Results Fifty-three patients were referred for LAT with an average age of 73 years. Twenty-two (42%) patients had either talc poudrage and IPC insertion (59%) or IPC alone (41%). Where patients survived until IPC removal (N=15), overall median time to IPC removal was 60 days. There was no difference in pleurodesis rate between IPC+talc and IPC alone (p=0.45). NEL was found in 26% LAT patients. Patients with NEL had a longer time to pleurodesis than those with expand-sile lung.

Discussion This small retrospective study surprisingly found no difference in pleurodesis rate between IPC alone and talc poudrage plus IPC. Expandable lung appears to be a better predictor of pleurodesis than use of talc. Limitations are small sample size and retrospective nature and thus further work needed.

REFERENCES

Introduction Eosinophilic Lung Diseases (ELDs), including Chronic Eosinophilic Pneumonia (CEP), Eosinophilic Granulomatosis with Polyangiitis (EGPA) and Allergic Bronchopulmonary Aspergillosis (ABPA) are uncommon conditions linked to asthma. Fungi are implicated in ABPA but the aetiology of other ELDs is unknown. No studies have yet described the fungal communities in CEP or EGPA.

Objectives To determine the fungal biomass and characterise the fungal communities in the upper and lower airways of ELD patients.

Methods Bronchoscopic evaluation of the Eosinophilic Airway Microbiome (BEAM) was a cross-sectional observational study. Subjects undertook questionnaires, blood tests and spirometry. Each provided an oropharyngeal throat-swab (OTS) and endo-branchial brushings. Samples underwent DNA extraction, 18S quantitative PCR and massively-parallel next-generation ITS2 sequencing. Data were pre-processed in Quantitative Insights Into Microbial Ecology (QIIME) 2 and analysed in R. Samples were rarefied; Those with <1,000 reads were excluded from downstream analyses.

Results Twenty-one subjects were recruited: 11 ELD patients (7 CEP, 3 EGPA, 1 ABPA) and 10 healthy controls. The mean (SD) age was 50.6 yrs (9.8) in cases and 51 (9.4) in controls. All cases (no controls) were using inhaled corticosteroids (ICS). The blood eosinophil count was 0.39x10^9/L (0.4) in cases and 0.08x10^9/L (0.1) in controls. Fungal biomass was significantly higher in OTS than brushes: OTS mean 20,675 18S copies/sample vs brushes 4,950 copies/sample (P=0.036). Fungal biomass did not correlate with blood eosinophil count or FEV1. Twelve OTS and 7 brushes had >1,000 reads. Data analysis revealed fungal diversity was low in all samples with each being dominated by a single genus. The most common genera in OTS were Candida, Aureobasidium and Cladosporium, and in brushes Candida and Papiliotrema. Brushings from all three EGPA subjects were dominated by Papiliotrema.

Conclusions Differences were observed between the dominant organisms in healthy controls (usually Aureobasidium), and ELDs (Candida-dominance of the upper and lower airways, Cladosporium [upper airways] and/or Papiliotrema [lower airways]). Such differences may be influenced by ICS use. The results of this study suggest mechanistic studies of potential immune-modulatory actions of fungi in ELDs are warranted to determine whether fungal dysbiosis is a trigger for and/or perpetuator of disease.

Background Allergic bronchopulmonary aspergillosis (ABPA) is a severe hypersensitivity reaction to Aspergillus species colonising the airways of asthmatic patients and may be a cause for deterioration. There is increasing evidence that monoclonal antibody therapy used to treat severe allergic asthma can be beneficial in treating patients with ABPA in steroid or antifungal dependant refractory disease with several phase 3 clinical trials in progress.

Aim To assess the real-world effectiveness of biological therapies targeting atopic inflammation in ABPA.

Methods Retrospective single-centre analysis of patients with ABPA as defined by the ISHAM criteria and use of any monoclonal therapy between 2014–2022. Clinical outcome was assessed at 12 months post commencement including validated symptom questionnaires, exacerbation frequency, corticosteroid use and clinical multidisciplinary team (MDT) consensus. Baseline characteristics were used to determine ABPA phenotype and impact on monoclonal antibody efficacy.

Results 74 patients with ABPA received monoclonal antibody therapy during the study period. Mean age was 56.3 years with 50% female. 32% received anti-immunoglobulin E (anti-IgE) therapy, 65% anti-Interleukin-5 (anti-IL5) therapy and 3% anti-interleukin 4-R alpha (anti IL4-Ra) therapy. Overall n=48 (65%) of patients were deemed by clinical MDT review at 12 months to have had a successful response with ≥ 50% reduction in oral corticosteroid (OCS) use. 26 (35%) stopped or changed biologic during the follow-up period due to either side effects (n= 3), failed clinical response (n=21) or other medical co-morbidities that required cessation (n=2). There was a significant reduction in ACQ-6 score, exacerbation frequency and maintenance OCS use following monoclonal antibody initiation as shown in table 1. Multivariate analysis will be further presented to analyse how ABPA endotyping, based
on radiology and microbiological fungal burden, affects efficacy of monoclonal antibody therapy.

**Conclusion** This retrospective study highlights the potential effectiveness of monoclonal antibody therapy in some individuals with ABPA with a significant reduction in exacerbation frequency, symptoms and OCS use following monoclonal antibody therapy highlighting the importance of ongoing phase 3 clinical trials. Given a significant proportion of patients had no clinical response, further research is required to understand how ABPA endotypes can affect monoclonal antibody response.

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**Abstract S143 Table 1**

<table>
<thead>
<tr>
<th>Monoclonal Antibody</th>
<th>ACQ-6 Pre Therapy</th>
<th>ACQ-6 Post Therapy</th>
<th>P Value (95% CI)</th>
<th>Exacerbation/12 months Pre Therapy</th>
<th>Exacerbation Rate/12 months Post Therapy</th>
<th>P Value (95% CI)</th>
<th>Maintenance Prednisolone Use (mg) Pre Therapy</th>
<th>Maintenance Prednisolone Use (mg) Post Therapy</th>
<th>P Value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Monoclonal</td>
<td>3.0 (1.49)</td>
<td>1.69 (1.81)</td>
<td>&lt;0.0001 (-0.81, -1.40)</td>
<td>4.0 (4.0)</td>
<td>1.0 (1.0)</td>
<td>&lt;0.0001 (-1.74, -3.09)</td>
<td>5.0 (10.0)</td>
<td>3.0 (5.0)</td>
<td>0.0173 (-0.26, -3.6)</td>
</tr>
<tr>
<td>Antibodies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-IgE</td>
<td>2.7 (1.14)</td>
<td>1.0 (2.2)</td>
<td>0.0004 (-0.55, -1.64)</td>
<td>2.0 (3.0)</td>
<td>1.0 (2.0)</td>
<td>ns</td>
<td>5.0 (6.25)</td>
<td>3.0 (5.5)</td>
<td>0.0662 (0.12, -5.07)</td>
</tr>
<tr>
<td>All Anti-IL5s</td>
<td>3.29 (1.57)</td>
<td>1.83 (1.5)</td>
<td>-0.0080 (-0.49, -1.43)</td>
<td>4.0 (1.0)</td>
<td>1.0 (3.25)</td>
<td>&lt;0.0001 (-3.03, -3.71)</td>
<td>5.0 (10.0)</td>
<td>2.5 (5.0)</td>
<td>0.1641 (0.31, -2.78)</td>
</tr>
<tr>
<td>Bensalizumab</td>
<td>2.59 (0.96)</td>
<td>1.99 (2.44)</td>
<td>0.1060 (0.28, -1.54)</td>
<td>5.0 (2.0)</td>
<td>2.0 (4.0)</td>
<td>0.0156 (-0.81, -5.18)</td>
<td>0.0 (25.0)</td>
<td>0.0 (25.0)</td>
<td>0.9999 (2.67, -2.13)</td>
</tr>
<tr>
<td>Mepolizumab</td>
<td>3.5 (1.89)</td>
<td>1.77 (0.41)</td>
<td>-0.0001 (-0.7, -1.66)</td>
<td>4.0 (2.75)</td>
<td>1.0 (2.5)</td>
<td>&lt;0.0001 (-1.48, -3.13)</td>
<td>5.0 (10.0)</td>
<td>0.0 (5.0)</td>
<td>0.2714 (0.55, -2.90)</td>
</tr>
</tbody>
</table>

Data presented as median (interquartile range) and P value (95% confidence interval)

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**Question:** How does the ubiquitous environmental mould, *Aspergillus fumigatus*, impact bronchial epithelial cells (BECs) during injury? This study aimed to assess an in vitro model of host-pathogen interaction with the underlying hypothesis that *A.f.* infection disrupts lung epithelial repair in disease.

**Background** *A.f.* causes a broad spectrum of life-threatening invasive and allergic respiratory diseases in over 18 million individuals worldwide. The impact of *A.f.* infection during co-morbid acute and chronic respiratory diseases has been identified but the underlying mechanistic basis of this is unclear.

**Methodology** To mimic lung barrier damage, we employed a scratch assay on CM-DiI labelled 16HBE14o- cell (BEC) monolayers on 0.4 μm pore transwells cultured in MEM containing 10% FBS. Scratch closure in the presence and absence of transgenic GFP+ *A. fumigatus* was measured using timelapse fluorescence microscopy. Epithelial migration velocity was calculated using non-linear regression with the Levenberg-Marquardt algorithm. To determine epithelial uptake of spores, BEC were isolated at different time points of the culture and spore uptake was measured via flow cytometry.

**Results** While we found wound closure occurred within 12–18 hours (mean maximum closure 97.2%), this was prevented in the presence of live *A.f.* spores (MOI 10:1, mean maximum closure 54.9%). Spore inhibition of wound closure was associated with presence of mycelium growth. Furthermore, addition of spores to BEC cultures 24h prior to scratch wounding dramatically inhibited wound closure (mean maximum closure 3.9%). Despite this, epithelial velocity during wound repair was higher (mean 0.50–0.66 μm/h). Finally, flow cytometry analysis showed that spores were not internalised by epithelial cells (uptake 0.50–0.66 μm/h).

**Conclusions** BEC wound repair accelerates and then fails during *A.f.* infection in a dose-dependent manner. Further research should explore the reproducibility of these preliminary findings and the mechanisms underlying wound repair failure. Potential candidates include *A.f.* secreted factors as mediators of altered BEC cytoskeletal function and epithelial migration.

Please refer to page A288 for declarations of interest related to this abstract.

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**Abstract S145**

**THE FUNGAL BURDEN IN NONTUBERCULOUS MYCOBACTERIAL PULMONARY DISEASE**

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**Introduction and Objectives** Fungal lung infections may complicate the clinical trajectories of individuals with nontuberculous mycobacterial pulmonary disease (NTM-PD). It remains unclear whether NTM infection or therapies predispose to fungal disease. We hypothesised that there are differences in pulmonary fungal burden in NTM-PD according to NTM species, NTM treatment use and underlying structural lung diseases. We aimed to quantify this longitudinally in people with NTM-PD.