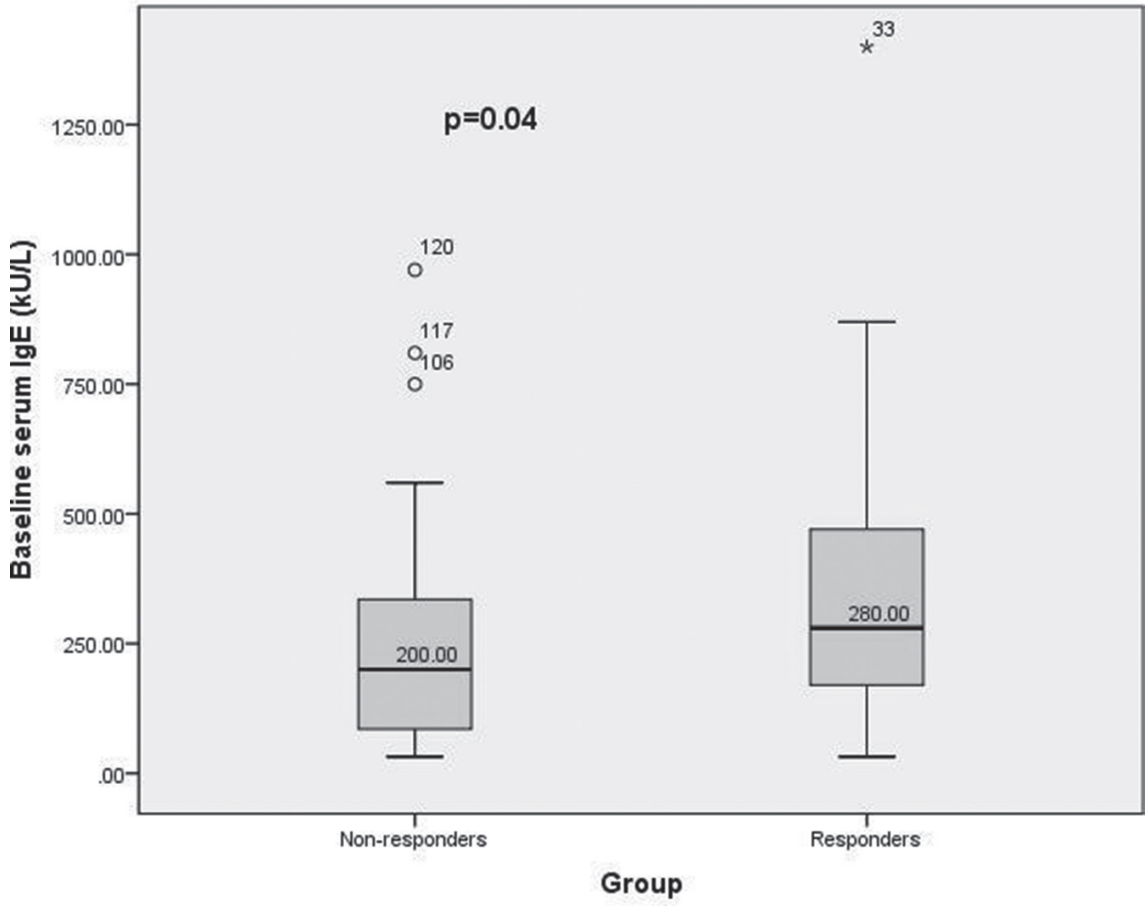
Methods n = 14 ICS treated asthmatic patients (Mean age 46 years, FEV1 86% predicted, R5 160% predicted, ICS 693ug/day),were randomised in cross-over fashion to receive either IND 150ug alone (ICS/LABA) or in combination with TIO 18ug once daily (ICS/LABA/LAMA) for 4 weeks with 2 week run-in and washout periods. Mannitol sensitivity (PD15) and reactivity (RDR), airway resistance (R5,R5-R20), reactance (AXE) and FeNO were measured at 24 hours after the first and last doses.
Results There were significant improvements in mannitol PD15 and RDR with IND or IND/TIO vs baseline after single but not chronic dosing (Figure) . There was also a significant difference in RDR between single and chronic dosing for both treatments. R5,R5-R20 and AXE were significantly improved with both treatments compared to baseline after single and chronic dosing . There were no significant differences between treatments after chronic dosing for either mannitol or IOS . In contrast FeNO was unchanged with either treatment compared to baseline.
Conclusions There were significant improvements in mannitol sensitivity and reactivity with either IND or IND/TIO after single but not chronic dosing, while FeNO remained unchanged . Airway resistance and reactance were significantly decreased to the same degree with both treatments after chronic dosing . This in turn suggests that the mechanism by which LAMA reduces exacerbations is unlikely to be related to AHR, FeNO or airway geometry.

P240 LOW IGE AND NOT BLOOD EOSINOPHILS PREDICTS LACK OF RESPONSE TO OMALIZUMAB IN UHSM COHORT

[1]TB Morris, [1]HV Patel, [1]M Demirbag, [2]LJ Holmes, [2]R Daly, [2]D Ryan, [1]RM Niven. *[1]University of Manchester, Manchester, UK; [2]University Hospital of South Manchester, Manchester, UK*

10.1136/thoraxjnl-2016-209333.383

Background Omalizumab is an anti-IgE monoclonal antibody therapy used in patients with inadequately controlled persistent allergic IgE mediated asthma who require continuous or frequent treatment with oral corticosteroids. Previous studies have tried to predict a patient's response to omalizumab based on pre-treatment baseline characteristics. Most recent data has suggested that baseline blood eosinophils, serum periostin or FeNO may be predictive of response to omalizumab in the T_H2 phenotype.
Aims This study will attempt to identify a characteristic that may explain why some patients suffering with severe asthma in a single severe asthma centre do not achieve a response when treated with the anti-IgE monoclonal antibody, omalizumab.
Methods The target population was represented by all patients previously treated or undergoing treatment with omalizumab at the Severe Asthma Service at University Hospital South Manchester (n = 185). The study population was those for whom records could be found within the study period (n = 154). Demographic and clinical data was collected retrospectively from patient medical records.



Abstract P240 Figure 1 Comparison of baseline IgE in true nonresponders and true responders

Results 16.2% of patients at UHSM did not show response to omalizumab at 16 weeks. Baseline serum IgE levels in the non-response group were on average 77.28 kU/L lower than those in the response group, statistical analysis of the two groups show that this difference was significant ($P = 0.04$). Mean eosinophils in the true non-responder group were actually higher than those in the true responder group, however this difference was not statistically significant. No other demographic or disease specific measures predicted a lack of response to omalizumab.
Discussion The results from the study indicate that a lower baseline serum IgE may predict non-response to treatment with omalizumab. The results also show that non-response rates at the NWLC were lower than those demonstrated in clinical trials (INNOVATE), were consistent with other real life studies (PERSIST/APEX I and APEX II) but markedly lower than those quoted in the eXpeRience registry.

P241 EOSINOPHIL APOPTOSIS IS NEGATIVELY ASSOCIATED WITH BODY MASS INDEX IN ASTHMA

[1]A Thavakumar, [2]AKA Wright, [1]MA Ghebre, [2]T Thornton, [1,2]CE Brightling. [1]*Department of Infection, Immunity and Inflammation, University of Leicester, Leicestershire, UK*; [2]*Institute of Lung Health, NIHR Leicester Respiratory Biomedical Unit, University Hospitals of Leicester NHS Trust, Leicestershire, UK*

10.1136/thoraxjnl-2016-209333.384

Background Obese asthmatics are known to have reduced eosinophils in sputum, as well as poor control of asthma symptoms.[1] We have shown that, compared to non-obese patients, there is an elevated number of eosinophils in the airway submucosa of obese asthmatic patients.[2] This study aims to determine whether a differential susceptibility to apoptosis, between obese and non-obese patients, could contribute to these clinical observations.
Method Patients with a clinical diagnosis of asthma were recruited (n = 28) and consented at Glenfield Hospital for blood donation to study eosinophil apoptosis; the patients recruited had varying severities of asthma and BMI. Eosinophils were isolated from whole blood by negative immunomagnetic selection using CD16 microbeads to a purity of mean ± SD 95.7% (± 4). Purified eosinophils (Time 0) were placed into culture in RPMI (1640 + GlutaMAX-1 supplemented with 10% FBS and 1% penicillin and streptomycin) and harvested at 17 and 21 hours later to measure apoptosis by flow cytometry using Annexin V and Propidium Iodide (Becton Dickinson). Cells were considered apoptotic if they were Annexin V positive/PI negative and reported as a percentage of total eosinophils.
Results At 0 hours, the mean% of annexin V positive cells was 0.47% and there was no significant association with BMI (r = −0247, p value = 0.245). At 17 and 21 hours there were 12.68% and 21.0% annexin V positive cells, respectively, and we noted a significant negative Pearson's correlation between eosinophil apoptosis and BMI at time 17 (r = −0.449; p = 0.028) and time 21 (r = −0.448; p = 0.028). These correlations were independent of lung function, steroid medication and percentage eosinophil purity.
Conclusion Eosinophils from obese asthmatic patients are less susceptible to apoptosis compared to those from non-obese patients. This may contribute to the differential presence of eosinophils in the lamina propria and airway of obese patients compared to non-obese individuals.

REFERENCES

1 Haldar P, Pavord ID, Shaw DE, *et al*. Cluster analysis and clinical asthma phenotypes. *Am J Respir Crit Care Med* 2008;**178**(3):218–224.
2 Desai D, Newby C, Symon FA, *et al*. Elevated sputum interleukin-5 and submucosal eosinophilia in obese individuals with severe asthma. *Am J Respir Crit Care Med* 2013;**188**(6):657–663.

P242 THE AIRWAY MICROBIOTA IN HUMAN RHINOVIRUS INDUCED ASTHMA EXACERBATION

EHC Wong, J Dhariwal, L Cuthbertson, P James, M Cox, M Moffatt, W Cookson, S Johnston. *National Heart and Lung Institute, Imperial College London, London, UK*

10.1136/thoraxjnl-2016-209333.385

Background Acute asthma exacerbations (AEs) cause significant morbidity. Up to 60% of AEs may be associated with respiratory viral infections, particularly human rhinoviruses (HRVs). The role of bacteria in AEs is unclear, yet antibiotics are frequently prescribed. Recent studies have demonstrated a greater abundance of potentially pathogenic bacteria (e.g. *Haemophilus* spp.) within the airway microbiota in asthma, whilst a greater abundance of commensals (e.g. *Prevotella* spp.) were observed in health. The aim of this study was to examine the changes within the airway microbiota in asthma in the context of a HRV-induced AE and evaluate if such changes correlate with clinical symptoms and lung function changes.
Methods Eleven moderate asthmatic (BTS step 3–4) and 12 healthy subjects were experimentally infected with HRV-16 and bronchoscopy was performed at baseline, 3 and 8 days following HRV-infection. Subjects completed daily symptom diary and spirometry. DNA was extracted from bronchoalveolar lavage and PCR amplification of the V3-V5 region of bacterial 16S rRNA gene was performed to evaluate microbiota community composition.
Results The microbiota composition did not significantly differ between healthy and asthmatic subjects at baseline, though healthy subjects exhibited significantly greater relative abundance of *Prevotella* spp. following HRV-infection ($p < 0.05$). At day 3 post-HRV infection, greater *Prevotella* spp. relative abundance was associated with lower symptom scores ($R2 = 0.56$, $p < 0.05$). In contrast, at day 8 greater *Neisseria* spp. relative abundance was associated with greater peak flow decline ($R2 = 0.41$, $p < 0.05$). Furthermore, HRV-16 viral load exhibited a significant linear relationship with the degree of microbiota community change (as measured by beta-diversity) ($R2 = 0.61$, $p < 0.05$).
Conclusion Following HRV infection, greater *Prevotella* spp. relative abundance was associated with less symptoms whilst greater *Neisseria* spp. was associated with greater peak flow decline, suggesting an imbalanced microbiota may exacerbate airway inflammation and ultimately severity of AE. Viral load significantly correlated with degree of microbiota community change, implying HRV infection may directly perturb the airway microbiota. Further studies are needed to confirm these findings and explore the roles of *Prevotella* spp. and *Neisseria* spp. in exacerbating airway inflammation.