Background The introduction of the pneumococcal conjugate vaccines into infant vaccination schedules, has led to a change in the serotype prevalence causing adult pneumococcal disease, through the process of herd immunity. Whilst there are national surveillance programmes informing the changes in serotype in invasive pneumococcal disease, there are no comparable data to demonstrate the ongoing vaccine effect on non-invasive pneumococcal community acquired pneumonia (CAP), the most common clinical manifestation of pneumococcal disease in adults.

Methods Consecutive adult patients admitted to 2 hospitals, covering the catchment area of a large UK city, with a diagnosis of CAP were studied prospectively, over a 1 year period between September 2014 and 2015. A novel multiplex assay capable of detecting 24 serotypes/serogroups of Streptococcus pneumoniae was performed on patient urine. Pneumococcal infection was determined by identification of the organism from either sterile sites and/or detection of pneumococcal antigen or serotype in urine samples.

Results Of 478 individuals admitted with CAP, pneumococcal disease was diagnosed in 166 (34.7%) cases. Pneumococcal CAP diagnosis was made by blood culture, pneumococcal urinary antigen detection and urinary serotype detection in 23 (13.9%), 61 (36.8%) and 149 (89.8%) cases respectively. A definitive single serotype was identified in 116 individuals; the most commonly observed were serotypes 3 and 8 (31 cases each, 26.7%), followed by serogroup 15 (14 cases, 12.1%), 17F (10 cases, 8.6%) and 33A/B/D/E (9 cases, 7.8%).

Conclusion This is the first report on extended serotype distribution implicated in adult pneumococcal CAP, 9 years after the introduction of the UK infant vaccination programme. In this era of high infant vaccine coverage, whilst the majority of isolates are non-vaccine types due to the effects of serotype replacement, serotype 3 remains a common cause of adult pneumococcal CAP and may reflect inadequate serotype specific vaccine effectiveness.

Abstract S105 Figure 1 Serotypes isolated in adult pneumococcal CAP

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Conclusion Serum neutrophils in bronchiectasis are primed and activated compared to healthy volunteers. The pro-resolving mediator LXA4 stabilised the neutrophil whilst promoting neutrophil phagocytosis.

Pulmonary Hypertension

GENOTYPE-PHENOTYPE ASSOCIATIONS IN PULMONARY ARTERIAL HYPERTENSION CAUSED BY BMPR2 AND EIF2AK4 VARIANTS

Introduction Idiopathic pulmonary arterial hypertension (IPAH) is a rare and incurable disease. Causal mutations in BMPR2 are found in 17% of patients. Pulmonary veno-occlusive disease (PVOD) and pulmonary capillary haemangiomatosis (PCH) are rarer forms of pulmonary hypertension and have a worse prognosis. Biallelic mutations in EIF2AK4 have been described in PVOD and PCH. We hypothesised that mutations in these genes are associated with specific phenotypes or endotypes.

Methods Whole genome sequencing was performed on genomic DNA from PAH patients recruited to the NIHR BRIDGE Study (n = 679). Rare (absent from BRIDGE control cohorts [n = 5906] and minor allele frequency < 0.0001 in the ExAC database [http://exac.broadinstitute.org]) and predicted deleterious (CADD score >15 and Polyphen not benign) variants were selected for association testing with phenotypic and metabolomic data. Plasma samples from 288 patients were sent to Metabolon (USA) for a high-throughput metabolomic screen.

Results Mutations in BMPR2 (82 single nucleotide variants and 13 deletions) were identified in 14% of PAH patients. Unexpectedly, 22 rare and predicted deleterious EIF2AK4 variants were found in 17 patients with IPAH. Biallelic EIF2AK4 variants were found in 1% of patients (5 homozygous variant carriers and 4 potential compound heterozygotes). Additionally, there were 8