obtained by timing the movement of the mucus using visual light. Cilia beat frequency (CBF) was measured from video images obtained by NIR illumination of endogenous mucus produced by the specimen as well as after infusion of artificial mucus (1.6% solution of polyethylene oxide in phosphate buffer saline, 1.0 ml).

Results: MTV was 6.3 mm/min (SD 2.1) and CBF 11.1 Hz (SD 2.4) immediately after mounting of the trachea (n=10). NIR illumination (810nm and 920 nm) allowed the visualization of ciliary motion through the thick layer of the artificial mucus.

Conclusion: Near-infrared high video microscopy is an effective tool in visualization of ciliated epithelium. Narrow band illumination in visual and NIR spectra results in clear high contrast image of live tissue.

E1634**Effect of salbutamol on upper airway wall impedance in children**

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Background: Respiratory impedance (Zrs) may easily be measured in children using the forced oscillation technique. However, the bronchial response to bronchoconstrictors estimated by change in Zrs is underestimated when pressure is oscillated directly at the mouth (standard generator, SG) because of the upper airway wall impedance (Zuaw). The artefact may be minimized 1) by applying pressure around the head (head generator, HG) or 2) by expressing the bronchial response as change in respiratory admittance (ΔAr), assuming Zuaw is unaffected by the provocation agent (Eur Respir J, 1999; 13: 761–766). ΔAr s could also be useful to assess the bronchial response to salbutamol (S), provided there is no effect of S on Zuaw.

The aim of the study was therefore to test whether S alters Zuaw.

Methods: 31 children (4 – 12 years) suspected of asthma were tested. Zrs was measured at 12 Hz, using both SG and HG, before and after S. Zuaw was estimated

MONDAY, SEPTEMBER 17TH 2007

by combining SG and HG data using simple modelling (Pediatr Pulmonol, 1992; 13: 28–33) and expressed as upper airway wall resistance (Ruaw) and apparent elastance (Euaw).

Results: Ruaw was not significantly different before (5.9 ± 0.6 hPa.s/L) and after S (5.7 ± 0.6 hPa.s/L). However, there was a small but significant decrease in Euaw after S (from 1026 ± 85 hPa/L to 907 ± 74 hPa/L, $p = 0.05$).

Conclusions: The study indicates that Euaw – but not Ruaw – is decreased by S. Further studies are needed to assess whether the small effect of S on Euaw significantly impacts on usefulness of Δ Ar during routine assessment of airway response to S.

E1635**Changes in airway and tissue mechanics in ventilated COPD patients after nebulized bronchodilator agent**

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The low-frequency respiratory impedance (Zrs) has been shown to reflect the respective contributions of the airway and tissue mechanical properties accurately in healthy subjects. Little information is available, however, on the changes in airway and tissue parameters derived from low-frequency Zrs data in COPD patients after bronchodilator therapy. Zrs was measured between 0.4 and 6 Hz at three PEEP levels (3, 7 and 10 hPa) before and after nebulized Berodual in 19 mechanically ventilated COPD patients including 10 with severe acute exacerbations. Airway resistance (Raw) and inertance (Iaw), and constant-phase tissue damping (G) and elastance (H) were estimated from Zrs spectra by model fitting. Raw, G and H decreased with PEEP, and on the administration of Berodual at all PEEP levels (Table 1). This indicates both bronchodilation and a progressive recruitment of previously closed regions of the lung. There was no change in Iaw and hysteresivity (G/H), suggesting that the peripheral airway inhomogeneity was not markedly affected by the intervention. However, the model fitting to Zrs data obtained in some patients and at low PEEP levels resulted in unrealistic parameter values (not included), which indicates the limits of relevance of the homogeneous modelling in COPD.

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Table 1

PEEP (hPa)	Raw (hPa*s/l)	Rawi (hPa*s/l)*	G (hPa/l)	Gi (hPa/l)*	H (hPa/l)	Hi (hPa/l)*
3	6.9±3.8	4.2±1.3	10.5±6.1	8.7±5.2	24.9±7.8	21.6±5.7
7	6.2±2.6	3.8±1.6	12.3±5.8	9.5±6.3	28.9±14.3	21.0±7.3
10	4.8±1.9	2.9±1.2	9.2±5.0	6.5±3.9	23.9±7.1	18.8±5.4

* $p < 0.05$ by Wilcoxon signed rank test, i = after inhalation; values: mean±SD

E1636**Correlation between respiratory mechanical and structural changes in sensitized rabbits: effects of methacholine and allergen administrations**

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Although lung response to constrictor stimuli is frequently assessed by measuring changes in lung function indices or by imaging techniques to identify the site of anatomical alterations, the relationship between mechanical and morphometric parameters have rarely been characterized. We correlated changes in the respiratory mechanical parameters to those obtained from chest imaging with synchrotron radiation. Low-frequency forced oscillations (FO) and K-edge subtraction imaging technique (KES) using Xenon as contrast agent were performed in normal and ovalbumine(OVA)-sensitized rabbits under control conditions and following iv infusion of methacholine (MCh) and iv injection of OVA. Airway conductance (Gaw) and elastance (H) were determined from the FO measurements, while surface area of the two main bronchi (SA) and the area of well ventilated zones in the lung periphery (VA) were quantified from the KES images. MCh induced marked decreases in Gaw that were closely related to those in the square of SA ($R^2 = 0.81$, $P < 0.001$), while the changes in H were mild and exhibited looser correlations with VA ($R^2 = 0.43$, $P < 0.02$). In contrast, larger elevations in H were observed after OVA challenges. Besides the decrease in Gaw; these changes showed a stronger correlation between H and VA ($R^2 = 0.96$, $P < 0.001$) than between Gaw and SA ($R^2 = 0.60$, $P < 0.02$). These results suggest that bronchoconstriction can be reflected by KES images and central airway parameters obtained from lung mechanical measurements, while KES imaging technique is more sensitive in detecting mild alterations in the lung periphery not associated with airway closure and consequent change in H.

E1637**Deposition of nanoparticles in the infant lung**

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In the first few years of life, the human lung undergoes a dramatic increase in structural alveolation via the development of new secondary septa from the primary septa. We hypothesize that this substantial change in alveolar structure might result in the rate of deposition of aerosols in infants being significantly different from that in adults. To test this hypothesis, we modelled the flow in two model alveoli; one with an aspect ratio $A = \text{depth}/\text{width} = 1/2$ (for the infant lung) and the other with $A = 1$ (for the mature lung), and computed the rate of deposition of 5nm and 50nm particles in both model alveoli. The equations governing the flow and concentration were solved numerically over a full breathing cycle using purpose-built programs which include the simulation of the lung's expanding geometry. Major differences in the flow structure were found in the two model alveoli. The flow in the deeper mature alveolus ($A = 1$) comprised one large recirculation region. In contrast, the flow in the shallower infant alveolus ($A = 1/2$) had two recirculation regions in tandem. Conflicting results were found for the rate of deposition of particles onto the surface of the two alveoli. Whereas the fractional deposition of 50nm particles for the infant alveolus was considerably lower than for the mature alveolus, the fractional deposition of 5nm particles showed the opposite trend, suggesting the importance of the alveolar structure and the interaction between convective and diffusive transport. We conclude that the deepening of alveoli, due to structural alveolation, changes the alveolar flow field, which in turn alters the rate of mixing and deposition of nanoparticles in an age- and size-dependent manner. Supported by NIH HL070542, HL074022, HL054885.

E1638**Dexamethasone increases sheep visceral and parietal pleura permeability**

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Pleural effusions are a common medical problem. The knowledge of pathophysiology of pleural effusions will improve the diagnosis and therapy of this disorder. The objective of this study was to investigate the effect of dexamethasone on the transmesothelial permeability of sheep visceral and parietal pleura.

Intact sheets of visceral and parietal pleura were mounted among Ussing-type chamber. Dexamethasone 10^{-6} M was added both apically and basolaterally in both pleurae. Potential difference and transmesothelial resistance (R_{TM}) were measured before and after the addition of dexamethasone. The R_{TM} is inversely correlated with the membrane permeability.

There was a decrease in the R_{TM} after the addition of dexamethasone both apically and basolaterally on the visceral and parietal pleura. This decrease was started the 1st or the 3rd min after dexamethasone's exposure and lasted about 30 minutes. The maximal effect for visceral pleura was a 64% decrease in R_{TE} at the apical side whereas at the basolateral side was observed 66% decrease of the R_{TE} . In the parietal pleura, R_{TE} was decreased 60% apically and 58% basolaterally.

These findings suggest that dexamethasone leads to increased permeability of sheep pleura. Dexamethasone has been found to induce the expression of aquaporin 1 and increase transcellular water transport in rat peritoneum. Dexamethasone it is possible to induce the same effect in the pleura.

E1639**Development of standardisation criteria for the measurement of lung clearance index in a multi-centre study**

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Background: Lung Clearance Index (LCI) measured by multiple breath washout of inert gas is a sensitive marker of small airway disease. We have adapted a novel gas analyser (Innocor) to measure LCI. We present standardisation of equipment and measurement methods aimed to minimise variance during multi-centre clinical trials.

Methods: 3 Innocor devices were established in 3 geographically separate centres with different staff. In two centres, LCI was measured in distinct cohorts of healthy non-smoking adults. An analysis protocol was developed to account for physiological variability between patients. Variability between 3 observers was assessed by analysis of 10 CF patients' data, each with 9 washouts over 3 separate visits. Observers were blinded to others results.

Results: In healthy adults patients there was no significant difference between measurements across two sites: Mean (SD) LCI 6.7 (0.4) (N=47) vs. 6.8 (0.9) (N=12), $p = 0.4$. A comparison of CF patients is provided in Table 1. Data were cross-analysed separately. Mean differences in LCI and FRC between sites were consistent. Analysis of variation showed no significant difference ($p = 0.9$).

MONDAY, SEPTEMBER 17TH 2007

Conclusions: Measurement of LCI at different sites is reliable across equipment and observers. This is the first study to support the use of LCI measurements in multi-centre trials.

Site	1 vs 2		1 vs 3		2 vs 3	
	Mean Difference	95% Limit of Agreement	Mean Difference	95% Limit of Agreement	Mean Difference	95% Limit of Agreement
LCI	0.015	-0.72-0.75	0.078	-0.86-1.02	0.061	-0.81-0.93
FRC (L)	0.037	-0.5-0.58	0.023	-0.26-0.3	-0.013	-0.61-0.58

E1640**Respiratory mechanics in pathogenesis of airway hyperresponsiveness in obese subjects**

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Background: Over the last ten years the prevalence of obesity and asthma increased in the Western Countries. While perspective studies suggested a possible role for obesity in the airway hyperresponsiveness and asthma onset and many hypotheses have been put forward, the dominating pathogenetic process leaves unknown. A potential mechanism enabling obesity to modify the airway responsiveness could be the decrease of the Functional Residual Capacity (FRC). **Methods:** 6 (5 male) healthy morbidly obese subjects (Body Mass Index >40 kg/m²), aged 37-67 yrs, with normal lung function tests, underwent both methacholine (direct) and mannitol (indirect) challenge in sitting position. To test this mechanism also 6 (3 male) normal subjects, aged 24-46 yrs, with normal lung function tests, performed both methacholine and mannitol challenge in the supine position.

Results: All obese subjects showed airway hyperresponsiveness to methacholine (PD20FEV1=224.5±347.0 mcg), but not to mannitol. There was a negative correlation ($r^2=0.68$, $p<0.05$) between PD20FEV1 and Body Mass Index. The assumption of supine position in normal subjects decreased FRC from 3.3±0.6L to 2.4±0.4L ($p<0.001$). Five normal subjects showed airway hyperresponsiveness to methacholine (PD20FEV1=1392.9±979.8 mcg), but not to mannitol in supine position. There was a positive correlation ($r^2=0.63$, $p<0.01$) between FRC %predicted (seated in obese and supine in normal subjects) and respective PD20FEV1.

Conclusions: These results suggest that the reduction of FRC, and not airway inflammation, increases airway responsiveness in obese subjects raising doubts about the usefulness of methacholine challenge to support the diagnosis of asthma in these subjects.

E1641**The effect of ferric oxide nanoparticles on pulmonary morphology, redox system and some immune components**

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The nanoparticles entering into circulation can penetrate the biological membranes. The effect of Fe₂O₃ nanoparticles was studied on the morphology, redox system and some immunological factors of the lungs.

In vivo and in vitro studies: *In vivo* (Sprague-Dawley) male rats were treated intratracheally with Fe₂O₃ (1mg/animal). Lungs of the animals were elaborated sequentially by morphological, immunological (IgA, IgG, IgM in the blood and bronchoalveolar lavage-BAL, ELISA) and biochemical methods (total glutathione - GSH - and extracellular superoxide dismutase - EC-SOD - in the lungs). *In vitro*: in the culture of type II pneumocytes (T2) and alveolar macrophages (AM) cell membranes were studied; in the supernatant: MCP-1 and MIP-1 α (macrophage chemoattractant protein, macrophage inhibitory protein, ELISA) were determined.

Results: 1. by the end of the 1st month, chronic, multifocal pneumonitis developed with moderate fibrosis; 2. by the end of the 2nd week, Fe₂O₃ decreased significantly the IgA level in blood, IgG and IgM levels in BAL; 3. GSH and EC-SOD did not alter; 4. cell membranes were damaged at high concentration (LC50); 5. expression of MCP-1 and MIP-1 α increased although not significantly.

Conclusions: 1. Fe₂O₃ nanoparticles gave rise to chronic, multifocal pneumonitis; 2. showed immunosuppressive effect; 3. caused moderate damage to the membranes.

E1642**Novel sub-classifications of mast cells in human lungs: differential alterations in smokers and COPD**

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Mast cells (MCs) have recently been assigned key roles in innate immunity and tissue remodelling. In the lungs MCs have, beyond allergic diseases, been

surprisingly little studied despite high MC numbers in healthy individuals and COPD patients. This study characterizes MC populations in anatomical sites of the lungs using resected tissues from patients with COPD (n = 16, GOLD I and II), smokers (n = 10) and non-smoking controls (n = 6). Sections were double-stained for tryptase⁺ cells (MC_T) and tryptase⁺chymase⁺ cells (MC_{TC}). Through detailed cell size analysis MC_T and MC_{TC} could be divided into further subgroups; Large MC_{TC}, present in pulmonary vessels, and a population of significantly smaller MC_{TC} in airway walls ($p<0.001$). MC_T cells displayed a reversed pattern; i.e. large MC_T cells in the airways and small MC_T in vessels ($p<0.001$). The site-dependent sub-groups were equally manifested in all patient groups and could by triple staining be corroborated by distinct expressions of IL-9R, VEGF, 5-LO, LTC₄S. The present extended sub-grouping of MC_{TC} and MC_T allowed detailed comparisons of MCs among the patients groups. Surprisingly, 5-LO was absent in airway MC_{TC} from COPD and smoking patients. This change was site specific since vascular or alveolar MC_{TC} populations in the same patients had unchanged or increased 5-LO expression, compared to controls. In conclusion, MCs in peripheral airways display a marked heterogeneity with different phenotypic expressions depending on localisation and underlying disease. We suggest that to properly assess MCs in diseased lungs the prevailing categorization into MC_T and MC_{TC} should be divided into further site and size-restricted sub-populations.

E1643**Fast clearance of inhaled ultrafine particles from airways is reduced in a knockout mouse model with cilia deficiency**

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In a MDHC7^{-/-} knockout (ko) mouse model the mouse dynein heavy chain 7 gene was deleted. This protein is very important for sufficient ciliary activity in the airways and elsewhere. Homozygous ko mice are viable, but males are infertile, because of asthenozoospermia. Theegarten et al. (abstract in 46th Congress of German Pneumology Association, 2005) described the MDHC7^{-/-} mice as a model for cilia deficiency in COPD.

Aims: In this study we measured total and regional deposition of ultrafine particles in the lungs of wild type and homozygous MDHC7^{-/-} mice, respectively.

Methods: Total and regional deposition of 20 nm radio-labeled ultrafine insoluble iridium particles (UF-IR) were determined after a one-hour particle exposure during spontaneous breathing (nose-only). Mice were killed 0-hours and 24-hours after administration and all organs and tissue samples as well as the remainder and excretion were analyzed quantitatively by gamma-spectrometry.

Result: The fast cleared UF-IR fraction from airways in MDHC7^{-/-} mice was significantly lower than in the wild type mice, 27% versus 38% of deposited UFP, respectively.

Conclusion: The cilia deficiency in airways of the MDHC7^{-/-} mice clearly resulted in a reduced clearance of UFP from the airways but did not completely diminish UFP clearance from the airways.

E1644**Analysis of quiet breathing in COPD using fiber grating vision sensor**

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Pulmonary functions of COPD patients are evaluated by spirometry. However, it requires considerable efforts of both patients and technicians to obtain reproducible data and is always difficult for patients with severe respiratory failure. An easier and more consistent technology to evaluate pulmonary functions is expected. Fiber Grating (FG) vision sensor is a type of active image sensor to achieve non-contact respiration monitoring. It can detect changes in volumes of interested area by measuring vertical movement of hundreds of laser spots beamed on the body, which can analyze quiet breathing without a nose-clip and a mouthpiece. We evaluated the usefulness of FG vision sensor for the assessment of pulmonary functions in COPD and analyzed changes in respiratory indices by this system before and after treatment with inhaled tiotropium.

On quiet breathing, minute volume (MV) increased in patients with COPD (n = 12) compared to control subjects (CTL) (n = 10, $P<0.05$). Tidal volume (TV) also tended to increase in COPD. Ratio of inspiratory to expiratory time (Ti/Te) significantly decreased in COPD compared to CTL ($P<0.01$). Time-flow curve by FG sensor demonstrated that the peak in expiratory flow in thorax was delayed to that in abdomen in COPD patients. The delay (Dex(T-A)) was greater in COPD than in CTL ($P<0.01$). After treatment with tiotropium, TV ($p<0.01$) and Dex(T-A) ($p<0.05$) significantly decreased and MV and Ti/Te tended to be improved in COPD.

These results suggest that analysis of quiet breathing by FG sensor contributes to evaluation of pulmonary functions in COPD. Since FG vision sensor is a non-invasive and non-contact system, it would be most valuable for patients with respiratory failure.

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E1645**Leptin influence the transmesothelial permeability of isolated sheep visceral and parietal pleura**

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The pleural effusion in ovarian hyperstimulation syndrome (OHSS) and Meigs syndrome has not been thoroughly investigated. In the present study a possible role of leptin, to an increased fluid accumulation in pleura space, in these disorders was investigated.

Intact sheets of visceral and parietal pleura were mounted as the planar sheet in an Ussing-type chamber. Leptin was placed both apically and basolaterally in both visceral and parietal pleura and transmesothelial resistance (R_{TM}) was measured. The transmesothelial resistance is inversely correlated with the membrane permeability. Measurements were conducted before and after the addition of leptin 1 ng/ml, 50 ng/ml and 100 ng/ml.

There was a decrease in R_{TM} after addition of leptin in all of the samples examined. This decrease was started between 1st and 5th min after hormone's exposure and lasted in all length of the experiments (20–30 minutes). The maximal effect for visceral pleura was a 63% decrease in R_{TM} , whereas in the parietal pleura the R_{TM} was decreased 67%.

These results suggest that leptin induce an increase in pleural permeability. This change in permeability might provide a great contribution to the pathophysiology of pleural effusions in OHSS and Meigs syndrome patients.

E1646**Endothelium function assesment with radial artery tonometry in COPD patients**

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Reduced FEV1 has been clearly linked to increased cardiovascular mortality. Radial Arterial Applanation Tonometry (RAAT) provides a non-invasive method of measuring arterial endothelial function prior to atheroma. We hypothesize that endothelium function assessment by RAAT is capable of evaluating endothelium dysfunction, and therefore of estimating cardiovascular risk in COPD patients.

Methods: 14 male COPD patients were enrolled in this study, 5 severe COPD (64±3 yr, FEV₁ 30±3%) and 9 moderate COPD (58±3 yr, FEV₁ 68±3%). 15 male controls with normal lung function, 8 smokers (51±3 yr) and 7 never smokers (52±2 yr). Radial arterial waveform was recorded (SphygmoCor Px Version 6.0 ATCOR, Australia). The radial AIx was defined as the ratio of the second to the first peak of pressure wave expressed as a percentage. 4 measurements with reproducibility criteria were taken at baseline. Afterwards, 400 µg of Salbutamol were administered. Measurements were performed every 5 min for 20 min. Then sublingual nitroglycerine (GTN) was given and a new measurement was made after 5 min.

Results: Peripheral AIx at baseline was significantly higher in both severe and moderate COPD patients compared to healthy subjects. Changes in AIx after Salbutamol showed correlation with FEV1. Decrease in AIx after GTN was significantly higher in healthy subjects and smokers (46.3±6.6 and 44.3±5.1, respectively) compared to severe and moderate COPD patients (27.4±3.8 and 22.3±4, respectively). There was also a strong correlation between this decrease and FEV1.

Conclusion: RAAT is an effective method to assess endothelium dysfunction in COPD patients. There is a correlation between arterial stiffness and severity of COPD.