PAI-1 IS THE PREDOMINANT BIOLOGICAL FACTOR ASSOCIATED WITH SEPTATION FORMATION IN PLEURAL INFECTION

1,2,3EO Bedawi, 1,N Kanellakis, 4,5Y Zhao, 1,A Sundaralingam, 1,D Addala, 1,6M Ellayeh, 1,R Halilックス, 6JP Corcoran, 1,2AM Condiffe, 1,2,4NM Rahman. 1Oxford Pleural Unit, Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Foundation Trust, Oxford, UK; 2NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK; 3Department of Infection, Immunity and Cardiovascular Disease, University of Sheffield, Sheffield, UK; 4Laboratory of Pleural and Lung Cancer Translational Research, Nuffield Department of Medicine, University of Oxford, Oxford, UK; 5Chinese Academy of Medical Sciences, China Oxford Institute, Nuffield Department of Medicine, University of Oxford, Oxford, UK; 6Department of Chest Medicine, Mansoura University, Mansoura, Egypt; 7Interventional Pulmonology Service, University Hospitals Plymouth NHS Trust, Plymouth, UK

Introduction Plasminogen Activator Inhibitor-1 (PAI-1) plays an essential role in the pathogenesis of lung and pleural injury. PAI-1 levels in pleural infection have been shown to be significantly elevated compared to malignant pleural effusions and heart failure. A significant variation was seen in levels of PAI-1 protein and activity in the pleural fluid from participants with pleural infection recruited to the MIST-2 study. Rabbit models of pleural injury have demonstrated that, along with other pro-inflammatory cytokines, PAI-1 is an important contributor to impaired fibrin cleavage and subsequent pleural loculation. To date, this has not been studied in the context of prospectively collected pleural fluid samples from patients with confirmed pleural infection and documented baseline ultrasound septation status.

Methods Pleural fluid samples (n=214) prospectively collected from patients recruited to the Pleural Infection Longitudinal OuTcomes study (PILOT) were analysed. Protein measurement assays were performed using a commercial Luminex assay for Serpin E1/PAI-1 (Luminex high performance assay, R&D) and analytic of interest in addition to TNF-alpha, MCP-1/CCL-2, IFN-gamma, urokinase plasminogen activator (uPA) and D-dimer. The independent samples T-test was used to compare mean values for each protein between two groups (septated vs non-septated). A multirnogression model was performed to assess the independent predictive ability for each protein to septation status as an outcome.

Results Complete ultrasound data was available for 166 cases, and these were used in the final analysis. There was a significant difference in the PAI-1 levels between the septated group (n=122; mean=1790.59 ng/mL, SD=2027.28) and non-septated group (n=44; mean=948.82ng/mL, SD=911.41); t(166)=2.65, p=0.009 (Normal ref 2–46 ng/mL). In the multirnogression model, PAI-1 was the only significant independent predictor of septation status (β=0.000, p=0.003).

Conclusion These data confirm that whilst several biological factors may contribute to impaired fibrinolysis and subsequent septation formation in pleural infection, PAI-1 appears to be the most important. These data imply that PAI-1 is likely to be the most useful target for further studies involving intra-pleural fibrinolytic therapy in pleural infection. Further work assessing the effect of baseline PAI-1 levels on clinical outcomes in this dataset is ongoing.