



Abstract P66 Figure 1

**Conclusion** Our data suggests that inhibition of HDAC activity by CBHA may attenuate TGF- $\beta$ 1-induced PAI-1 expression in human pleural mesothelial cells through modulation of cellular signaling at multiple levels. HDAC inhibitors may be employed as potential therapeutic agents for pleural fibrosis.

#### P67 OUTCOMES FROM SURGICAL MANAGEMENT OF PLEURAL INFECTION: 12-YEAR EXPERIENCE FROM A TERTIARY CARDIOTHORACIC CENTRE

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**Introduction and Objectives** Thoracic empyema affects >65 000 patients/year in the US and UK. Up to 50% require surgical drainage, and 15% die. We describe clinical features, microbiology, risk factors and surgical outcomes from referrals to a regional specialist cardiothoracic centre over 12 year.

**Methods** Patients were identified by searching the hospital Clinical Data Repository for a diagnosis of 'pyothorax' from 1999 to 2010. A retrospective observational study was conducted using case note and database review.

**Results** 406 distinct empyemas were identified. Patients were predominantly male (n=301, 74.1%), with median age of 53 years (IQR=37–69). Pyothorax predominantly developed secondary to community-acquired pneumonia, although 51 (12.6%) were hospital-acquired; 70 (17.2%) were receiving steroids or immunosuppressants, 35 (8.6%) had concurrent malignancy, 33 (8.1%) were diabetic and 14 (3.4%) patients were HIV-infected. Empyemas were right-sided in 233 (57.3%, p=0.03); four were bilateral. A causative organism was identified in 229 (56.4%) patients. Positive cultures were obtained from sputum in 59 (14.5%), pleural fluid in 174 (42.9%) and blood in 61 (15.0%) patients. Organisms identified included *Streptococcus milleri* (n=18, 4.4%), *Streptococcus pneumoniae* (n=39, 9.6%), other streptococci (n=10, 2.5%), *Enterobacteriaceae* (n=12, 3.0%), anaerobes (n=32, 7.9%), methicillin-sensitive *Staphylococcus aureus* (n=36, 8.9%), methicillin-resistant *Staphylococcus aureus* (n=25, 6.2%), *Enterococcus* (n=14, 3.4%), *Mycobacterium tuberculosis* (n=36, 8.9%), non-tuberculous mycobacteria (n=1, 0.2%), other bacteria (n=25, 6.2%), and fungi (n=9, 2.2%); 34 (8.4%) cultures were polymicrobial. 277 (68.2%) patients were managed by open thoracotomy. 116 (28.6%) underwent video-assisted thoracoscopic surgery (VATS), of whom 17 (14.7%) were converted to open. Three (0.7%) required a Clagett window; 10 (2.5%) were managed with tube thoracostomy alone. A significant trend towards increased use of VATS over time was noted (p=0.0002). All-cause complication rate was 20.7%, and 28-day mortality was 5.7%. Low preoperative haemoglobin was predictive of mortality (p=0.04), but admission and peak C-reactive protein were not.

**Conclusions** In this large series of empyemas from a tertiary referral centre, microbiological diagnosis was achieved in only half the patients. The identification of tuberculosis in 36 cases means routine screening for mycobacteria is necessary. Use of VATS has increased significantly, and mortality was lower than previously reported and associated with preoperative anaemia.

**Contributors** DJBM and MF contributed equally to this work.

#### P68 SURGERY FOR MESOTHELIOMA: THE CASE FOR MACROSCOPIC COMPLETE RESECTION

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**Objective** The role for radical surgery for Malignant Pleural Mesothelioma (MPM) remains controversial. There are advocates of less radical 'debulking surgery' who argue against the need for removal of diaphragm and pericardium because of increased morbidity. We test the hypothesis that survival is increased by the more radical operations intended to remove all visible tumour and achieve macroscopic complete resection (MCR).

**Methods** Over a 13-year period, 362 patients underwent therapeutic surgery for MPM: in-group MCR: 232 (64%) patients underwent either extra-pleural pneumonectomy (135 patients (37%)) or radical pleurectomy-decortication (97 patients (27%)) with resection of diaphragm and pericardium. Whilst in group D: 130 (36%) underwent debulking surgery leaving macroscopic tumour in situ (55 patients (15%) by thoracotomy and 75 patients (21%) by VATS). The patients in the MCR group were younger (mean age 57.9 vs 66.1, p<0.0001) and more had epithelioid subtype (167 (72%) vs 86 (66.2%), p<0.0001). We compared the hospital outcomes and overall survival between these two groups.

**Results** The mean length of stay was longer in group MCR than in group D (16.0 days vs 9.6 days, p<0.0001) but 30-day mortality was similar (12 (5.2%) vs 8 (6.2%), p=0.811). In univariate analysis, overall survival was significantly longer in the MCR group (mean survival 22 months vs 13 months, p<0.0001). A similar benefit was observed for the epithelioid pathological subgroup (mean survival 25.8 months vs 16.6 months, p<0.0001). Cox regression showed that surgery intended to achieve MCR was associated with a significantly reduced hazard of death after adjusting for age and pathological subtype (HR 0.72, 95% CI 0.55 to 0.93, p=0.014).

**Conclusions** Surgery to increase survival in mesothelioma should be based on an intent to achieve macroscopic complete resection. This strategy should form the basis of future trials to evaluate the role of surgery in this disease.

#### P69 MESOTHELIOMA IN THE 21ST CENTURY. A 1-YEAR SURVEY OF MALIGNANT MESOTHELIOMA IN THE SOUTH WEST OF THE UK

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**Introduction** Malignant mesothelioma (MM) is a cancer that most commonly arises within the pleura, and carries a poor prognosis. There is a strong association with past asbestos exposure so incidence varies across the UK. In the South West of the UK there is a high incidence with many cases being due to asbestos exposure in the ship-building industry.

**Aims** To describe the demographics, treatment strategies and survival of patients presenting with MM across the Peninsula cancer network, a population of around 1.7 million people, over a 1-year period.

**Method** Cases of MM diagnosed in 2007 were identified retrospectively and reviewed following interrogation of cancer, MDT,

pathology and post mortem databases for the five hospitals in the network. A full review of the clinical records was performed.

**Results** 81 patients were identified. Average age was 72 and 94% were male. 82.7% of patients had a performance status of 0 or 1 at presentation but 21% had a significant co-morbidity, most commonly cardiac in nature. 77.8% of patients had definite or probable asbestos exposure. At presentation symptoms had been present for a mean of 3.7 months, the commonest being breathlessness and chest pain. A definitive diagnosis was made in 84% of patients, either on histology (75%) or cytology (9%) and the epithelioid subtype was most common (40.7% of cases). VATS was the main diagnostic modality (61.7%). Despite 61.7% of patients technically being fit for chemotherapy, only 29.6% received it. Mean survival was 269 days (8.8 months). Survival was longer in those with a better performance status at presentation (PS0=344 days, PS1=270d, PS2=125d, PS3=89d), and in those who received chemotherapy (448d vs 269d).

**Conclusion** MM remains a common problem in the South West of the UK. Despite recent treatment advances the prognosis remains poor, with our survival data being similar to that described in earlier population based studies and in chemotherapy treatment trials. Only a small proportion of our patients received chemotherapy and this may reflect the lack of NICE guidance for use of pemetrexed which was only issued in 2008. However, those patients who received chemotherapy had a better survival time (14.7 months vs 8.8 month).

#### P70 TALC SLURRY PLEURODESIS: DOES MIXING TALC WITH 50% DEXTROSE RATHER THAN NORMAL SALINE INCREASE SUCCESS RATE?

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**Introduction** Symptomatic malignant pleural effusions can be managed effectively with talc pleurodesis. Various studies document the success rate for talc pleurodesis around 80%. In these studies, talc was mixed with normal saline to make the slurry prior to pleurodesis. We audited the success rate for pleurodesis in our hospital using slurry made by mixing talc with normal saline and slurry made by mixing talc with 50% dextrose to see if changing the 'solvent' made any difference to the success of the procedure. The hypothesis that 50% dextrose, being 'stickier' than normal saline, will achieve a better success rate was thus tested.

**Method** In group 1, 28 patients underwent pleurodesis using slurry obtained by mixing talc with normal saline. The findings were presented to BTS in 2008. Subsequently we re-audited our practice with group 2, in which 18 patients were pleurodesied using slurry obtained by mixing talc with 50% dextrose.

**Results** Procedure success was defined as absence of fluid reaccumulation requiring intervention at 3 months post pleurodesis. The success rate for the first group was 34% while the success rate for the second group was 76%. The second group underwent more rigorous protocol ensuring drain clamping for 1-h post procedure and use of suction in 100% compared to 80% and 87.5% in the first group. However, subgroup analysis of the first group did not reveal a statistically significant difference in success rate for these variables. Use of NSAID analgesia for 28% patients in group 1 compared to none in group 2 could have influenced the results significantly. Lastly, better patient selection and operator bias might have resulted in better success rate in the second group as recommendations from first audit were implemented in second cycle. Overall best success rate of 76% was inferior to that reported in previous studies due to more liberal patient selection.

**Conclusions** Use of 50% dextrose rather than normal saline to mix talc for talc slurry with strict patient selection and a rigorous

pleurodesis protocol as recommended by BTS guidelines can result in better success rate. This is possibly because of the resulting stickier inert slurry. However, research with a randomised control trial is required to assess this question further.

## Paediatric lung diseases

### P71 REDUCED AIRWAY BETA-DEFENSIN 2 LEVELS IN CHILDREN WITH CYSTIC FIBROSIS AND VITAMIN D-DEFICIENCY

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Vitamin D (vD) levels have been reported to correlate with (a) lung function in healthy populations and (b) disease severity in pulmonary TB, COPD and asthma. The proposed mechanism, supported by in vitro studies, relates to vD response elements in the promoter regions of genes encoding molecules involved in innate immunity such as defensins and cathelicidin (LL-37). As patients with CF are at risk of fat and fat-soluble vitamin malabsorption, we sought to explore this relationship in a cohort of CF children. Frozen serum and bronchoalveolar (BAL) fluid samples, which had been donated for research at the time of a clinically-indicated bronchoscopy were available from 49 children with CF. Mean age at the time of the procedure was 6.8 years (range 0.03–15.99). 44 (90%) were biochemically pancreatic insufficient and were prescribed pancreatic enzyme supplementation and fat-soluble multivitamins. Serum 25OH vD3 was measured using HPLC and mass spectrometry. BALF human beta defensin-2 (hbd2) and LL-37 were quantified using ELISA. vD deficiency was defined as <20 ng/ml based on internationally-accepted criteria. Deficient and sufficient groups were compared with Mann–Whitney tests and Spearman's correlations were performed. 16 (33%) children were vD-deficient (including two of the five pancreatic sufficient patients); they did not differ in age from the vD sufficient group. BALF hbd2 was significantly lower than in the vD sufficient group (median (range) 185.3 (7.8–615.7) pg/ml vs 385.5 (7.8–1002) pg/ml;  $p < 0.05$ ). In contrast, no relationship was observed between serum vD and BAL LL-37. As this molecule is known to be highly sensitive to proteolysis, we considered the possibility that degradation could be masking an effect of vD on LL-37 expression. However, no inverse relationship with neutrophil elastase or MMP-9 was found to support this hypothesis. Children with CF are at risk of low vD levels even if they are clinically pancreatic sufficient or if vitamin supplements are being prescribed. vD deficiency is associated with low levels of antimicrobial defence molecules within the airway. Whether this is a clinically important phenomenon leading to susceptibility to infection and increased inflammation will be the focus of future work.

### P72 FEASIBILITY OF RECRUITING NEWBORN BABIES WITH CYSTIC FIBROSIS DIAGNOSED BY NEWBORN SCREENING TO A CLINICAL STUDY WITH INVASIVE OUTCOME MEASURES

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**Background** Newborn screening (NBS) for cystic fibrosis (CF) has been available throughout the UK since 2007. Such screening is only