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PSEUDOMONAS AERUGINOSA IMPAIRS GROWTH OF ASPERGILLUS FROM CF AIRWAY SAMPLES

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10.1136/thorax-2020-BTSabstracts.275

Objectives Fungal infection is associated with poor lung health in CF but may go undetected. The low sensitivity of standard fungal culture is well recognised but poorly understood. *Pseudomonas aeruginosa* (Pa) has been shown to inhibit growth of *Aspergillus* (Asp) *in vitro*. We hypothesised that similar inhibitory mechanisms may, in part, account for the poor sensitivity of Asp cultures.

Methods We retrospectively studied sputum/BAL standard culture results from all CF patients in our centre between 2012–2017. 16,736 positive airway samples were identified from 1001 subjects. Correlation analysis identified relationships between pairs of relevant CF-pathogens. As part of a previous study, 318 sputum samples had Internal transcribed spacer-2 (ITS2) fungal sequencing data. Samples with <1000 reads were excluded; >1% of total reads aligned to the genus of interest were considered positive. Contingency tables examined fungal culture performance compared with ITS2 sequencing with co-infecting bacteria, using relative risk (RR, [95% CI]) and Fisher's exact test.

Results We observed a strong bias towards single rather than dual growths in patients who had isolated Pa and Asp over the study period. This was not observed with other bacterial/fungal combinations. In the 48% (149/311) of samples Asp positive by ITS2 sequencing, only 19% (28/149) were positive on culture. 39% of the culture results were considered to be false negative for Asp (fn-Asp). Fn-Asp cultures were more likely in Pa-infected than Pa-free samples (RR 1.6 [1.1–2.4], p=0.01). This effect was only seen when non-mucoid (nm)-Pa was present and not when mucoid (m)-Pa was present alone (nmPa (RR 1.90 [1.2–3.0], p=0.006); mn+mPa (RR 1.91 [1.3–2.9], p=0.002), mPa (RR 1.22 [0.8–1.9], ns). The Asp-fn risk was not increased by co-infection with other bacteria. Furthermore, Pa did not impact on fn-culture of *Candida* or non-aspergillus filamentous fungi.

Conclusions In patients who have serial cultures demonstrating both Pa and Asp infections, dual positive cultures are uncommon. Molecular analysis demonstrated a significantly increased false negative Asp culture in the presence of Pa, particularly in it's non-mucoid form. These data suggest that Pa can inhibit Asp growth *in vivo* and/or during culture of sputum and presents an important area for future research.

The nuts and bolts of ILD clinical management

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HOME SPIROMETRY AS A CLINICAL ENDPOINT IN FIBROTIC ILD: LESSONS FROM THE INJUSTIS INTERIM ANALYSIS

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10.1136/thorax-2020-BTSabstracts.276

Home handheld spirometry enables repeated measurements of forced vital capacity (FVC), offering opportunities for longitudinal evaluation in interstitial lung disease (ILD). Whilst recent studies have not blinded participants to their home spirometry performance, they support feasibility in participants with idiopathic pulmonary fibrosis (IPF). However little data exists for the utility of home spirometry in non-IPF ILD. We assess correlation, agreement and non-inferiority of blinded daily home spirometry over three months relative to hospital spirometry, informing the feasibility of remote monitoring as a primary endpoint in clinical settings.

We utilised interim data from the ongoing INJUSTIS study (NCT03670576). Participants with fibrotic ILD were offered a handheld spirometer linked via bluetooth to a smartphone application and asked to perform daily, blinded FVC for three months. Hospital spirometry was concurrently obtained at baseline and three months. Home FVC values were based on week averages at study timepoints. Correlation, Bland-Altman plots and equivalence tests were used to compare baseline, 3 month and delta. Sensitivity analysis was performed where test dates matched.

82 participants with ILD were included. Mean age was 69.8 ± 8 years, 72.3% were male and mean FVC was 2.96 ± 0.88 L. Median adherence to daily spirometry was 79.5%, four participants had an adherence <10%. At the time of

| FVC sample | | Comparison | | | Agreement | | | Correlation | | Non-inferiority | |
|------------------|----|------------------|-------------------|-------------------|---------------------|--------------------|---------|-------------|---------|------------------|-----------------------|
| | N | Mean Lab (SD) | Mean Home (SD) | Mean diff (SD) | N Outside limits | % Within limits | r | R2 | р | 95%CI | Non-inferiority |
| Baseline | 82 | 2.96 (0.88) | 2.65 (0.88) | -0.31 (0.46) | 8 | 90.2 | 0.8644 | 0.7472 | <0.0001 | -0.39; - 0.22 | True within 400 |
| Date- matched | 45 | 2.93 (0.93) | 2.70 (0.94) | -0.23 (0.44) | 2 | 95.7 | 0.8897 | 0.7916 | <0.0001 | -0.34; - 0.12 | True within 400 ml |
| 3 months | 35 | 2.88 (0.96) | 2.77 (1.11) | -0.13 (0.61) | 2 | 94.3 | 0.8131 | 0.6611 | <0.0001 | -0.33; 0.07 | True within 400 ml |
| 3 m ∆ | 35 | -0.05 (0.19) | -0.01 (0.54) | 0.03 (0.58) | 3 | 91.4 | -0.0884 | 0.0078 | 0.614 | -0.16; 0.23 | True within 400 ml |

censorship, 35 participants had 3 month data for both home and hospital spirometry, 45 participants had date-matched values. High correlation was observed between home and hospital spirometry at baseline (r=0.86) and three-months (r=0.81), changes in 3 month ΔFVC were not correlated (r=-0.09). At least 90% of home spirometry values were within agreement limits of hospital values at baseline (mean difference -0.31L/min,95%CI -0.39;-0.22), three-months (-0.13L/min,95%CI -0.31;0.05) and 3 month ΔFVC (-0.03L/min,95%CI -0.13;0.20). Home values more frequently underestimated hospital values but non-inferiority was confirmed within 400 ml.

Home spirometry in fibrotic ILD is feasible and non-inferior to hospital spirometry. This is particularly relevant in the context of the current covid-19 pandemic, where an urgent need has arisen to consider remote monitoring of lung function. Adherence to daily spirometry was high in blinded participants, but variability in home values was observed when using week-averages, supporting importance of longitudinal modelling for clinical endpoint precision.

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THE ROLE OF VITAMIN D IN PULMONARY SARCOIDOSIS AND INFLAMMATION

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10.1136/thorax-2020-BTSabstracts.277

Introduction and Objectives Sarcoidosis is a multisystem disease of unknown aetiology characterized by a Th1 granulomatous immune response. Granuloma formation has been linked to a failure of the innate immune system, which could be related to a deficiency in vitamin D. Previous studies have documented low levels of vitamin D in patients with sarcoidosis. We aimed to explore the role of vitamin D in sarcoidosis and its relationship to biomarkers of disease activity and severity.

Methods Baseline demography, mode of presentation, Scadding CXR stage and need for treatment was recorded for 184 patients. Additional data including biochemical markers of disease activity and serum vitamin D levels were performed in 66 patients within a 4-week study period. Disease activity was assessed using lymphocyte trend, inflammatory markers, LFT, serum ACE and IgG, physiological and radiological measures as well as the need for treatment. Vitamin D levels were grouped into 'sufficient' (>50 nmol/L) and 'insufficient or deficient' (<50 nmol/L). Univariate analysis was performed on all data collected.

Results Baseline data was similar between the study group and cohort. In this cohort the average age was 57.6 with median length of disease of 4.8 years (2.1–8.0), the treatment rate was 48%. The majority of patients were sufficient in Vitamin D (64%) at time of testing. A positive association between the need for treatment and previously recognised indicators; including lymphocyte trend, higher CXR staging, and mode of presentation was found. Preliminary analysis suggested an inverse correlation between vitamin D and levels of systemic inflammation -CRP (OR 3.61 p-value 0.01) and ESR (OR 9.59 p-value <0.005). Interestingly lower levels of Vitamin D trended towards a lower treatment need. There was no relationship between levels of vitamin D and CXR stage or lymphocyte trend.

Conclusions The majority of patients were sufficient in Vitamin D. Levels correlated inversely with markers of inflammation but did not appear to be associated with need for

treatment or disease severity. This data suggests a link between Vitamin D and systemic inflammation in sarcoidosis and warrants further investigation. Given deficiency may also mimic many symptoms encountered in active sarcoid measurement is useful in robust assessment.

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INTEGRATING AMBULATORY OXYGEN ASSESSMENTS INTO A SPECIALIST INTERSTITIAL LUNG DISEASE (ILD) CLINIC

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10.1136/thorax-2020-BTSabstracts.278

Introduction Ambulatory oxygen (AO) increases walking distance, reduces exertional breathlessness and has been shown to improve quality of life in patients with exertional desaturation. Patients with ILD often have a high burden of hospital appointments. In response to patient feedback we trialled colocating AO assessment alongside the specialist ILD clinic rather than at separate AO assessment.

Method Patient experience and service data was collected prospectively for all patients referred for AO assessment over a 6 month period. All patients with ILD were offered AO assessment alongside their appointment in ILD clinic.

Results There were 26 ILD referrals during pilot, 11 in the same time period of the previous year. Other Respiratory disease referrals 40 in pilot, 17 in previous yr. Males 40 in pilot, 12 previous yr. Mean age was 67.8 yrs pilot (range 39–86) and 62.1 yrs (range 33–82) previous yr.

All patients with ILD elected for appointments alongside their specialist ILD appointment. Non-attendance rate in ILD AO clinic was 4% compared to 36% in general AO clinic. Average wait for ILD AO clinic was one week compared to 12 weeks in general AO clinic.

There was no difference in reported patient experience between ILD AO and general AO clinics. 100% (n = 43) of patients would recommend the service. 98% of patients felt involved in decisions about their oxygen prescription and 93% reported feeling better able to manage their condition. Patient and staff feedback favoured AO intgegration into ILD clinic figure 1.

Conclusion Integrating AO assessments into specialist ILD clinics significantly reduced non-attendance rate and waiting times; these efficiencies have enabled us to meet increased



Abstract P133 Figure 1

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