P159 THE IMPLICATIONS OF EMPHYSEMA ZONE FOR DIAGNOSIS OF ALPHA-1-ANTITRYPSIN DEFICIENCY

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Introduction: Patients with alpha-1-antitrypsin deficiency (AATD) classically exhibit lower zone predominant emphysema, unlike individuals with usual chronic obstructive pulmonary disease (COPD). However, phenotypic variation is recognised[1] and with the advent of specific treatment for AATD[2] it is more critical to identify deficient individuals. In the presence of atypical disease a diagnosis of AATD may not be considered.

Methods: All PiZZ subjects from the UK AATD registry with a quantitative chest computed tomography (CT) scan were studied (n = 369). Emphysema was quantified at −910 HU with slices representing the upper zone and lower zone, respectively. Subjects with a normal voxel index in either zone[3] were excluded. Emphysema zone was determined by the difference in voxel index between lower and upper zone slices (LZVI–UZVI). Subjects diagnosed due to lung disease (index cases) were compared with subjects diagnosed through family screening or for other reasons (non-index cases).

Results: Index cases were younger, had smoked more and had lower zone dominant emphysema (LZDE) in over 88% of cases (see table). Almost 30% of non-index subjects had a CT scan diagnostic of upper zone dominant emphysema (UZDE). Index status remained a significant predictor of emphysema zone after correction for age, smoking and gender ($p = 0.005$, $B = 4.90$), such that it accounted for 15% of variability in emphysema zone score, compared with 6.9% for smoke exposure.

Conclusions: There are several interpretations of these results. Non-index cases may be at an earlier disease stage, suggested by their age, and implying that upper zone disease occurs first, consistent with previous evidence.[4] Second, there may be ascertainment bias, such that subjects with UZDE are less likely to be tested for AATD. Third, UZDE may be a different disease entity, influenced by other genetic factors.[5] Testing for AATD should therefore be offered to all subjects with COPD to ensure optimum management.

1. **Needham,** Stockley. *Thorax* 2004;**59**:441–5.
2. **Dirksen,** *et al*. *AJRCCM* 2008;**177**:A419.
3. **Soejima,** *et al*. *AJRCCM* 2000;**161**:1264–73.
4. **Holme,** *et al*. *Thorax* 2007;**62**:A140.
5. **DeMeo,** *et al*. *AJRCCM* 2007;**176**:42–8.

Abstract P159 Table

	Index cases	Non-index cases	p Value
LZDE (%)	88.55	70.89	<0.001
LZVI–UZVI	15.52 (0.86)	8.71 (1.39)	<0.001
Age (years)	51.74 (0.63)	48.33 (1.11)	0.009
Gender (%male)	64.62	53.85	0.085
Pack years smoked	18.00 (7.50–25.50)	5.25 (0–18.25)	<0.001
FEV_1 (% predicted)	35.41 (1.20)	75.14 (4.13)	<0.001
KCO (% predicted)	63.74 (1.41)	81.15 (2.54)	<0.001

LZDE, lower zone dominant emphysema; LZVI–UZVI, lower and upper zone voxel index.

Clinical aspects of pleural disease

P160 ABSENCE OF *PNEUMOCYSTIS JIROVECII* IN PLEURAL INFECTION: A GENETIC AMPLIFICATION STUDY

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Introduction: Up to 26% of pleural infections have no pathogens identified using standard microbiological and genetic amplification techniques. Possible explanations for this phenomenon include previous use of antibiotics, microbiologically different pleural fluid locules, or difficulty isolating organisms using conventional techniques. *Pneumocystis jirovecii* (previously *carinii*) causes pneumonia in immunocompromised hosts. Previous studies have demonstrated an asymptomatic carrier state in immunocompetent individuals—*P jirovecii* DNA was detected in the bronchoalveolar lavage fluid of 18% of patients with lung disease, 4.4% with bacterial pneumonia (both without HIV) and in the oropharynx of 20% of healthy individuals. We hypothesised that *P jirovecii* may account for some microbiologically obscure pleural infections and that co-infection with *P jirovecii* and bacteria may occur in pleural infection. The aim of this study was to assess the prevalence of *P jirovecii* in pleural infection, using highly sensitive and specific genetic detection techniques.

Methods: Pleural fluid was obtained from participants in the MIST1 trial (a double-blind, placebo-controlled trial of intrapleural streptokinase in pleural infection). Criteria for pleural infection were purulence, culture positivity, Gram staining positivity, or pH below 7.2, with clinical evidence of infection. Samples from 100 patients (randomly selected from 454 patients recruited) were analysed using highly sensitive real-time PCR targeting part of the *P jirovecii* heat shock 70 (HSP70) gene sequence. Potential inhibition of *P jirovecii* HSP70 PCR was assessed by the use of the SPUD assay.

Results: There was no evidence of *P jirovecii* DNA in any sample. Samples with possible inhibition of PCR were diluted and retested; these samples remained negative for *P jirovecii* DNA despite recovery of the SPUD amplicon.

Conclusions: Having given consideration to the possible inhibition of PCR, there was no evidence of *P jirovecii* DNA in any sample using the highly sensitive real-time HSP70 PCR technique. Therefore, *P jirovecii* is neither a common pathogen nor co-pathogen in those with pleural infection, an important negative finding given its prevalence as a co-pathogen in pneumonia. There is no need to investigate for *P jirovecii*, nor for its blind treatment, in pleural infection unless a patient is severely immunocompromised.

P161 PLEURAL EFFUSION IN PRIMARY LUNG CANCER: PREVALENCE AND RISK FACTORS

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Introduction: In patients presenting with lung cancer, pleural involvement has significant implications on disease staging, prognosis and treatment. Computerised tomography (CT) is significantly more sensitive than plain radiographs in identifying pleural effusions but the prevalence of pleural effusion detected by CT in patients presenting with lung cancer is unknown.

Aims: To determine the prevalence of pleural effusion on CT in patients presenting with lung cancer and during the subsequent disease course. To identify factors associated with the presence of pleural effusions.

Method: Retrospective review of 200 consecutive patients presenting to two UK hospitals.

Results: Pleural effusions were common. CT scan was more sensitive for detecting pleural effusions than chest *x* ray (CXR), detecting an effusion in 50 (25%) versus 27 patients (13.5%), respectively ($p<0.001$, McNemar test). 16 (32%) were cytologically confirmed to be malignant. A further 11 (5.5%) patients developed an effusion as their disease progressed, giving an overall prevalence of 30.5%. Patients with small-cell lung cancer (SCLC) were more likely (relative risk 1.8, $p = 0.026$) to develop an effusion. Age, gender, and location of the tumours were not predictive of the presence of pleural effusions (see table). All patients with SCLC and a pleural effusion had extensive disease.

Abstract P161 Table Summary of patient variables and associated risk of effusion

Variable	No of patients	No with effusion at diagnosis (%)	Relative risk	p Value
All patients	200	50 (25)		
Gender				
Male	124	28 (23)	0.9	NS
Female	76	22 (29)	1.2	NS
Age (years)				
<60	28	7 (25)	1.0	NS
60–69	73	19 (27)	1.0	NS
70–79	64	15 (22)	0.9	NS
>79	35	9 (26)	1.0	NS
Histology				
Small cell	25	11 (44)	1.8	0.026
Non-small cell	140	31 (22)	0.9	NS
Undifferentiated	54	11 (20)	0.8	NS
Squamous	45	7 (16)	0.6	NS
Adenocarcinoma	38	13 (34)	1.4	NS
Bronchoalveolar	2	0 (0)	0	NS
Carcinoid	1	0 (0)	0	NS
No histology	35	8 (23)	0.9	NS
Side of primary				
Left	83	20 (24)	1.0	NS
Right	111	28 (25)	1.0	NS
Lobe				
Upper	115	25 (22)	0.8	NS
Middle	5	0 (0)	–	NS
Lower	49	16 (33)	1.3	NS

Conclusion: Pleural effusions are common in lung cancer and usually present at diagnosis. CT is a more sensitive test for their presence than CXR, with a detection rate of 25% at diagnosis. Investigations to establish whether effusions are malignant or paramalignant in origin are undertaken infrequently.

P162 DO NON-STEROIDAL ANTI-INFLAMMATORY DRUGS DECREASE SUCCESS OF TALC PLEURODESIS?

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Introduction: Talc slurry pleurodesis has a reported success rate of over 80%. Our impression was that in clinical practice we were not achieving this. We audited our recent pleurodeses to see if this was the case and what factors may have influenced the success of the procedure.
Methods: Between January 2005 and June 2007 we identified 28 patients who underwent a total of 40 pleurodeses. We audited our practice against BTS guidelines and looked at what factors may have influenced outcome. Success was defined as the absence of significant reaccumulation of fluid within the first 3 months post-pleurodesis, excluding patients who did not survive one month.
Results: The median time to reaccumulation was 27 days (mean 74.9, range 2–600) and to death 65 days (mean 136, range 1–780). Nine patients died within 1 month, two were lost to follow-up. Of those who survived a month, the 3-month success rate was 10 of 29 (34%). The site of the primary, the grade of the requestor, the number of previous pleurodeses attempted and the chest *x* ray appearances prior to pleurodesis had no significant association with success rates. Drainage rate <150 ml/day pre-pleurodesis and suction post-pleurodesis did not affect success rates. One of nine patients who were on steroids were successful compared with nine of 20 who were not on steroids ($p = 0.107$ by Fisher's exact test). None of the eight patients on non-steroidal anti-inflammatory drugs (NSAID) were successful compared with 10 of 21 patients who were not on NSAID ($p = 0.0265$ by Fisher's exact test).
Discussion: The high early death rate and the low success rate suggest we are pleurodesing patients with more advanced disease than those in previous studies. Better identification of those in the terminal phase of their illness is required. Despite the small sample size, NSAID were significantly associated with pleurodesis failure and there was a non-significant trend against steroid use. This may be due to confounding factors as patients on these drugs are likely to have had more advanced disease. However, animal studies have demonstrated similar findings. Consideration should be given to using alternative analgesia during pleurodesis.

P163 SPECIALIST CLINIC IMPROVES DIAGNOSIS AND REDUCES LENGTH OF STAY IN EXUDATIVE PLEURAL EFFUSIONS

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Introduction: Exudative pleural effusions (EPE) are common and are associated with sinister pathology. Timely, thorough investigation into underlying aetiology is therefore essential. Current British Thoracic Society (BTS) guidelines include a diagnostic algorithm for the investigation of unilateral effusions. A retrospective audit of the management of EPE in a large district general hospital against BTS guidelines revealed deficiencies in the diagnostic pathway, resulting in low diagnostic rates compared with published data. We subsequently established a specialist pleural effusion clinic (SPEC) and prospectively audited the management of EPE in the clinic's first year. We report on comparative data from the two audits.
Methods: The retrospective cohort consisted of cases identified from clinical coding over an 18-month period. Their clinical records were reviewed and data from 100 patients with confirmed or likely EPE were analysed. 75 new patients were seen in the SPEC in the first year. Patients were referred from general practice (n = 25), general medicine (n = 17) and other specialties including oncology (n = 8). 25 of those seen had a diagnosis at referral and were therefore excluded. Data on the SPEC cohort was collected prospectively.
Results: The mean age of the retrospective cohort and the SPEC cohort was 68 years and 65.8 years, respectively. 50% (50/100) of the retrospective cohort had chest physician input compared with all of those in the SPEC cohort. 26/100 (50%) of the retrospective cohort had all recommended investigations on the first pleural tap. This is compared with a rate of 30/50 (60%) in the SPEC cohort (100% when first tap was in SPEC). An underlying diagnosis was confirmed in 26/100 of the retrospective cohort compared with 44/50 (88%) of those seen in SPEC. The pleurodesis rate in appropriate patients was 3/7 in the retrospective cohort and 7/7 in the SPEC cohort. Median length of inpatient stay was 12 days (range 1–55) in the retrospective cohort and 1 day (range 0–272) in the SPEC cohort.
Conclusions: In a district general hospital setting we have improved adherence to BTS recommendations using a SPEC. We achieved a higher diagnostic rate and decreased the inpatient bed day requirement.

P164 USE OF PORTABLE ULTRASOUND FOR PLACEMENT OF CHEST DRAINS FOR PLEURAL EFFUSION: A SNAPSHOT SURVEY OF JUNIOR DOCTORS ACROSS THE THAMES TRAINING REGION

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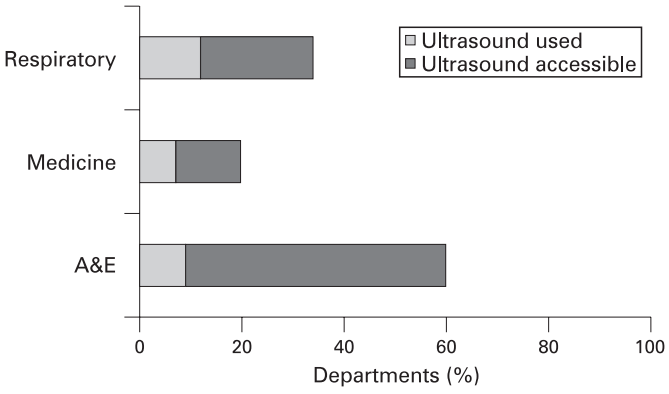
In May 2008, the National Patient Safety Agency strongly advised the use of ultrasound when inserting a chest drain for fluid. Increasingly, portable ultrasound machines are becoming available

for use by clinical teams across the hospital. The aim of this project was to establish to what extent these are available and being used by A&E, medical and respiratory teams for guiding chest drain insertion.

A telephone survey was conducted, interviewing a junior doctor working in each of the A&E, medical admissions and respiratory departments in all training hospitals across the Thames region (this represents 168 clinical teams in 58 hospitals). This was performed over a one-week period in July 2008.

Portable ultrasound machines were accessible for use by A&E clinicians in 60% (33/55) of A&E departments. However, they were only used to assist with guidance of chest drains in five of these 33 departments (15%). The anatomical approach was suggested as the most common approach used in A&E (88%). A&E clinicians commented in 15 hospitals (27%) that they would refer the patients to the medical team rather than insert the drain themselves (see fig).



Abstract P164 Figure Accessibility and use of portable ultrasound for the placement of chest drains for pleural fluid.

Portable ultrasound machines were accessible for use by medical juniors in 20% (11/55) of hospitals; however, they were only used for drain insertion in four hospitals (with involvement of the respiratory team in all cases). In the remaining hospitals, if ultrasound was needed, input from the radiology department was required (93%). Only three departments (5%) had a policy to use ultrasound guidance for all cases.

In respiratory departments, doctors had access to portable ultrasound in 34% (20/58) of hospitals and this was utilised for drain placement in seven hospitals. Only four departments (7%) had a policy to use ultrasound guidance for all cases.

44 of 168 (26%) doctors could identify their training lead for chest drain insertion. In 77% of cases, this was a member of the respiratory team.

This survey documents that across the Thames region, the use of ultrasound in chest drain placement is not routine current practice. Even when portable ultrasound is available clinicians are still relying on an anatomical approach as first line.

P165 THE USE OF AUTOLOGOUS BLOOD PATCH FOR PLEURODESIS IN TREATMENT OF SECONDARY SPONTANEOUS PNEUMOTHORAX: A RETROSPECTIVE STUDY IN CYSTIC FIBROSIS PATIENTS

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Background: Pneumothorax is common in patients with cystic fibrosis (CF). It is often treated with autologous blood patch pleurodesis (ABPP) as it is well tolerated and has less impact on transplantation. However, its effectiveness has never been adequately assessed in the treatment of secondary spontaneous pneumothorax. In our study we look at CF patients with spontaneous pneumothorax who were treated with this procedure to determine the efficacy and any complications.

Methods: Retrospective analysis of patients with CF who presented with pneumothorax between January 1993 and January 2008. We looked for recurrence and any complications with the procedure.

Results: We found a total of 17 patients with pneumothorax who were treated with ABPP, three patients who only had intercostal chest drain and another two who were treated with talc pleurodesis. The time period for observation for recurrence varied from 6 months in the case of the most recent admission to 15 years. All 17 patients had large (>2 cm) symptomatic pneumothorax on admission. Of these, six (35.2%) patients had a recurrence of pneumothorax on the same side, four within 6 weeks, one 13 months and one patient 17 months later. One recurrent patient presented with tension pneumothorax and was treated with talc pleurodesis with no subsequent recurrence. The remaining five patients were treated with repeat blood pleurodesis and three had no further recurrence over the next 2 years, two had another recurrence and were then treated with talc pleurodesis with no further recurrence. There were no immediate complications in any of the patients and none developed pleural infection, which has been reported in previous studies. Of the three patients who were treated with chest drain alone, two had recurrence within 4 months and were treated with blood pleurodesis with no further recurrences over the next 2 years. The two patients who were treated with talc alone did not have any recurrence afterwards.

Summary: Autologous blood patch pleurodesis appears to be a well tolerated and safe procedure that is useful in patients who may later be candidates for lung transplantation. However, it does not appear to be as effective as talc in preventing a recurrence.

Understanding disease mechanisms in vitro/in vivo

P166 IDENTIFYING A GENE EXPRESSION SIGNATURE FOR PROGRESSIVE PULMONARY SARCOIDOSIS

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In recent years, DNA microarray technology has progressed from a means of identifying potential genes involved in disease causation to a technique that can be used to find subclasses in disease states and identify biological markers associated with disease outcome. In sarcoidosis, one of the key questions in clinical management is which subset of patients will progress to chronic disease and whether treatment in this group of patient will alter the natural history of the disease. There are currently no markers that can be applied at disease presentation to identify patients at risk of disease progression. It is thus also not possible to assess whether early treatment will improve outcome in this group. We question if a global gene expression pattern in the lungs might predict the subset of patients with pulmonary sarcoidosis that progresses to chronic disease. We hypothesise that in patients with progressive pulmonary sarcoidosis, a different set of genes are activated to drive the route of inflammation towards that of a fibrotic pathway. In the first part of the study, we examine the viability of gene profiling of RNA obtained from bronchoscopic transbronchial biopsies and if differences in gene expression pattern can be observed in the lungs from biopsy-confirmed sarcoid patients with asymptomatic disease and Scadding stage 1–2 chest *x* ray (CXR) changes compared with patients with persistent symptoms, Scadding stage 2–3 CXR changes and abnormal pulmonary function test (n = 8 patients, non-smokers, no treatment, excluding Loefgren's