Introduction Recurrent exacerbations are a characteristic feature of uncontrolled asthma, often due to viral or bacterial infections. We have reported in a retrospective study that immune deficiency is common in asthma and correlates with reduced lung function. We set up a prospective study to determine if this predisposes to a more severe disease.

Aim Our aim is to ascertain if immune deficiency is associated with a more severe disease potentially with radiological changes and clinically with low lung function and frequent exacerbations.

Methods We prospectively collected data from new patients attending the regional asthma and fungal clinics. Demographics, markers of disease severity and specific antibody levels to Haemophilus influenzae (HI) and Streptococcus pneumoniae (SP), were recorded. Patients with specific antibody deficiency (HI: ≤ 0.15 iu and SP: ≤ 0.35 iu to 6+ of 12 strains tested) received appropriate vaccination(s) in primary care (Pneumovax®).
and Meniotrix®), with repeat samples collected two months later. We also recorded blood and sputum eosinophil counts, radiological findings such as bronchiectasis and bronchial wall thickening, total IgE, smoking status, exacerbations in the last year and ITU admissions.

**Results**
101 patients were followed up (69 asthma, 32 fungal) 67 admissions.

We also recorded blood and sputum eosinophil counts, radiological findings such as bronchiectasis and bronchial wall thickening, total IgE, smoking status, exacerbations in the last year and ITU admissions.

**Conclusion**
Specific antibody deficiency is commonly seen in patients with asthma and fungal disease. Vaccination can provide protection and should be considered in this patient group. We need further analysis with a larger cohort of patients to study the association between antibody deficiency, lung function, radiological changes and disease progression.

**P245**

**WHOLE BLOOD LEVELS OF MICRORNA-34A PREDICT SURVIVAL AND REGULATE GENES ASSOCIATED WITH PULMONARY ARTERIAL HYPERTENSION**

J Lin, J Iremonger, J Pickworth, A Rothman, H Casbolt, N Arnold, C Elliot, R Condiffe, D Kiely, A Lanzier. University of Sheffield, Sheffield, UK

**Introduction**
Despite advanced therapies for pulmonary arterial hypertension (PAH), the hyperproliferative pulmonary vasculopathy persists. Circulatory microRNAs (miR) offer considerable promise as both a prognostic biomarker, and to identify molecular mechanisms underlying PAH. Previous study from our lab identified whole blood miR-34a as downregulated in patients with PAH.

**Objectives**
To validate changes in whole blood miR-34a levels in patients with PAH and relate them to disease severity and survival, and determine the phenotypic effect on pulmonary artery smooth muscle cells (PASMC).

**Methods**
Whole blood RNA was isolated from 27 treatment-naive patients with PAH, 12 age-matched healthy volunteers (HV) and experimental models of PAH (Monocrotaline-MCT, Sugen5416/hypoxia-SuHx and controls, n = 5/group). Whole blood miR-34a-5p and −3p levels were measured by qPCR. The phenotypic effect of miR-34a-5p and −3p levels was assessed on PASMC in-vitro. Differences between groups were determined by Student’s t-test or ANOVA-Tukey.

**Results**
Whole blood miR-34a-5p was reduced in patients with PAH (p < 0.0001) and experimental models of PAH (MCT p < 0.05, SuHx p < 0.001). Receiver operating characteristic curve identified that miR-34a-5p levels discriminates patients with PAH from HV (AUC = 0.86, p = 0.001). MiR-34a-5p levels were significantly lower in patients with severe PAH, as defined by a cardiac index of <2 vs >2.5 l/min/m² (p < 0.05) and NT-proBNP > 300 vs <300 ng/l (p < 0.001) and predict survival at 5 years. MiR-34a-5p levels were negatively correlated with pulmonary vascular resistance (r = −0.4, p < 0.05) and pulmonary arterial wedge pressure (r = −0.4, p < 0.05). Preliminary data showed that whole blood miR-34a-3p was reduced in patients with PAH (p = 0.0267) and experimental models of PAH (MCT p < 0.01, SuHx p < 0.01); and delineates patients with PAH from HV (AUC = 0.925, P = 0.01). Transfection of PDGF-stimulated PASMC with miR-34a-5p or −3p inhibitor