Conclusion These results confirm the presence of acid reflux as a typical finding in patients with CF with a history of reflux cough. Furthermore, there may be a characteristic physiological abnormality in patients with CF with high frequency of TLOSR and increased oesophageal acidification.

S97 ASSESSMENT OF DIAPHRAGM FATIGUE FOLLOWING HIGH INTENSITY EXERCISE IN PATIENTS WITH CYSTIC FIBROSIS

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Introduction There is an increased load placed on the respiratory muscles in cystic fibrosis (CF). Whether this predisposes the diaphragm to fatigue following exercise is unknown. The aim of this study was to examine whether patients with CF develop low frequency fatigue of the diaphragm after cycle exercise to exhaustion.
Methods Six male patients (median (range) age 22 (20–33) years) with CF (forced expiratory volume in 1 s (FEV_1) % predicted 50% (31–80%)) were studied. The study was conducted on two occasions, 1 week apart. The first visit, to determine each subjects' maximum work load (W_{max}) and peak oxygen consumption (VO_{2peak}), involved an incremental exercise test to exhaustion on a cycle ergometer. On the second visit patients performed an endurance exercise test above 80% of their predetermined W_{max} at a constant pedal rate (50–60 rpm) to exhaustion. Twitch transdiaphragmatic pressure (TwPdi), elicited by bilateral anterolateral magnetic phrenic nerve stimulation (BAMPS), to assess the presence of low frequency fatigue, was measured before and at 20, 40 and 60 min postexercise.
Results Endurance exercise duration was 10.5 min (6–20) achieving 110% (100–121) of VO_{2peak}. There were no significant differences in TwPdi at any time point postexercise compared with baseline (median (range) TwPdi 25.0 cm H_2O (16.0–46.0) at baseline, 26.5 cm H_2O (17.5–44.0) at 20 min, 26 cm H_2O (17.5–44.0) at 40 min and 26.0 cm H_2O (16.0–43.0) at 60 min postexercise ($p<0.005$)).
Conclusion Patients with CF do not develop low frequency fatigue of the diaphragm after high intensity, exhaustive constant load cycle exercise.

S98 THE USE AND PERCEIVED BENEFITS OF NON-INVASIVE VENTILATION FOR HYPERCAPNIC ADULTS WITH CYSTIC FIBROSIS IN A REGIONAL CENTRE

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Introduction Non-invasive ventilation (NIV) improves gaseous exchange and aids secretion clearance in patients with cystic fibrosis (CF). A recent study demonstrated that NIV improved chest symptoms and exercise tolerance, and reduced maximal nocturnal CO_2 levels in this patient group. The objectives of this study were to examine the reasons for NIV initiation, and the perceived benefit in adults with CF with hypercapnia.
Method We conducted a retrospective observational study of adult patients treated with NIV during admission to a regional CF centre over an 18-month period. We recorded indication for treatment, perceived benefit in terms of work of breathing, symptoms of hypercapnia (early morning headache) and sputum clearance. Patient tolerance of NIV was also noted.
Results 19 patients, 5 of which were on the active lung transplantation list, were treated with NIV over 34 episodes during the 18-month period. Mean percentage predicted forced expiratory volume in 1 s (FEV_1) on admission was 22% (range 10–53%) and 10 patients were female. Seven (20%) NIV episodes were initiated for treatment of decompensated respiratory acidosis, 24 (71%) episodes were in patients with compensated hypercapnic respiratory failure and in 3 (9%) episodes NIV was used exclusively as an adjunct to airway clearance. In patients with decompensated respiratory acidosis, NIV use resulted in a reduction in $PaCO_2$, from 11.4 ± 6.1 kPa to 6.25 ± 2.2 kPa (mean $\pm$ SD, $p = 0.2$) and an increase in pH, from 7.26 ± 0.14 to 7.49 ± 0.12 ($p<0.04$). In 68% of episodes the patient was discharged from hospital ($n = 23$), 16 with domiciliary NIV and 7 without NIV. 89% ($n = 17$) of patients reported subjective benefits from the NIV, including decreased work of breathing ($n = 8$), decreased hypercapnic symptoms ($n = 5$) and improved sputum clearance ($n = 4$).
Conclusion NIV was used successfully to treat and control symptoms of hypercapnic respiratory failure and was generally well tolerated, with a number of subjective benefits reported by patients.

New techniques in diagnosis and treatment of respiratory diseases

S99 COMPARISON OF THE MEASUREMENT OF BRONCHODILATOR RESPONSE IN PATIENTS WITH ASTHMA AND HEALTHY VOLUNTEERS USING SPIROMETRY AND IMPULSE OSCILLOMETRY

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Introduction Reversible airflow obstruction is often used as a criterion to support a clinical diagnosis of asthma. Bronchodilator reversibility is conventionally measured by forced expiratory spirometric manoeuvres, but is effort dependent and requires patient cooperation. Impulse oscillometry (IOS) is an effort-independent and patient-friendly lung function technique which appears to be an attractive alternative, but there are limited data correlating the bronchodilator response using the two techniques in adults with asthma and healthy volunteers.
Objectives To correlate clinical measurements performed by spirometry and IOS in response to administration of a bronchodilator in adults with asthma and healthy volunteers.
Methods The study was a prospective audit of ptients with asthma and healthy volunteers attending routine screening at a research unit in a university teaching hospital. Reversibility testing was carried out using standardised ATS/ERS criteria after administering 400 μg of sallbutamol via a valved spacer device. Spirometric (forced expiratory volume in 1 s (FEV_1)) and IOS measurements (R5, R20, X5) were as per ERS/ATS guidelines.
Results Ninety-five patients with asthma and 61 healthy volunteers underwent screening. The mean percentage predicted (SEM) baseline prebronchodilator FEV_1 was 83.99 (2.23) for those with asthma and 99.25 (1.72) for healthy volunteers. Baseline percentage predicted oscillometry indices in the group with asthma were 162.22 (7.5) for R5; 154.73 (4.71) for R20; and 441.72 (173.86) for X5. In the healthy volunteers this was 111.01 (3.96) for R5; 127.75 (4.12) for R20; and −229.80 (125.75) for X5.R5 was the only impulse oscillometry measure that showed correlation with spirometric indices (FEV_1). The mean percentage predicted (SEM) postbronchodilator change in FEV_1 and R5 in the group with asthma was 6.35 (0.65) and −33.78 (4.43), respectively; correspondingly in healthy volunteers it was 2.24 (0.32) and −14.91 (2.48). A negative correlation was demonstrated $r = -0.40$, $p<0.001$ between the two indices. Linear regression modelling demonstrated that a 1 unit change in $\%FEV_1$ corresponds to a 2.5% change in %R5.

Conclusions Low frequency IOS (R5) and spirometric measurements correlate. Linear regression allows prediction of this change. Further studies need to be carried out to ascertain the reproducibility of this measure prior to use in clinical practice.

S100 COMPARISON OF FORCED EXPIRATORY VOLUMES MEASURED WITH STRUCTURED LIGHT PLETHYSMOGRAPHY AND PNEUMATACH SPIROMETRY

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Introduction This abstract presents a non-invasive monitoring method called structured light plethysmography[1] (SLP) (PneumaScan) and compares its measurements of forced expiratory volumes with those from pneumatach spirometry (PNT).

Methods Simultaneous SLP and PNT measurements were made on 27 healthy subjects (20 males; age 9–61 years; body mass index 15.9–33.6) during a forced expiratory manoeuvre. A grid of black and white squares was projected onto the subjects' chest and abdominal wall, ensuring coverage from the sternal notch superiorly to the anterior superior iliac crests inferiorly. Movements of the grid were captured by two digital cameras and recorded changes in volume. Algorithmic data reconstruction and analysis enabled forced expiratory volumes to be calculated. Subjects wore a plain, light coloured and tight-fitting T-shirt whilst standing against a black backdrop. The subjects' backs were fixed to the wall at three different points (the occiput, the scapulae and the sacrum) to minimise movement. Concurrent measurements were made using a MasterScope spirometer and exported via the manufacturer's J-scope software. Data were normalised to forced vital capacity (FVC), and drifts resulting from BTPS (body temperature and pressure and saturated with water vapour) corrections and integration errors were removed to allow direct comparison of SLP and PNT data.

Results Using paired Student t test, SLP data showed a high degree of agreement with PNT for forced expiratory volume in 1 s (FEV_1) and FEV_1/FVC ($p = 0.085$ and $p = 0.1752$, respectively). Pearson correlation coefficients for FEV_1 and FEV_1/FVC were both >0.85. In addition a Bland–Altman analysis showed no volume-related changes in trend differences.

Conclusion Forced expiratory volumes from SLP are comparable with those obtained by traditional pneumatach spirometry. SLP thus provides an alternative to pneumatach spirometry for measurement of forced expiration. Ongoing work is being undertaken to automate and refine the method.

1. **Usher-Smith JA,** Wareham R, Cameron J, *et al*. Structured Light Plethysmography in infants and children: a pilot study. *Arch Dis Child* 2009;**94**(Suppl I):A38.

S101 MEASUREMENT OF TIDAL BREATHING: A COMPARISON OF STRUCTURED LIGHT PLETHYSMOGRAPHY WITH PNEUMATACHOGRAPHY

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Introduction Measurements of tidal breathing can be used in the diagnosis of respiratory disease. We present a novel, non-invasive lung function device, structured light plethysmography[1] (SLP) (PneumaScan), and the results of a comparison of tidal breathing measured by SLP with those measured by traditional pneumatachography.

Abstract S101 Table 1

	SLP		Pneumatach		Difference (SLP–Pneumatach)		
Parameters	Mean	SD	Mean	SD	Mean	SD	95% CI
Respiratory rate (breaths/min)	15.36	5.01	15.45	5.02	−0.0998	0.224	0.046 to 0.154
Tidal volume (litres)	0.97	0.47	1.00	0.447	−0.0304	0.124	0.001 to 0.060
Inspiratory time (s)	2.16	0.81	2.12	0.783	0.0479	0.170	0.007 to 0.089
Expiratory time (s)	2.23	1.03	2.25	1.04	−0.0192	0.159	0.019 to 0.057

SLP, structured light plethysmography.

Method SLP utilises two digital cameras to track the 3D position of a checkerboard grid projected onto the subject's anterior chest and abdominal wall. Data from 23 healthy adult subjects, aged 19–61, wearing relatively tight clothing, were collected in lying, sitting and standing positions (n = 69). Algorithmic data reconstruction and analysis enabled tidal breathing parameters to be calculated. Simultaneous pneumatach and SLP signals were collected for 1 min in each position. Parameters investigated were respiratory rate (RR), tidal volume (TV), inspiratory (IT) and expiratory (ET) times. As SLP currently produces relative volumes, data were scaled to the pneumatach data in order to obtain real number volumes for comparative purposes.

Results Pearson correlation r^2 values were calculated for RR ($r^2 = 0.999$, $p<0.001$), TV ($r^2 = 0.964$, $p<0.001$), IT ($r^2 = 0.978$, $p<0.001$) and ET ($r^2 = 0.988$, $p<0.001$). Paired Student t test analysis showed no statistically significant difference between means in RR ($p = 0.9071$), TV ($p = 0.6968$), IT ($p = 0.7328$) or ET ($p = 0.9134$). Analysis of the differences in measurements between the SLP and pneumatach data is summarised in table 1. Different body positions made no statistically significant difference in correlation between SLP and pneumatach.

Conclusions Excellent correlation was seen between SLP and the pneumatach across all parameters. CIs for the means of differences were narrow. In this application SLP is a clinical device comparable with a pneumatach. Good agreement in the supine position may lead to application in continuous surveillance of tidal breathing. Ongoing work will enable independent automatic volume calibration of the SLP system.

1. **Usher-Smith J,** *et al*. Structured Light Plethysmography in infants and children: a pilot study. *Arch Dis Child* 2009;**94**(suppl):A38.

S102 EVALUATING BRONCHOALVEOLAR LAVAGE CELLULAR PROFILES USING FLOW CYTOMETRY IN PATIENTS WITH PULMONARY AND SYSTEMIC DISEASE

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Background Bronchoalveolar lavage (BAL) cell fluid analysis can be helpful in the diagnosis and management of certain pulmonary diseases. This is generally performed using microscopy, with immunohistochemistry delineating specific cell subtypes. However, this is labour-intensive, time-consuming and potentially subject to operator bias. Flow cytometry allows rapid, automated and high-volume cell enumeration. Here we evaluate its use in assessing BAL differential cell counts in a hospital, respiratory population.

Abstract S102 Table 1

Final clinical diagnosis	No. of cases	Lymphocytes, % of total cells	Lymphocyte CD4:CD8 ratio	Neutrophils, % of total cells
Pulmonary sarcoidosis	21	26 (16.5–43.3)	4 (2.8–9.5)	3 (2.5–6)
Bacterial infection/ pneumonia	18	11 (5.5–29)	0.6 (0.4–1.4)	15 (8–30)
Tuberculosis	13	51 (30–61)	1 (0.2–2.8)	3 (1–9)
Pneumocystis jirovecii pneumonia	6	15 (13–19)	0 (0–0.3)	8 (4–24)
Non-tuberculous mycobacteria	5	21 (14–23)	3 (2–5.7)	12 (3–33)
Other interstitial lung disease	4	8 (5.5–35.1)	0 (0.1–0.5)	21 (12–25)
Mediastinal lymph node sarcoidosis	4	10 (4–17.8)	1 (1–1.3)	8 (6–25)
Extrathoracic sarcoidosis	3	16 (14.9–35.4)	1 (1–1.3)	8 (6–25)
Fungal pneumonia	3	8 (8–8)	1 (0.61–0.65)	4 (3–5.5)
Bronchiectasis	3	3 (2.5–4)	0 (0.2–1.8)	14 (10.5–17.5)
Unknown	24	9 (4.3–15.5)	2 (0.8–2.1)	11 (5.3–21.8)

Methods A single-centre, retrospective review of adults with a clinical indication for BAL between October 2006 and June 2009. Using a four-colour flow cytometer, a filtered and concentrated portion of the sample was stained using combinations of monoclonal antibodies against CD45 (pan-leucocyte marker), CD3, CD4, CD8 (lymphocyte), CD15 (neutrophil) and CD23 (eosinophil marker). A minimum of 100 000 events were captured, yielding at least 5000 events within lymphocyte or granulocyte pools. Outcome measures were intra-assay variability (IAV) and the relationship between BAL cellular differential count and final clinical diagnosis.

Results Complete clinical and laboratory information was available on 118 of 124 patients. IAV was assessed using 10 randomly selected samples, with assays run in triplicate. The coefficient of variance was good, with a median value of <2% (range 0–9%). 31 patients had suspected pulmonary sarcoidosis prebronchoscopy. In the 20 (65%) who had the diagnosis confirmed, the median CD4:CD8 ratio was 4.4 (interquartile range (IQR) 2.7–8.3) compared with 0.7 (0.5–1.0) in the remainder who had an alternative diagnosis ($p<0.001$). Eight of 33 suspected tuberculosis cases were confirmed to have it. Their median lymphocyte percentage of total BAL cells was 59% (IQR 51–61%) vs 9% (4–24.5%) in the other 25 cases ($p = 0.001$). The percentage of neutrophils in the BAL cell population was significantly higher in bacterial infection (median 15%, IQR 8.8%–30%) compared with other non-bacterial infections (4%, 2–10%, $p = 0.007$). Table 1 gives median (IQR) cellular differentials for conditions with >2 cases ($n = 104$).

Conclusions BAL fluid can be analysed using flow cytometry in a routine laboratory setting. The technique is straightforward, precise and appears to discriminate specific clinical processes. Further work needs to determine whether this adds value to other current diagnostic investigations.

S103 COMBINING EBUS-TBNA WITH STANDARD BRONCHOSCOPIC TECHNIQUES FOR THE DIAGNOSIS OF PULMONARY SARCOIDOSIS

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Introduction Transbronchial lung biopsies (TBLBs) and endobronchial biopsies (EBBs) are standard techniques for the diagnosis of pulmonary sarcoidosis with yields of up to 75%. Cohort studies suggest endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) may be a useful tool for the diagnosis of sarcoidosis. However, no data are currently available on the safety and efficacy of combining standard bronchoscopic techniques with EBUS-TBNA. A prospective study was therefore carried out to evaluate the diagnostic yield from EBUS-TBNA, TBLB, EBB and their combination in patients with suspected sarcoidosis, for whom pathological confirmation was clinically required.

Methods Patients with enlarged mediastinal lymph nodes and suspected sarcoidosis (stages 1 and 2) underwent EBUS-TBNA. In all patients the EBUS scope was withdrawn and replaced with a standard videobronchoscope under conscious sedation and TBLB and EBB were performed.

Results Twenty-seven patients with suspected sarcoidosis underwent EBUS-TBNA and bronchoscopy. Overall 16 patients were diagnosed with sarcoidosis, 7 had tuberculosis, 2 had reactive lymphadenopathy, 1 had lymphoma (diagnosed on EBUS-TBNA) and 1 remains in follow-up. The sensitivity of EBUS-TBNA for obtaining non-caseating granulomas in patients with sarcoidosis was 81%. The sensitivity of standard bronchoscopic techniques alone was significantly lower at 44% ($p = 0.029$). Yield per procedure according to stage of sarcoidosis is summarised in table 1. In patients with negative EBUS-TBNA, non-caseating granulomas were obtained by TBLB of radiologically normal lung parenchyma in one patient and EBB of normal endobronchial mucosa in one patient. The sensitivity of combined EBUS and standard bronchoscopic techniques was 94%. No major complications related to EBUS-TBNA or sedation were observed. One patient undergoing TBLB experienced a pneumothorax, requiring admission but not intercostal drainage.

Abstract S103 Table 1 Diagnostic yield of EBUS-TBNA and bronchoscopy according to stage of sarcoidosis

	No. of patients with positive diagnostic yield (%)			
	EBUS-TBNA (%)	Transbronchial lung biopsy (%)	Endobronchial biopsy (%)	Combined EBUS+bronchoscopy (%)
Stage 1 sarcoidosis (n = 8)	6 (75)	1 (13)	0 (0)	7 (88)
Stage 2 sarcoidosis (n = 8)	7 (88)	5 (63)	1 (13)	8 (100)

EBUS-TBNA, ultrasound-guided transbronchial needle aspiration.

Conclusion Combining EBUS-TBNA with standard bronchoscopic techniques is a safe procedure and optimises the diagnostic yield in patients with pulmonary sarcoidosis. Further prospective studies with economic analyses are warranted to determine whether the combination of EBUS-TBNA with standard bronchoscopic techniques can avoid mediastinoscopies in patients with suspected sarcoidosis for whom pathological confirmation is required.

S104 EXPERIENCE OF A TERTIARY CENTRE WITH REMOVABLE SELF-EXPANDABLE METAL STENTS

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Introduction and Objectives The use of self-expanding metallic stents (SEMS) in the management of large airway obstruction and sealing of fistulae has become more established with the advent of removable stents. As a tertiary centre we have significant experience in the insertion of airway stents. We report our

experience and evaluate the clinical efficacy and safety of removable SEMS.

Methods We conducted a retrospective study between January 2005 and July 2009. Data analysis was carried out using SPSS.

Results 36 stents were inserted in a total of 33 patients (20 males and 13 females). The mean age was 59.7 ± 14.4 years (range 22–81). 32 stents (84.2%) were deployed for malignant conditions and 4 (10.5%) for benign diseases. 81.8% of patients had malignant airway obstruction and 6.1% had tracheo-oesophageal fistulae. Obstruction was located to the trachea in 44.4% of cases. 88.9% of patients reported improvement in symptoms in the first 24 h. 62.9% of patients were in severe respiratory distress prior to SEMS insertion, with immediate improvement thereafter. Complications were reported in 14 stents, with 2 presenting within 24 h. We recorded 1 case of stent fracture, 6 cases of migration, 5 cases of mucus plugging, 1 minor bronchial tear associated with stent placement, and 1 case of stent-associated respiratory tract infection. 12 stents were easily removed, with no associated complications. 17 deaths were reported, none related to stent insertion and all were in patients with advanced malignant disease. Survival for these patients ranged from 7 to 430 days poststent insertion.

Conclusions SEMS provide an effective, safe and feasible therapeutic modality in patients with benign and malignant airway stenoses. Although associated with significant complications, they have the advantage of providing immediate relief from breathlessness and imminent asphyxia. In patients with malignancy, SEMS enable definitive oncological treatment to be given electively, and in greater safety, and are easily removed after completion of treatment.

COPD: cells and genes

S105 FIBRINOPEPTIDE Aα360: A FOOTPRINT OF NEUTROPHIL ELASTASE ACTIVITY

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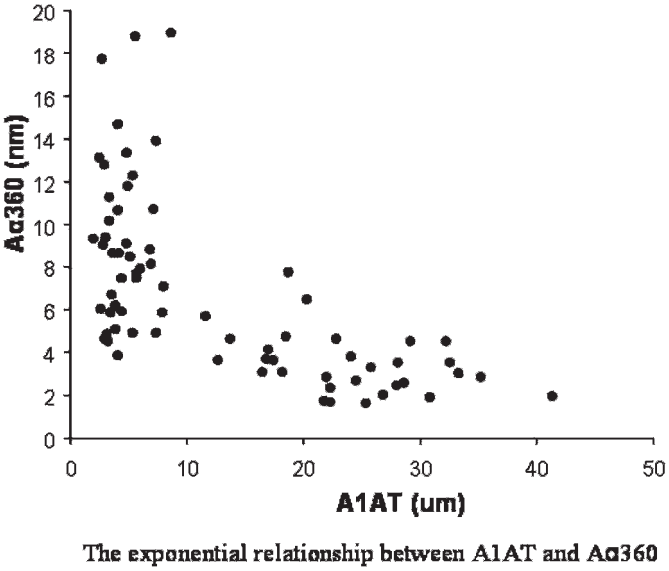
Initial descriptions of the association between α-1-antitrypsin deficiency (AATD) and lower zone pulmonary emphysema[1] were closely followed by the confirmation that neutrophil elastase (NE) could induce emphysema in animal models.[2] Mathematical and in vitro models have demonstrated an exponential relationship between released enzyme activity and distance from the neutrophil[3 4] and since the neutrophil NE concentration at release is substantially higher than the physiological concentration of AAT an area of obligate proteolytic damage will occur, which is substantially larger in patients with AATD. This process of quantum proteolysis is a simple concept that explains the increased susceptibility of subjects with AATD to emphysema, but, since it occurs in the neutrophil microenvironment, it has been difficult to demonstrate in vivo. The aim of this study was to explore the relationship of a specific (preinhibition) NE cleavage product of fibrinogen (Aα360) to AAT and the presence of airflow obstruction in deficient subjects.

Methods Plasma Aα360 was measured in a group of 68 subjects with a wide range of plasma AAT levels. Subsequently, postbronchodilator spirometry was related to plasma Aα360 concentrations in a further 72 patients (49 male and 23 female) with PiZ AATD in the stable state. Correlations were determined using non-parametric statistical tests.

Results Aα360 showed an exponential relationship to plasma AAT concentration that increased at levels <11 μm (the putative protective threshold), as shown in fig 1, consistent with theoretical modelling and in vitro experiments. The mean forced expiratory volume in 1 s (FEV_1) and FEV-:vital capacity (VC) were 50.7% predicted and 37.26%, respectively, and 61 patients had an FEV_1:VC <70%. There was no relationship between Aα360 and age, height, gender or smoking status. However, Aα360 correlated with FEV_1 ($p = 0.01$), FEV_1:VC ($p = 0.008$) and residual volume ($p = 0.013$).



Abstract S105 Figure 1. A1AT, α-1-antitrypsin.

Conclusion The Aα360 concentration is a direct measure of the destructive activity of neutrophils, relates (as predicted) to the AAT level and correlates with spirometric markers of severity in patients with AATD.

1. *Clin Radiol* 1992;**45**:260–6.
2. *Am Rev Respir Dis* 1985;**132**:362–6.
3. *Biochemistry* 1995;**34**:16171–7.
4. *J Immunol* 1996;**157**:2624–31.

S106 DIESEL EXHAUST PARTICLES POTENTIATE INFLAMMATION AND RENDER IT RESISTANT TO IL-1 ANTAGONISM IN VITRO

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Introduction and Objectives Inhalation of small particulate matter is a major cause of airway inflammation, with fragments of bacteria, viruses and various environmental pollutants causing inflammation and potentiation of human respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma. Diesel exhaust particles (DEPs) are the major component of air pollution. The influence of DEPs on the interactions between resident epithelial cells and infiltrating leucocytes remains unexplored. In this study we investigated the potential for DEPs to induce inflammation in the airway, and subsequently explored its capacity to modulate the inflammatory response to pathogenic stimuli, a situation that will commonly occur during inhalation of environmental particulates and microbial products.

Methods The effects of DEPs were studied in co-cultures of primary human monocytes and the immortalised bronchial epithelial cell line, BEAS-2B. Co-cultures, or monoculture controls, were treated with DEPs in the presence or absence of Toll-like receptor 4 (TLR4) and TLR5 agonists (lipopolysaccharide (LPS) and flagellin, respectively) and an interleukin-1 (IL-1) receptor antagonist (IL-1ra). Changes in cytokine release were measured by ELISA.