(n=2) and 30 minutes of NOS inhibition [with 1 mM: L-N-Ornithine, 1400W and S-Methyl-L-thiocitrulline] reduced baseline CBF by 20% to 9.6 Hz SD±0.9 ($p<0.001$) but the $P2X_4$ inhibitor [10 μM brilliant blue G] had no effect.

Conclusion $P2X_4$ and nNOS are expressed in human airway cilia but do not co-localise. NOS inhibition reduced CBF whilst $P2X_4$ inhibition did not, suggesting that blocking $P2X_4$ activity alone is not sufficient to modify NOS activity or CBF.

P257 HUMAN CYTOMEGALOVIRUS BINDING TO NEUTROPHILS TRIGGERS A PRO-SURVIVAL SECRETOME THAT MODULATES MONOCYTE MIGRATION, ACTIVATION AND PHENOTYPE

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Neutrophils provide the body's first line of defence against invading pathogens. They respond to infection by releasing an array of chemokines, cytokines, and superoxide anions that initiate cascades of other immune mediators and cell types. Although the rapid response and flexibility of neutrophils make them an integral part of the body's immune system, human cytomegalovirus (HCMV), paradoxically, may use neutrophil activation for its own evolutionary advantage. Here we report that human peripheral blood neutrophils exposed to a clinical strain of HCMV display a profound survival phenotype that occurs independent of viral gene expression. The initial HCMV driven survival response was partially dependent on ERK1/2 activation and profoundly inhibited by inhibition of NF-kB. Intriguingly, this initial survival event triggered by virus binding was augmented by a cytokine mediated effect whereby supernatants from infected neutrophils provided uninfected neutrophils with substantial protection against apoptosis – a protection which was PI3K as well as ERK1/2 and NF-kB dependent.

Concomitant with a transferable survival effect the HCMV-neutrophil secretome also markedly manipulated autologous donor monocytes. Enhanced migration and subsequent differentiation to a permissive phenotype for HCMV infection was suggestive of a mechanism for efficient viral dissemination from the site of initial infection. Fascinatingly, although differentiation to a permissive phenotype was observed this was concomitant with down-regulation of a number of key activators of the adaptive immune response. Overall, these data illustrate the manipulation of an anti-viral response by a pathogen to enhance the outcome of infection which, intriguingly, involves a cell type not productively infected by the pathogen itself. These data further illustrate the complexity of pathogen interactions with the host immune system as well as providing new clues into the mechanisms HCMV exploits for efficient viral dissemination which could have implications on our understanding for HCMV pathogenesis.

Improving the care of sleep apnoea

P258 CHANGE IN SLEEP STUDY AND CPAP PROVISION FOLLOWING THE NIHCE CPAP TA

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Introduction We have assessed whether Primary Care Trusts' (PCTs) commissioning of sleep services has improved following the NIHCE 2008 technology appraisal on CPAP.

Methods We wrote to all PCTs in England, (under the Freedom of Information Act, 2000) for information on sleep studies commissioned, and CPAP prescriptions issued, for the years ending 31 March, 2008, 09, and 10. The PCTs were also asked who provided sleep studies or CPAP on their behalf (NHS hospital, GP, private, or other provider). Some PCTs did not reply, or claimed not to hold data, so we contacted appropriate NHS hospitals to obtain further information. Sleep study data was only obtained from approximately 75% of PCTs or associated hospitals. An alternative set of data, on the Department of Health (DH) website, was also used. Limited sales data from CPAP companies was also available for comparison.

Results In almost all PCTs, sleep studies and CPAP provision were from NHS hospitals. The incomplete data from PCTs showed that sleep studies rose from about 30,000 in 2007/8 to 48,000 in 2009/10, a 3-year increase of about 60%. Data on sleep studies published by DH rose from over 61,000 in 2007/8 to over 86,000 in 2009/10, a 3-year increase of 41%. For CPAP prescriptions issued, only 66% of PCTs submitted data for 2007/8, rising to a 75% response by 2009/10. On the basis of this incomplete information and with some assumptions, annual CPAP prescriptions rose from less than 17,000 in 2007/8 to over 37,800 by 2009/10, a three year increase of 126%. There may be some under-reporting in the earlier years, and the industry sources suggested a 3-year lower increase of nearer 80%. In addition there are likely to be errors of coding. However, there was wide variation between PCTs suggesting patchy performance.

Conclusions We believe that the results show a clear improvement in the number of sleep studies and CPAP prescriptions over this period. Thus, following the NIHCE TA there has been an improvement in patient access to the diagnosis and treatment of sleep apnoea, though we are concerned that the wide variation suggests there is a substantial element of post-code lottery.

P259 PREFERENCE OF PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS) FOR CONVENTIONAL CONTINUOUS POSITIVE AIRWAY PRESSURE(CPAP) OR BI-LEVEL CPAP (CFLEX) AND CHANGES IN RESISTANCE TO EXPIRATION

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CFlex (Respironics) Bi-Level device lowers expiratory PAP (EPAP) early in expiration returning EPAP to the set inspiratory PAP (IPAP) before the start of the next inspiration. Most patients with OSAS will express a preference for either CPAP or CFlex at the time of treatment initiation. We investigated the possibility that choice of CFlex was related to interaction of breathing pattern and the CFlex device in 43 newly diagnosed patients with OSAS in a single-blind study. Inspiratory and expiratory time (Ti, Te) were measured by rib-cage and abdominal inductance belts. IPAP and EPAP were measured at the mask by pressure transducer. In 23 patients we recorded simultaneous flow in the CPAP circuit and by using mask specific leak rates derived values for inspiratory tidal volume (Vt insp): (Vt insp = (Mean Inspiratory Circuit Flow x Ti) - (Mask leak x Ti)) Patients tried CPAP or CFlex in random order for periods of 10 minutes or until breathing was stable. One minute epochs of stable breathing were used to calculate mean values for Ti, Te, IPAP, EPAP and Vt insp

Results 19 patients stated a preference for CFlex (CFlexpref), 20 for CPAP (CPAPpref). 4 had no preference and received CPAP. We included them in the CPAP. pref group for analysis. For the whole group (n=43) there was a small but significant fall in mean EPAP on CFlex compared with mean EPAP on CPAP (10.4 vs 11.5 cm H_2O).

Comparing CPAP. pref with CFlexpref we found no significant difference between mean EPAP on CPAP and mean EPAP on CFlex making it unlikely that preference for CFlex was based only on EPAP reduction. In the 23 patients (CPAPpref=13, CFlexpref=10) who had Vt insp measured we derived an index of the flow resistive load to expiration (Table). The CFlexpref group demonstrated a significant fall in this index of expiratory load. The changes in the CPAPref group were more variable. The findings are consistent with CFlex preferers generating and sensing a larger reduction in expiratory load on CFlex.

Abstract P259 Table 1

Resistance to Expiration (mean EPAP/mean Expiratory Flow) Geometric mean (SD) cm H_2O l^{-1} s			
CPAP		CFlex	
CPAP Preferred (n=13)	CFlex Preferred (n=10)	CPAP Preferred (n=13)	CFlex preferred (n=10)
70.8 * (38.3–131)	67.6** (51.6–88)	60.25* (34.5–105)	54.9** (40.6–74.3)

Paired t test: * p NS;** p<0.03v

P260 HAEMATOLOGICAL CHARACTERISTICS OF PATIENTS REFERRED FOR INVESTIGATION OF OBSTRUCTIVE SLEEP APNOEA

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Introduction Obstructive Sleep Apnoea (OSA) is a condition with increasing prevalence. Individuals with severe OSA have significant intermittent nocturnal hypoxia. Erythropoiesis is stimulated through the renal secretion of erythropoietin in response to hypoxia, and is responsible for polycythaemia found in chronic respiratory failure. There are case reports of secondary polycythaemia attributed to OSA, but there are limited data assessing the relationship of OSA physiological parameters and haemoglobin. We aimed to investigate this.

Methods Clinical information was collated prospectively from patients assessed at the Newcastle Regional Sleep Service with suspected OSA. None of those included had been referred to investigate polycythaemia. All patients included underwent either a domiciliary or in-patient sleep study as per standard clinical practise, and had a Full Blood Count (FBC) taken.

Results There were 103 patients included: 70% males, mean (SD) age 52 years (range 26–76 years), BMI 36.1kg/m^2 (8.3), Epworth Sleepiness Scale 13 (5), daytime SpO_2 on air 96% (2.7) [six patients had SaO2 <92%]. Sleep study results showed the Apnoea-Hypopnea Index (AHI) to be <5 in 13% [no OSA], ≥5 and <15 in 30% [mild OSA], ≥15 and <30 in 19% [moderate OSA], and ≥30 in 38% [severe OSA]. Analysis of FBC results showed no statistical difference in Haemoglobin between the four patient groups; mean (SD), no OSA 14.3g/dl (2.1), mild 14.6g/dl (1.5), moderate OSA 14.5g/dl (1.2), severe OSA 14.7g/dl (1.4). There was no correlation between Haemoglobin (Hb) and AHI, oxygen desaturation index (ODI), % time SpO_2<90%, % time SpO_2<80%, or awake SpO_2. There was no significant difference in haematocrit or RBC between groups. A weak positive correlation was observed between total WBC and ODI, r=0.319, p=0.001, but there was no statistical difference between patient groups.

Conclusions In this sleep clinic patient group, we found no correlation between haemoglobin and any OSA severity marker. This suggests that the nocturnal intermittent hypoxia which occurs in OSA alone does not lead to secondary polycythaemia. Further work will evaluate the prevalence of OSA in people with secondary polycythaemia, and whether the OSA is contributory or reflects the general population prevalence of OSA.

P261 ANALYSIS OF THE PREVALENCE AND PREDICTORS OF OBESITY HYPOVENTILATION SYNDROME IN A COHORT OF OVERWEIGHT PATIENTS WITH SUSPECTED SLEEP DISORDERED BREATHING

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Introduction The need for early detection of Obesity Hypoventilation Syndrome (OHS) is clear because delay in the diagnosis and treatment is associated with significant morbidity and mortality.

Objective To determine the prevalence of obesity hypoventilation syndrome among obese patients with suspected sleep apnoea and determine the validity of previously reported predictors of OHS such as serum bicarbonate level.

Methods A retrospective analysis of prospectively collected sleep clinic data on 525 consecutive obese patients referred to sleep clinic from January 2009 to January 2011 to a university hospital was performed. Subjects with suspected sleep disordered breathing were evaluated according to our clinical protocol and capillary blood gases were measured in obese (BMI> 30) subjects.

Results 525 consecutive patients (mean age 51.44±12.7, 65.71% males, mean BMI 34.59±8.1) were evaluated. A total of 344 (65.52%) were obese (mean age 52.29±12.4, 63.66% males) of which 128 (37.2%) were morbidly obese (BMI>40 kg/m^2). Daytime hypercapnia ($paCO_2$>6 kPa) was detected in 20.63% (71/344) obese and 22.1% (61/275) obstructive sleep apnoea (OSA) patients. Univariate analysis of potential predictors of OHS showed significant correlations between $paCO_2$ and BMI, FEV1, FVC, AHI, mean nocturnal SpO_2, minimum nocturnal SpO_2, sleep time spent with SpO_2 <90%, paO_2 and serum HCO_3. Following stepwise multiple regression, paO_2 and HCO_3 were found to be independent predictors of OHS explaining 27.7% of paCO2 variance (p<0.0001).

On logistic regression analysis, serum HCO_3 cut-off of >27 mmol was found to have 85% sensitivity and 90% specificity for diagnosis of OHS.

Conclusion We confirmed high prevalence of OHS in obese patients with OSA (22.1%) that would be possible to diagnose by measuring serum HCO_3 levels, thereby eliminating the need for arterial blood gas sampling.

P262 AGE AND GENDER SPECIFIC DIFFERENCES IN EXCESSIVE DAYTIME SLEEPINESS

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Introduction The pictorial Epworth Sleepiness Scale (ESS) (Ghiassi et al., Thorax 2011) has been developed and validated against the traditional ESS and allows subjects to intuitively answer the questions related to daytime sleepiness with pictorial items. Although non-specific, the ESS has been validated for sleep apnoea