Poster presentations

Lung cancer: the patient journey

P001 DELAY IN LUNG CANCER CLINIC APPOINTMENT: AUDIT OF GP REFERRALS

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The NICE (National Institute for Health and Clinical Excellence) guidelines for the diagnosis and treatment of lung cancer[1] advise that patients with a chest *x* ray (CXR) suggestive of lung cancer should be referred urgently to a respiratory physician (1.1.5). They advise that a copy of the CXR report be sent to the lung cancer multidisciplinary team (MDT) for an appropriate action (1.2.1). The referral pathways of these patients differ between hospitals. In Burnley the report of an abnormal CXR is sent to the patient's GP who then refers the patient to the fast-track lung cancer clinic.

We audited retrospectively the GP referral letters marked ''2 week rule'' in 2005 (n = 80) and the patients' case notes with an aim of assessing the potential delay in the lung cancer clinic appointment caused by the practice of receiving referrals from GPs. We did this by calculating the number of days between (1) date of first CXR and date of GP referral to the lung cancer clinic; (2) date of GP referral and date of first appointment for the two week lung cancer clinic.

Discussion: In Burnley General Hospital the outpatient CXRs are reported on the same day and the report faxed to the GP by the next working day. The lung cancer specialist nurse receives a copy of the CXR report and reminds the GP if a referral is not received within the next 7 days, but the MDT does not intervene in any other way. Our audit showed that there was a median delay of 10 days from the date of chest *x* ray (that is, 9 days from receiving CXR report) to the date of sending a referral to lung cancer clinic.

Conclusion: This audit reveals that direct action by the lung cancer MDT on the abnormal *x* ray reports would potentially cut considerable time (median 9 days) to the date of lung cancer clinic appointment. The results of our audit support the recommendation 1.2.1 in NICE guidelines

1. **NICE**. Clinical Guideline 24. The diagnosis and treatment of lung cancer. February 2005. Available at http://www.nice.org.uk/page.aspx?o = cg024niceguideline (accessed September 2006).

Abstract P001 Delay for the 2 week rule lung cancer clinic appointment.

n = 80	Time from CXR to referral by GP (days)	Time from GP referral to clinic date (days)	Time from CXR to clinic date (days)
Mean	16.34	12.26	28.46
Median	10	11	20

P002 IMPACT OF A TWO-STOP CLINIC ON DIAGNOSTIC TIMES, TREATMENT DELAYS, AND TREATMENT INTENT IN PATIENTS REFERRED WITH SUSPECTED LUNG CANCER

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Background: The NICE (National Institute for Health and Clinical Excellence) guidelines for the diagnosis and treatment of lung cancer (2005) recommend early diagnosis clinics for patients with suspected lung cancer on the basis that resection rates, and hence survival, may be improved. As yet this is unproven therefore we assessed the impact of a two-stop lung cancer clinic on diagnostic times, treatment delay, and treatment intent at our trust.

Methods: Diagnostic and treatment data were collected on patients referred to clinic with suspected lung cancer over a six month period in 2004 and then over a similar period in 2005 following the introduction of a two-stop clinic, in which the computed tomography scan of the thorax was the primary investigation.

Results: The results for two groups of patients are shown in the table.

Conclusions: The introduction of the two-stop lung cancer clinic was associated with a significant reduction in the time from referral to definitive treatment planning at the MDT meeting and a significant increase in the proportion of patients receiving specific anti-cancer treatment. There was a trend towards a greater proportion of patients undergoing radical treatment with a reduction in the time to receive this treatment, however this did not reach statistical significance. Further study is required to determine whether these improvements are associated with increased survival.

P003 CHEST PHYSICIANS AND LUNG CANCER NURSE SPECIALISTS: WHO PREDICTS THE MULTIDISCIPLINARY TEAM DISCUSSION OUTCOME BEST?

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Introduction: The role of the lung cancer multidisciplinary team (MDT) is to enhance the management of lung cancer by facilitating the diagnostic process and speeding the treatment plan, in the hope that this will improve the outcome. However, such MDTs are resource intensive and costly both in terms of the number of, and time spent by, specialist personnel. We wanted to find out whether the resource of the MDT could be better targeted towards difficult cases if ''straightforward'' patients could be could be managed separately. To do this, we assessed whether a chest physician (CP) or lung cancer nurse specialist (NS) alone would come to the same conclusion as the full MDT discussion in organising the management decision.

Method: We asked our CP and NS separately to go through all the information available for each patient, and then document the projected outcome from the MDT discussion. We then compared their opinions with each other, and finally to the ultimate outcome of the subsequent MDT discussion. Other core members of our MDT are radiologists, a pathologist, oncologists, palliative care specialists and thoracic surgeons.

Abstract P002

	2004	2005	
Audit period	May–Oct	June–Nov	
No of patients seen	165	171	
Final diagnosis of lung cancer	52 (32%)	49 (29%)	
Time from referral to MDT meeting	34 (11–80)	26 (6–56)	p<0.001
Specific anti-cancer treatment given	33 (63%)	42 (86%)	p = 0.009
Radical treatment intent	10 (19%)	13 (27%)	p = 0.262
Time from referral to radical treatment	95 (34–128)	73 (30–106)	p = 0.376

Data for diagnostic and treatment times are shown as median (range) days. MDT, multidisciplinary team.

Abstract P003

	O	S	SBx	PET	IS	DIS	ROS	CTBx	Other
MDT result	58	16	9	13	18	6	10	8	7
CP prediction	51	12	8	10	17	0	7	7	5
NS prediction	51	12	7	9	17	0	7	7	5

Results: The outcome of 153 consecutive patient discussions (mean patient age 71 years (range 36–95), 80 male) were studied. We categorised the outcome in these discussions as: Oncology (radiotherapy and/or chemotherapy) (O), Surgical resection (S), Surgical biopsy (mediastinoscopy/thoracoscopy) (SBx), staging PET scan (PET), interval CT scan (IS), discharge (DIS), referral to other cancer service (breast, colon, etc) (ROS), CT guided biopsy (CTBx), and others (see table). The MDT outcome matched that of the CP in 121 cases (79%) and that of the NS in 119 cases (78%), and both in 114 cases (75%). The outcome projection of CP matched that of the NS in 133 cases (87%).
Conclusion: This study shows that in the majority of cases, key members of the respiratory team can independently deduce the correct pathway steps in the management plan of lung cancer patients, indicating that those resource intensive MDT discussions may not be necessary for most patients. Such discussions may be best targeted towards more difficult cases, and we are now assessing protocols to enable this precious resource to be used more effectively.

P004 BODY COMPOSITION ASSESSMENT IN PATIENTS ATTENDING A RAPID ACCESS LUNG CANCER CLINIC

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Background: Cachexia is generally considered a late manifestation of lung cancer and associated with poor prognosis. Less extreme body composition abnormalities may go undetected. We explored the utility of routine bioelectrical impedance analysis (BIA) to determine body composition at the time of referral to a rapid access lung cancer clinic (RALC).
Method: All patients referred to RALC Clinic between 01/05–01/06 had BIA (Tanita 310). A height squared fat free (FFMI) and body mass index (BMI) were calculated and their effect on a variety of outcome measures determined.
Results: 216 (127 male) patients were assessed. 34 had a low BMI (<20 kg/m^2); 33 had a low FFMI (<15 kg/m^2 male, <16 kg/m^2 female); 18 of the 33 with low FFMI also had a low BMI and 15 a normal BMI (hidden loss of FFM). Overall 49 (22%) had altered body composition. 69 (34 male) patients were diagnosed with lung cancer (NSCLC n = 48, SCLC n = 5, non-histological clinical diagnosis n = 11, other n = 5). Of these, 8 had a low BMI-low FFMI, 7 normal BMI-low FFMI, and 8 low BMI-normal FFMI at presentation. A low FFMI was not more prevalent in those with a diagnosis of cancer than those where it was excluded, $p = 0.07$. A low FFMI was not more prevalent in (a) one histology group or (b) more advanced disease or (c) worse performance score (PS). The median (95% CI) survival of this outpatient referred group with diagnosed lung carcinoma was 61 (40 to 83) weeks. Body composition did not delineate a separate survival group, though survival was less in those with a worse PS or staging, $p<0.05$. Two of the 9 patients with intended curative surgery had a low FFMI. Two of the 15 patients with low FFMI received chemotherapy compared to 12 of the 54 with a normal FFMI.
Conclusions: BIA is easily incorporated into RALC assessment and allows the early detection of altered body composition which may affect survival though extended follow up period is required to assess this. Determination of body composition is not a surrogate for other recognised prognostic markers such as PS/histology/staging. However, altered body composition may have had a potentially unwarranted effect on management decisions taken.

P005 EFFECT OF RAPID ACCESS CLINICS ON STAFF: COMPARISON WITH OTHER DUTIES

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Introduction: Rapid access clinics are designed to compress and streamline the diagnostic process, for the ultimate benefit of patient care. However, little work has been done to look at the effect this pressure has on the staff of the multidisciplinary team (MDT), who have to work to tight deadlines in order to meet tough government targets. We therefore surveyed the staff working in our large and busy rapid access lung cancer clinic, which deals with up to 600 patients per year.
Method: We conducted an anonymous prospective survey of doctors (D), nurses (N) and technical and clerical staff (TC) working in our MDT. We used a questionnaire adapted from the NHS staff survey 2003 which contained questions on role enjoyment/satisfaction/awareness, feedback, emotional challenges and worry, rapport and patient contact, training/support, deadlines, and interference with other work activities (1 to 5 scale, 5 = strong agreement). We also asked them to compare the MDT work with their other duties.
Results: Thirty four members were surveyed (11 D, 15 N, and 8 TC), and all returned the questionnaire. Overall, staff spent an average of 26% of their time in the MDT role. The results (mean scores) are given in the table.

Abstract P005

Parameter	Usual role	MDT role	p Value
Role enjoyment	4.0	4.6	<0.002
Support	3.9	4.4	<0.05
Feedback	3.5	3.9	NS
Satisfaction	3.7	4.1	NS
Worry about the role	2.4	2.3	NS
Rapport	4.4	4.6	NS
Emotional challenge	3.4	3.1	NS
Patient contact	4.6	4.5	NS
Formal training	4.3	3.8	0.04
Working to deadlines	3.9	4.1	NS
Interference with other work	2.1	2.1	NS
Role awareness	4.3	4.3	NS

In the subgroup analysis, nurses were more satisfied, supported, and enjoyed colleague rapport, whereas doctors complained about lack of training and clerical and technical staff felt less supported.
Conclusion: Although the rapid access clinic work is challenging, staff seemed to enjoy it more than their normal work. Team spirit and colleague support play a part in this, and the absence of formal training and the need to meet deadlines did not affect the outcome. Creating a well supported environment is the key to establishing an effective MDT with good staff morale.

P006 THE LUNG CANCER MDT: WHO CONTRIBUTES TO DECISION MAKING?

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Introduction: The UK Cancer Plan states that the multidisciplinary team (MDT) is a mandatory part of every cancer unit, and in lung cancer the core team must consist of a Respiratory Physician (RP), Radiologist (R), Pathologist (P), Nurse Specialist (LCNS), Oncologist (O), Palliative Care Specialist (PCS) and Thoracic Surgeon (TS). Active participation and coordination between the team members should enhance patient care. We investigated the contribution of these members in our MDT meeting, where only patients with suspected lung cancer are discussed.
Method: We prospectively audited individual member's contribution to the MDT meetings, including their comments or questions, which patients they commented on, and the outcome of consecutive cases over an 13 week period. We did not include the presentation of a case or report as comment.
Results: 207 cases (mean age 70 years (range 36–95), 114 male) were audited. Of these, 203 (98.5%) were presented by a RP. There were a mean of 2.8 comments per case (0 to 8). Contribution by members: RP

136 (mean 0.65 per patient), TS 140 (0.85), R 176 (0.85), O 99 (0.47), P 11 (0.05), LCNS 16 (0.08), and PCS 7 (0.03). More comments were made where the outcome was resection (3.4 per patient) or thoracoscopy/mediastinoscopy (3.4) compared to CT guided biopsy (3.0), palliative care (2.7), oncological treatment (2.45), or simply radiological follow up (2.16). Respiratory physicians made more comments on patients with an outcome of palliative care (0.77 per patient) and those who were referred onward to another team (0.78). Input from TS was more in cases with outcome of surgery (1.26), CT guided biopsy (1.21), and PET scan (1.16). As expected, radiologists commented mainly on the outcome of CT guided biopsy (1.14) and those who required radiological follow up (1.08). PCS made the least comments overall but on patients with an outcome leading to palliative treatment. Although the LCNS knew more about most of the patients, they commented less (0.08). The pathologist made the least comments (0.05), but this normally had the greatest effect on treatment.

Conclusion: This study has identified active and passive participants in our MDT meetings. We intend to feedback the results to encourage members to participate more. We aim to use this to avoid herd behaviour and collective team thinking for groups of patient, ensuring that each patient has an individual discussion. We believe this model of feedback is important and refreshes the MDT members' outlook and attitude to the care of this unfortunate patient group.

P007 COMPARING CANCER REGISTRY DATA WITH LOCAL LUCADA DATA

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Introduction: The Cancer Peer Review utilises cancer registry data in two measures. Data from the cancer registry for our hospital appeared to be incorrect. We sought to compare data in the registry to our own local data, collected for the national LUCADA project.

Methods: The two databases were searched for all patients with a date of diagnosis in 2005. Results were collated onto spreadsheets. The data were then evaluated and the two datasets were compared. Mismatches between the data were investigated more thoroughly to ascertain any common factors.

Results: The cancer registry contained 76 patients, 70 of which were full details, 6 were death certificate details only. Of these latter 6, 2 received palliative care, 2 received active monitoring, 1 received chemotherapy, and 1 received radiotherapy. Only 1 patient was not on the local database—this patient was seen in 2004 and a diagnosis of lung abscess was made. The local database contained 94 patients and 18 of these were not on the registry list. One was probably a recurrence rather than a new patient, but had been included in the local database as new. 10 were outside of the WMCIU region (and presumably were picked up by another registry). Two were labelled as unknown primary by the registry and so did not appear as lung cancer, although they were dignosed as having lung cancer (one liver biopsy adenocarcinoma, one lymph node small cell carcinoma). This left 5 patients with a secure diagnosis of lung cancer who did not appear on the registry database: 1 FNA ''highly suspicious of small cell carcinoma'', 1 not biopsied—for active monitoring only, 1 FNA showing small cell carcinoma carried out at another hospital, 1 diagnosis made at end of 2005, but positive biopsy not until early 2006, 1 several biopsies, all negative, working diagnosis still lung cancer.

Conclusions: The local database appears to be the more comprehensive. There are numerous reasons why some patients do not get picked up by the registry. The registry data are only as good as the information given to them. More communication and data sharing is crucial if the data are to be accurate and trustworthy. Comparison of local databases and registry data is a useful way of auditing data collection.

P008 ESTABLISHMENT AND EXPERIENCE OF A NURSE-LED HAEMOPTYSIS CLINIC

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Background: At a time when we were having difficulty in meeting the target of seeing all urgent cancer referrals within two weeks, we noticed a significant number of patients being referred with haemoptysis and a normal chest *x* ray (CXR). An audit of such referrals over a year failed to reveal any cases of lung cancer, but a wide variety of other respiratory problems. We therefore decided to establish a nurse-led clinic for these patients. A literature review identified very little relevant or recent published data on this group of patients.

Pilot phase: Two experienced specialist respiratory nurses initially ran a clinic parallel to the rapid access lung cancer clinic with 44 patients being seen during this pilot phase. The initial consultation was with one of the nurses and included a full medical history and clinical examination. The results of any initial investigations were reviewed, including the CXR, spirometry, and the results of any relevant blood tests. The patients were then presented to the lead clinician and a differential diagnosis agreed which determined further investigation and management. None of these 44 patients had a final diagnosis of malignancy.

Establishment of clinic: As a result of this experience a management algorithm was developed after which an independent nurse-led clinic began with the nurses having the authority to discharge patients at first visit, but having immediate access to a consultant in the parallel clinic if required. As experience developed and the nurses were appraised, they were authorised to prescribe a range of antibiotics, to order CT scans, and request bronchoscopy.

Results: Between July 2003 and May 2006 202 patients (excluding the initial 44) have been seen in this independent nurse-led clinic. The mean age was 62 (range 19–90). The commonest final diagnoses included: infection (30%), idiopathic (16%), and bronchiectasis (15%). There was 1 case of tuberculosis and 12 cases of lung cancer (6%). In only 3 of these 12 were the CXRs, on review, entirely normal; so the incidence of lung cancer in patients with haemoptysis and truly normal CXR was only 1.5%. 62 patients (31%) were discharged at the first visit by the nurse alone, but all patients were seen by a consultant respiratory physician if they were called back for a second visit. 113/202 (56%) of the patients went on to have a CT scan. Only 17 patients had a bronchoscopy. Within the management algorithm, haemoptysis was split into ''major'' and ''minor'', based on the amount of blood expectorated and its duration. We found that higher volume haemoptyses were not associated with lung cancer, but more persistent haemoptysis (7 days or more) were. This observation would have to be tested in a larger population. In summary we have demonstrated the feasibility, safety, and effectiveness of a nurse-led haemoptysis service and consideration should be given to extending the role of specialist nurses into other areas.

P009 NATIONAL LUNG CANCER AUDIT: DATA COMPLETENESS

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LUCADA (LUng CAncer DAta) is a long term audit of lung cancer care in England. The audit is now commissioned by the Healthcare Commission and managed within the information centre for Health and Social Care by the National Clinical Audit Support Programme (NCASP) in partnership with the Royal College of Physicians. LUCADA began collecting data in 2004 and as at 30.6.06 had 23 539 patient records in total. The first annual report will be published in autumn 2006 and will present data on all cases of lung cancer with an initial date of referral in 2005. Data relating to this cohort of patients continued to be entered onto the database up until June 2006. This abstract describes the data completeness of this data set. A high level of data completeness is vital if we are to be in a position to carry out proper risk adjusted analyses in an attempt to explain wide regional variations in lung cancer treatment and outcomes.

For subsequent risk adjusted analysis LUCADA collects data on the following case mix variables: age, gender, postcode (and thereby deprivation index), cell type, cancer stage, performance status, and the presence of a comorbidity which would preclude a curative procedure. The first three variables are automatically populated from the ''Open Exeter'' database on entering the NHS number. Completeness for these variables is thus 100%. The table sets out completeness for the remaining key data fields.

Abstract P009

Data item	Completed	Completed excluding unknown
Histology/clin diagnosis	78%	Not applicable
Cancer stage	52%	48%
Performance status	65%	53%
Comorbidity	66%	46%

For ideal risk adjusted analysis to be carried out, all of the above key variables need to be available. In this 2005 data set only 36% of the cases have complete data for all case mix factors with no missing or unknown values.

Data completeness is a huge challenge and there are multiple factors which have an influence including time, organisation, and resources. The challenge for LUCADA is to achieve continuing high levels both of participation and data completeness in a difficult service environment. Autumn 2006 will see the first annual report but will not contain any risk adjusted analysis. The aim for 2006 is to ensure that the data for the next annual report will be of sufficient quality to make it possible for these analyses to be done. By 2007 we aim to be able to publish comparative performance and outcome data that will have the potential to influence the service improvement agenda.

P010 ARE WE GOING TO BE ABLE TO MEET THE ''31 DAYS TO TREAT FROM REFERRAL'' TARGET FOR LUNG CANCER PATIENTS?

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Introduction: In 2008 guidelines recommended by the National Health Service Cancer Plan will be implemented, recommending that all patients with lung cancer (LC) referred via the two week wait (2ww) process, should be diagnosed and have started treatment within 31 days of the initial referral date, except for good clinical reasons. We are a regional centre for LC serving a population of around 1 000 000.
Aim: To assess how close our centre is to achieving this target.
Method: We looked at our patients diagnosed with LC referred via the 2ww process, in the same six-month periods (January to June) over four consecutive years from 2003–06. This was a retrospective analysis of all patients referred as a 2ww for suspected LC as defined from our LC tracker database.
Results: During these six-month periods we received 334 2ww referrals in 2003, 305 in 2004, 362 in 2005, and 328 in 2006. The number of LC diagnoses made via the 2ww process for these periods was 115 (34.4% of the 2ww referrals) in 2003, 101 (33.1%) in 2004, 95 (26.2%) in 2005, and 83 (25.3%) in 2006. The mean number of days that our patients have waited from initial referral to treatment is 51.3 days in 2003, 49.3 days in 2004, 39.9 days in 2005, and 36.3 days in 2006. The median number of days from referral to first visit was 14 days in 2006.
Discussion: It is proving to be a challenge to initiate treatment for LC patients within 31 days of referral. However, our data support an improvement in the mean time to treat 2ww LC patients from referral, by 15 days ($p<0.001$), over the last four years. This improvement has arisen despite access to positron emission tomography (PET) scanning being limited and at a distant centre, which has added further complexity to the diagnostic pathway. We feel that the reason for this improvement is due to changes in our service as follows:

- A new clinic structure with a mini multidisciplinary team (MDT) meeting on Tuesday involving a radiologist, chest physician, MDT tracker, and specialist nurse, prior to the Tuesday clinic with new referrals.
- The implementation of an ultrasound neck and fine needle aspiration diagnostic service being offered on the day of the first clinic visit.
- Continuation of the main weekly MDT meeting on a Friday.

Conclusion: We have identified that at present we would not meet the ''31 days to treat from referral'' target. There are two potential areas for improvement. If the time between referral and first visit were shortened, many more of our 2ww patients would commence treatment within 31 days of referral. Secondly, local implementation of PET scanning will improve our diagnostic pathway duration.

P011 INCIDENCE OF LUNG CANCER IN PATIENTS RE-PRESENTING TO THE RAPID ACCESS LUNG CANCER CLINIC

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Introduction: Patients with features suggestive of lung cancer are now referred to rapid access clinics, where less than half will be diagnosed with the disease. However, the remainder is still at risk and may re-present at a later date, raising questions as to whether the tumour was apparent at the initial presentation and whether the clinical features prompting further referral have changed. Also, the incidence of cancer in these ''representers'' is unknown. To look at this further, we reviewed all cases who presented for the second time to our large rapid access clinic, which processes up to 600 cases per year, 45% of which have lung cancer.
Method: We interrogated our comprehensive database which records the method of referral, presenting features, demographics, and outcome of all referrals, looking for patients who presented more than once to the rapid access clinic. In the representers, we compared the data of those subsequently diagnosed with cancer with the remainder. All patients underwent a CT scan, and bronchoscopy when appropriate.
Results: Of 4839 patients processed over six years, 46 (1%) who did not have cancer at the initial referral were referred again with suspicious features (mean time to re-referral 27 months (range 5–59)). 18 (39%) were subsequently diagnosed with lung cancer (8 non-small cell, 2 adenocarcinoma, 3 small cell, 1 mesothelioma, 1 carcinoid, 3 clinical diagnosis). Although 25 patients represented with new symptoms, there was no difference between those with cancer and the remainder. There was no difference in clinical features between the two groups (see table, (mean + range)), but patients were less likely to be referred from primary care the second time (GP 1st referral 40/46 *v* 2nd referral 25/46, $\chi^2=11.80$, $p<0.001$), although these cases were more likely to have cancer (GP 1st referral 18/18 *v* 2nd referral 8/18, $\chi^2=13.9$, $p<0.001$).

Review of CT scans showed that the tumours in the representers were not visible at the first presentation, but 22% had contralateral changes, 17% had normal scans, and 61% had ipsilateral changes not indicative of the ultimate cancer.
Conclusion: In this small but important group of patients, the incidence of lung cancer was similar to that expected for new referrals. We were reassured that the lung cancer had not been missed at first presentation even though the average time to representation was just over two years: this illustrates the difficulties in screening high risk individuals for lung cancer. It is of note that primary care colleagues were less likely to re-refer patients, even when they had new symptoms indicative of lung cancer.

P012 MANAGEMENT OF LUNG CANCER IN THE ELDERLY

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Background: Lung cancer is common and has a poor prognosis.[1] Peak incidence is between 75 and 80 years.[2] Worthing has the largest percentage of over 85 year olds in Europe. This study was designed to review the management of patients with lung cancer at Worthing Hospital, comparing the elderly (over 75 years) population with the younger (under 75 years) patients, and assessing factors which influence survival.
Methods: Patients with a new diagnosis of lung cancer between January 02 and December 04 were identified from the lung cancer database and their medical records were reviewed.
Results: 367 patients were identified, 221 were aged under 75, 146 were 75 or older (range 31–95). Histological confirmation was achieved

Abstract P011

Parameter	Age	Male	Smokers	Re-presentation time (months)	FEV1%
Cancer	68 (52–82)	50	18	27 (9–59)	57 (22–102)
Non-cancer	67 (41–81)	50	29	27 (5–56)	67 (27–104)

in 79% of patients overall but only in 66% of patients over 75 years. 225 patients had non-small cell (NSCLC), 41 patients had small cell (SCLC) and 26 had mesothelioma. Most patients had good performance status (PS 0–2) 73%, but PS was not recorded in 16%. 96% of patients were formally staged. Of the patients with NSCLC 21% were early stage (1a–2b), 17% were stage 3a, 37% were stage 3b, and 47% were stage 4. Of the SCLC patients only 27% had limited stage disease at diagnosis. Younger patients were more likely to receive active treatment (surgery, chemotherapy or radical or palliative radiotherapy) 62% *v* 33%. Mean survival was 197 days in the under 75 years group and 172 days in the over 75 year olds, with no significant difference. Comparing active treatment (AT) against best supportive care (BSC) for under 75 year olds: the AT patients had a longer survival; a mean survival of 238 days compared with 145 days for those who received BSC ($p=0.01$). This pattern was also seen in the over 75 year olds whose mean survival was 221 days if actively treated *v* 137 days ($p=0.013$). The strongest predictor of improved survival was PS, followed by treatment type (active/BSC).
Conclusion: This study shows that elderly patients at Worthing are less likely to have histological confirmation and are less likely to receive active treatment despite having a good performance status. It is not clear whether this is due to clinicians' more conservative approach to management in the elderly, patient choice, or comorbidities. This study suggests regardless of age, patients with a good performance status have a survival advantage if they receive active treatment compared to best supportive care. We were unable to differentiate between outcomes of those treated with curative or palliative intent.

1. **British Thoracic Society**. *Burden of lung disease*, Second edition.
2. **Brown JS**, Eraut D, Trask C, *et al*. Age and the treatment of lung cancer. *Thorax* 1996;**51**:564–8.

P013 SURVIVAL FOLLOWING SURGICAL RESECTION OF LUNG CANCER: A DISTRICT EXPERIENCE

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Background: Surgical survival figures for lung cancer vary worldwide. In the UK results of surgery for lung cancer are not usually as good as those quoted internationally. Mountain quoted 1 year survival (5 year survival) for 1A 91% (67%), 1B 94% (57%), 2A 88% (55%), 2B 77% (39%), 3A 64% (23%).[1] NICE weighted average 5 year survival for 1A 69%, 1B 52%, 2A 45%, 2B 33%, 3A (T3) 33%, and 3A (N2) 25%.[2] We looked at survival in the district of Southend over a 15 year period.
Methods: We reviewed the notes from our database of patients who underwent surgery for lung cancer from the beginning of 1990 to the end of 2004, before the introduction of routine PET scans.
Results: 181 individuals had surgery in London: mean age 63.1 years (SD 8.8), FEV_1 2.18 L (0.62), FEV_1 % predicted 83% (30). 12 patients (0.6%) had a diagnosis of non-small cell lung cancer, 101 (56%) squamous cell, 49 (27%) adenocarcinoma, 1 (0.6%) bronchoalveolar carcinoma, 15 (8%) large cell, and 2 (1%) small cell. 56 patients (31%) had a pneumonectomy (P), 103 (57%) a lobectomy (L), and 22 (12%) had a thoracotomy but no curative surgery. 68 patients (38%) had stage I disease, 37 (20%) stage II, 53 (29%) stage III, 4 (2%) stage IV and 19 (11%) stage unrecorded. Chemotherapy was given preoperatively in 2 patients, and within 3 months in 3 L and 3 P patients, radiotherapy within 3 months in 7 L and 13 P. Mean survival from diagnosis to death for those undergoing L was 41.4 months (range 0–167), for P 36.1 months (range 1–177) and open and close 17.2 months (range 1–126). Mortality at 30 days was 5.4% for P, 2.2% for L. Mean survival for those with Stage I disease was 51.6 months, (range 1–170), stage II 36.4 months (range 8–162), stage III 28.1 months (range 0–158), and stage IV 11.7 months (range 6–19). Cerebral seconadaries developed in 7 P and 8 L in the first year post op (9.4% in total). Survival following L at 1 year was 80%, 2 years 60%, and 3 years 42%. Following P was 68%, 32% and 29% at 1, 2, and 3 years respectively. Overall survival at 1, 2, and 3 years for stage I disease was 88%, 66%, and 49%, stage II disease 70%, 46%, 32%, stage III disease 60%, 26%, 17%, and stage IV 25%, 0%, and 0%. Patients who underwent accelerated radical radiotherapy instead of surgery had survival figures as follows: 1 year 66%, 2 years 38%, and 3 years 27%.
Discussion: Survival following resection for lung cancer in our district appears to be shorter compared to international figures. We do not know the reason for the poorer survival figures in the UK, but our figures correlate with other UK reports.

1. **Mountain CF**. *Chest* 1997;**111**:1710–17.
2. NICE National Collaborating Centre for Acute Care. Diagnosis and treatment of lung cancer, February 2005.

Pulmonary vascular disease: clinical aspects

P014 PRIMARY THROMBOPROPHYLAXIS IN MEDICAL INPATIENTS: AN AUDIT OF OUR CURRENT PRACTICE WITHIN THE DIVISION OF MEDICINE OF A LARGE TEACHING HOSPITAL AND A POSSIBLE SOLUTION FOR CHANGE OF PRACTICE

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Introduction: 75% of inpatient mortality from venous thromboembolism (VTE) occurs among medical patients even though post-surgical VTE receives higher profile. Incidence of VTE among medical inpatients could be reduced by almost 50% with primary thromboprophylaxis (pTP). Despite the SIGN guidelines for pTP for medical inpatients being available on http://www.sign.ac.uk/guidelines, compliance with these is thought not to be optimal. We audited our compliance with these guidelines within the Division of Medicine of our 1000-bedded teaching hospital.
Methods: Case notes and drug cards of every inpatient on 11 medical wards during the four-day period of study (20/3/2006 to 23/3/2006) were scrutinised for the following data: demographic profile, length of stay up to day of study, primary diagnosis, secondary diagnosis, prescription (or not) of prophylactic low molecular weight heparin (LMWH) and where LMWH is contraindicated (c/i), the use (or not) of alternative methods (eg, TED stockings) of pTP. Patients were categorised into: **Group A:** Guideline recommended LMWH pTP given; **Group B**: Recommended pTP LMWH c/i, as the patient was on warfarin already for another indication; **Group C**: Recommended pTP LMWH c/i due to internal haemorrhage risk, so alternative pTP used; **Group D**: Guideline recommended pTP (LMWH or alternative) not followed; **Group E**: pTP not recommended; and **Group F**: Guideline recommendation not clear. Percentage of patients for whom the SIGN guidelines recommended pTP was calculated as: n(Groups A+B+C+D) ÷ n(all patients) × 100 and Compliance (%) = n(Group A+B+C) ÷ n(Groups A+B+C+D) × 100.
Results: 289 patients on 11 medical wards (including oncology) were studied in the four-day period. Following the SIGN guideline-recommendations, 240 (83.7%) should have received pTP though only 26 (Group A) actually received this (as LMWH) with a further 17 (Group B) receiving warfarin for another indication. Compliance within our Division of Medicine with the SIGN pTP guidelines therefore calculates to be 17.9%.
Conclusions: Our practice of pTP among medical inpatients could be optimised. Simple awareness of the SIGN pTP guidelines might not automatically mean it is applied. As per the SIGN guidelines, more than 80% of patients should have received pTP. A possible solution could be to consider pTP in every medical admission unless specifically contra-indicated.

Abstract P014

Group A	Group B	Group C	Group D	Group E	Group F	Total
n=26	n=17	n=0	n=197	n=27	n=22	n=289

P015 SEATED IMMOBILITY AT WORK IS A COMMON RISK FACTOR FOR VENOUS THROMBOEMBOLISM

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Background: The role of seated immobility in the pathogenesis of venous thromboembolism (VTE) associated with long distance travel is well recognised. However, whether seated immobility at work is also an important risk factor for VTE is uncertain. The aim of this case series was to determine the frequency of seated immobility at work as a clinical risk factor in patients admitted to hospital with a deep vein thrombosis (DVT) or pulmonary embolism (PE).
Methods: Patients aged <65 years attending an outpatient VTE clinic following a recent admission for DVT and/or PE were interviewed to obtain information regarding clinical risk factors. Seated immobility at work was identified as a risk factor if in the four week period prior to the onset of symptoms, the subject had been seated a maximum of ⩾8 hours per day *and* ⩾3 hours at a time without getting up, *or* had been seated a maximum of ⩾12 hours per day *and* ⩾1 hour at a time without getting up.
Results: There were 62 subjects studied in whom 49 had a DVT, 33 had a PE, and 20 had both DVT and PE. Prolonged seated immobility at work occurred in 21/62 (34%) of cases, representing one the most common risk factors together with family history (35%) and thrombophilic state (32%). Seated immobility secondary to prolonged air travel (>8 hours) was identified in 13/62 (21%) of cases Although other risk factors commonly occurred in subjects with seated immobility at work, in 4 subjects no other risk factors were identified. Of the 21 subjects with seated immobility at work 6 (29%) worked in the IT industry, 4 (19%) worked in management, and 2 (9.5%) were taxi drivers. Seated immobility, as a result of either work or travel, accounted for nearly half (48%) of all cases.
Conclusions: Seated immobility at work may represent an important independent risk factor for VTE. Further research is required to better understand its role, identify the high risk occupations and the efficacy of preventive measures. Overall seated immobility in different situation, included work and air travel, represented the most common risk factors for VTE, the term seated immobility thromboembolism (SIT syndrome), is proposed to include all cases of VTE which have occurred following seated immobility.

P016 PULMONARY EMBOLI AND DEEP VENOUS THROMBOSES: PRECIPITATING FACTORS AND RISKS IN PATIENTS WITH HEREDITARY HAEMORRHAGIC TELANGIECTASIA AND PULMONARY ARTERIOVENOUS MALFORMATIONS

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Introduction: Pulmonary emboli (PE) carry significant hazards in all patient groups. Authoritative guidelines including those from the British Thoracic Society, advise on appropriate prophylaxis to reduce the incidence of venous thromboemboli (VTE) in at-risk patients. In some groups of patients, risk-benefit considerations regarding prophylactic and therapeutic anticoagulation are complex. For example, patients with pulmonary arteriovenous malformations (PAVMs) are often hypoxaemic and polycythaemic, and, due to the presence of their right-to-left shunts, may be at risk of paradoxical embolic stroke from PEs. Many PAVM patients do not receive prophylaxis or full treatment for VTE however, because of underlying hereditary haemorrhagic telangiectasia (HHT, Osler-Weber-Rendu syndrome). HHT which causes epistaxis, chronic gastrointestinal haemorrhage and anaemia, is considered a relative contraindication to anticoagulation.
Methods: In order to determine the incidence of PE and DVT in patients with HHT and PAVMs, and to identify risk factors to improve prevention and management, we studied 311 consecutive patients with definite HHT reviewed in our specialised clinic between May 1999 and May 2005. 207/311 (66.6%) of patients had PAVMs, though these were diagnosed due to respiratory symptoms in only 44/207 (21.3%).
Results: (1) 22 out of 311 patients had confirmed DVT and/or PE (7.1%) at median age 61 (range 32–82) years. Univariate and binary logistic regression indicated that patients with thromboses did not have an excess of PAVMs, hypoxaemia, or polycythaemia. (2) Factor V Leiden heterozygosity was more common in DVT/PE patients ($p=0.0137$, Fisher's exact test). All VTEs in patients with Factor V Leiden followed a recognised precipitating clinical event, particularly a PAVM-induced brain abscess. (3) In a subgroup of 38 healthy HHT/PAVM patients, mean plasma Factor VIII:Ag (ELISA, Diagnostica Stago) was significantly higher than in 38 age and sex matched controls at 137.8 (119.1, 156.5)%, compared to 100 (89.3, 110.6)%. In a validation study in 125 healthy HHT clinic patients, service laboratory FVIII:Ag exceeded the normal laboratory range of 0.45–1.58 μ/ml (mean 1.94 (1.80, 2.07)μ/ml. (4) In the 125 clinic patients, FVIII:Ag was significantly higher in patients with thromboses than without thromboses, and in binary logistic regression, independently contributed to thrombotic risk ($p=0.012$, Wald test).
Conclusion: There is a significant incidence of venous thromboembolism in PAVM/HHT patients. Elevated FVIII:Ag may be an HHT-specific factor that contributes with known clinical and genetic risk factors, to overall thrombotic risk.
Funding support: Hammersmith Hospitals Trustees Research Committee.

P017 THE USE OF IMAGING IN THE DIAGNOSIS AND EXCLUSION OF PULMONARY EMBOLISM: DO THE BTS GUIDELINES REDUCE THE NEED FOR IMAGING?

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Introduction: We studied the use of radiological imaging for suspected pulmonary embolism (PE) over a four month period at the Countess of Chester NHS Foundation Trust. The diagnostic work up was compared with that suggested by the British Thoracic Society (BTS) guidelines (2003). Our aim was to test whether application of the guidelines could have prevented the need for imaging in a proportion of patients, and/or whether adherence to the guidelines would have resulted in missed diagnoses.
Methods: 173 patients were investigated for suspected PE. 65 computed tomography pulmonary angiograms and 108 perfusion scans were used as initial imaging. 13% were found to have pulmonary embolism on imaging. 46% had a respiratory diagnosis (infection, COPD, interstitial lung disease), while 18% had cardiovascular disease.

Clinical probability was poorly recorded in the notes. Retrospective calculation revealed that the positive predictive value for patients with high probability scores was only 38%. The negative predictive value of a low probability risk score was 96%.

D-dimer was often inappropriately used and poorly interpreted. The level set by the haematology department (255 units (u)) had 100% sensitivity but only 8% specificity for PE. We calculated that an optimum level of 400 u would have 100% sensitivity and 78% specificity.
Results: 114 patients with PE ruled out by imaging had low or intermediate clinical probabilities (76%). Of these, 28 had not had a d-dimer. Nine had a d-dimer of less than 255 u, and 20 had a d-dimer less than 400 u. Therefore with appropriate use of clinical probability and d-dimer testing, between 20 and 48 scans could have been avoided. 12 patients with proven DVT had unnecessary imaging studies.

Using the BTS guidelines, between 32 and 60 scans could have been avoided; a reduction of 18% to 35%. Application of the guidelines would not have resulted in any missed diagnoses.

P018 THE PATH AFTER V/Q SCANNING IN A SUSPECTED PULMONARY EMBOLISM

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Introduction: Although CT pulmonary angiography (CTPA) is being used increasingly in the investigation of pulmonary embolism (PE), ventilation/perfusion (V/Q) scanning is still widely used. In our hospital both investigations are available. We wished to establish whether V/Q scans were being appropriately requested and whether patients with indeterminate V/Q scans were being appropriately managed afterwards to ensure PE was not missed or unnecessary anticoagulation given. We also wished to assess the extent to which both imaging modalities were used to help define whether there is still a role for the V/Q scanning service. We compared management with that recommended in our local guidelines. These state that patients with an abnormal chest *x* ray (CXR) or existing respiratory disease should have a CTPA rather than a V/Q scan, that patients with a low probability V/Q scan but high clinical probability of PE should have a CTPA and that patients with an intermediate V/Q scan should have a CTPA. The audit focused on these points.
Methodology: Forty two consecutive patients with a suspected PE and who underwent V/Q scanning between 01/11/2003 to 31/10/2004 at Huddersfield Royal Infirmary were identified and their case notes analysed. The presence/absence of existing lung disease, clinical

probability of PE (Well's score) and V/Q scan result were noted. The subsequent clinical management was noted in terms of further radiological investigation and anticoagulant therapy.
Results: Eight of the patients (19%) were known to have existing lung disease but had a V/Q scan. 29 patients (69%) had a low probability V/Q scan. 13 of these had a high clinical probability of PE but only 2 of them (15%) were followed with further imaging, CTPA. Seven patients had an intermediate probability V/Q scan of which 3 (42%) went on to have CTPA. Six patients had a high probability V/Q scans and were treated as PE.
Conclusion: These findings indicate that the guidelines are not been strictly followed, as a result of which PE could be missed or unnecessary anticoagulation given. If our guidelines had been strictly followed, then 8 patients would have had CTPA rather than V/Q scanning initially and a further 15 patients would have had CTPA as a second imaging investigation. V/Q scanning led to a clear management decision in 22 (55%) of the 40 patients indicating that it still has a useful role when pressures on CT scanning services are increasing.

P019 V/Q OR CTPA AS INVESTIGATION FOR PULMONARY EMBOLUS: AN AUDIT

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Introduction: The BTS advocates imaging ideally within 24 hours for non-massive PE and within 1 hour for massive pulmonary embolus (PE). CT pulmonary angiogram (CTPA) and ventilation-perfusion (V/Q) scan are available at our hospital although currently CTPA is generally recommended only for those with an abnormal chest *x* ray or massive PE. We performed an audit to examine the adherence to local protocol (based on BTS guidelines) in the assessment of suspected PE and to assess the time taken for appropriate imaging.
Methods: We identified all patients who had CTPA or V/Q scan for the investigation of acute PE between April and July 2005. The notes were reviewed to assess evidence of documentation of pre-test probability (PTP) of PE, D-Dimer and the number of hospital days taken for the result of either V/Q scan or CTPA. If PTP was not recorded it was calculated retrospectively using information from the notes.
Results: Eighty six patients had a V/Q or CTPA performed. 16 patients were diagnosed with PE (19%) (9 CTPA, 7 V/Q scans). 56 had V/Q scans, 37 had a CTPA and 7 required V/Q followed by CTPA. One patient had a CTPA to exclude PE at a later date after a low probability V/Q scan. Five patients with non-diagnostic V/Q scans did not have any further imaging. Two were diagnosed and treated as PE. Only 12% had PTP documented and 28% had risk factors documented. Retrospective scoring showed 52% with a low probability, 44% with mod/high probability and 4% in whom a score could not be calculated. The time from request to result was 3.0 days (range 0–11) for V/Q scan and 1.6 days (range 0–11) for CTPA. 28/56 (50%) patients waited over 2 days for a V/Q scan compared with 6/37(16%) for a CTPA. An alternative diagnosis was forthcoming from CTPA in 22 patients. CTPA either diagnosed PE or provided significant alternative information with which to make a diagnosis in 31/37 (84%).
Conclusion: Clinicians remain poor at documenting clinical probability and risk factors in the assessment of PE. CTPA was performed significantly more quickly than V/Q scan which is likely to result in a shorter hospital stay. CTPA also provided information with which to make an alternative diagnosis in 59%. 13/56 (23%) of patients required further CTPA after non-diagnostic V/Q scans. However this did not occur in 5 cases. We propose that primary investigation of PE with CTPA instead of V/Q scan would result in less hospital days, fewer requirements for further imaging, and would provide an alternative diagnosis in a significant number of patients.

P020 AUDIT: THE OUTPATIENT MANGEMENT OF CTPA CONFIRMED PULMONARY EMBOLIC DISEASE

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Introduction: British Thoracic Society (BTS) guidelines support the outpatient treatment of low risk patients with computerised tomographic pulmonary angiography (CTPA) confirmed pulmonary thromboembolism (PTE).[1] This approach does not lead to significant adverse events, may save up to 5.5 days inpatient stay and is highly acceptable to patients.[2]
Aim: The primary aim of our audit was to find out if we are following the BTS guidelines on management of PTE. We also collected clinical data on each patient to help answer why some patients may not have been managed as outpatients. Finally we asked whether or not there may be a role for the outpatient management of low risk patients with suspected PTE to be investigated and treated entirely as outpatients (including outpatient CTPA).
Methods: CTPAs done at the Royal Devon & Exeter Jan–March'06. We randomly selected case notes of 64 patients. 30 day mortality score was then retrospectively calculated using simple 11 point patient characteristics.[3] We also collected data on patient clinical symptoms, signs, investigations and duration of inpatient stay.
Results: Forty four patients were included; Average age 66. 29% (12) of the CTPAs were positive. The average inpatient stay was 8.8 days the average wait for CTPA was 3.3 days (report 0.5 days) and the average duration of anticoagulation was 9.2 days. No low risk confirmed PTE were managed as outpatients but 57% (7) could have been according to BTS guidelines. 16% (7) of suspected VTE were managed entirely as outpatients but some of these were ''high risk'' on mortality scoring.

On review of ''low risk'' patient characteristics it appears they were more likely to have chest pain (64% *v* 60%) and higher clinical probability of PTE (wells score and d dimmer) than the inpatient group as a whole. This may be influencing the decision for outpatient treatment.
Conclusion: We are NOT following the BTS guidelines for the management of CTPA confirmed PTE. We propose the introduction of mortality scoring and expansion of existing outpatient DVT clinics.

Abstract P020

30 day mortality	Total inpatients	Total outpatients
0.8% (low risk)	24% (9)	29% (2)
2.5% (low risk)	32% (12)	29% (2)
4.3%	23% (8)	42% (3)
9.9%	13% (5)	0% (0)
27.1%	8% (3)	0% (0)

1. *Thorax* 2003;**58**:470–84.
2. *Thorax* 2005;**60**(Suppl II):S155.
3. *Am J Respir Crit Care Med* 2005;**172**:1041–6.

P021 MICROTHROMBI IN A SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENT COHORT: A PILOT HISTOLOGICAL STUDY

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Introduction: Although there is evidence for a hypercoagulative state in chronic obstructive pulmonary disease (COPD), there appears to be little morphological data published on the presence of microthrombi in the small vessels of COPD patients. During histopathological studies on lung specimens from severe COPD patients undergoing lung volume reduction surgery (LVRS), we have noted a significant incidence of vascular congestion and thrombosis in the alveolar capillary bed that prompted a formal pilot study of distribution. We have used both H&E staining and thrombomodulin immunohistochemistry to assess thrombotic potential in these vessels.
Method: Ten peripheral lung tissue blocks were selected at random from archival tissues originally obtained from patients undergoing LVRS at the Glenfield Hospital, Leicester. All tissues were obtained with full ethical consent. Samples were stained with H&E and graded according to overall lung pathology, the presence and distribution of vascular congestion and apparent microthrombi and then subject to thrombomodulin IHC to assess endothelial cell integrity as a putative marker of ''pre-thrombotic'' potential.
Results: Morphological assessment of lung samples showed a range of pathologies in the airways, blood vessel walls, and parenchyma consistent with inflammatory damage and post-inflammatory remodelling seen in severe COPD. With regards to the microvasculature, there was a widespread congestion of vessels, often associated with hyalinisation of the vessel wall and loss of capillary integrity, particularly in areas of emphysema. Many examples showed microthrombi disrupting the normal anatomy of the capillary wall. There was no apparent increase in the incidence of lesions in areas surrounding remodelled large vessels or within alveolar walls adjacent to active bronchiolitis. Thrombomodulin staining was very widely distributed throughout the sections with many examples of staining without overt association with microthrombi. Interestingly, there seemed to be a spectrum of thrombomodulin staining from marked in many ''normal'' capillaries through to a loss of staining in areas of active pneumonitis and then a ''reappearance'' of marked staining with overt microthrombosis.

Conclusion: This pilot study supports the idea that microvascular endothelial injury and microthrombosis are features of the natural history of severe COPD. Histological studies are underway in order to understand whether this is a primary lesion reflecting a hypercoagulative state or whether this is a secondary response to the loss of capillary integrity leading to microvascular stasis.

P022 ISCHAEMIC STROKE AND BRAIN ABSCESS DUE TO PULMONARY ARTERIOVENOUS MALFORMATIONS

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Introduction: Pulmonary arteriovenous malformations (PAVMs) are a recognised cause of hypoxaemia and haemoptysis. In the absence of symptoms or cyanosis however, many patients are not referred for treatment. Possible reasons include poor recognition of PAVM-induced ischaemic stroke and brain abscess risk, and the lack of published evidence that PAVM treatment by embolisation reduces these risks.
Methods: In order to determine risk factors for PAVM-induced ischaemic stroke and brain abscess, and risk reduction following embolisation, 219 consecutive PAVM patients reviewed between May 1999 and May 2005 were studied. 139 were referred for treatment of PAVMs, and 80 for investigation of known or suspected hereditary haemorrhagic telangiectasia (HHT). Presentation pattern, severity of any HHT, neurovascular risk factors and focal cerebral deficit of rapid onset lasting >24 hours were recorded, and if ischaemic (diagnosed by neurologists), brain abscess (by neurosurgical reports) or of other aetiologies. Pre embolisation, arterial oxygen saturation (SaO_2), and right-to-left shunt (^{99m}Tc scans) were measured. 192 patients were placed on a waiting list for embolisation (never >6 months), when PAVM features and the presence of untreatable PAVMs (feeding arteries ⩽2–3 mm) were recorded.[1] Confirmation of complete PAVM obliteration was by chest *x* ray, SaO_2 and R-L shunt performed at intervals for a mean of 3.7 (95% CI 2.6 to 4.8) years.
Results: In a predominantly asymptomatic population, excluding ascertainment bias, 40/203 (19.7%) individuals experienced ischaemic stroke or brain abscess. Overall, 31 patients experienced at least one ischaemic stroke, 28 a brain abscess, and one patient experienced both events. 39/60 (65%) had no pre-existing diagnosis of PAVM. Of the 21 patients with a pre-existing PAVM diagnosis, only 10 (48%) had been treated, and median PAVM diagnosis to stroke interval was 7.0 (Q_1 1.5; Q_3 11.5) years. The median age at stroke was 45 (Q_1 38; Q_3 53) years. Significant persistent neurological defects were present in 30/49 (62%) of abscess/stroke patients at a median interval of 8.0 (Q_1 1.5;Q_3 11.5) years, and 12/15 (80%) of brain abscess patients were unable to return to their former occupation. In univariate analyses, and Cox proportional hazards models with embolisation as a time-dependent covariate, none of six quantitative markers of PAVM severity or structure was associated with ischaemic stroke or brain abscess. PAVM embolisation significantly reduced ischaemic stroke and brain abscess rates. However, for patients diagnosed after 1985, the mean delay to treatment was significantly longer when the risk of stroke/abscess was not recognised (incidental diagnosis 6.6 (95% CI 3.4 to 9.8) years; respiratory symptom diagnosis 4.0 (2.6 to 5.4) years; diagnosis by HHT screening programme 1.5 (0.4 to 2.7) years; diagnosis after stroke/abscess 1.1 (0.7 to 1.6) years.
Conclusions: Ischaemic stroke and brain abscess occur commonly in patients with PAVMs. Opportunities for preventative treatment are being missed.

Funding support: HHT patient donations

1. **Gupta**, *et al. Am J Roent* 2002;**179**:347–55.

P023 PULMONARY ARTERIAL PRESSURE, PULMONARY ARTERIOVENOUS MALFORMATIONS (PAVMS), AND PAVM EMBOLISATION

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Introduction: Pulmonary arteriovenous malformations (PAVMs) are abnormal dilated vessels that provide a direct capillary-free communication between pulmonary arteries and veins. The majority of PAVM patients have underlying hereditary haemorrhagic telangiectasia (HHT, Osler-Weber-Rendu syndrome). PAVMs lead to hypoxaemia, haemorrhage, and paradoxical embolic stroke. Increasing evidence is supporting the use of embolisation to treat PAVMs. PAVMs provide low resistance pathways for pulmonary blood flow, and patients with PAVMs would be predicted to have low pulmonary vascular resistance (PVR) and pulmonary arterial pressure (PAP), as demonstrated in a series of 7 patients.[1] However, pulmonary hypertension has been recognised in a small number of PAVM patients, as a result of diverse aetiologies including HHT-associated pulmonary hypertension.[2] The presence of pulmonary hypertension is considered a relative contra-indication to embolisation of PAVMs.
Aims: (1) To examine the distribution of PAP in patients with PAVMs. (2) To establish whether embolisation increases the PAP, in particular in patients with pre-existing pulmonary hypertension.
Methods: A prospective study of contributory factors and PAP measurements was performed in 143 PAVM patients undergoing embolisation. 131/143 patients (92%) had underlying HHT. Pulmonary artery pressure measurements were made prior to contrast injection, and, where clinically indicated, following embolisation.
Results: The mean PAP mean was 14.00 (SD 5.01) mmHg (range 6–40 mmHg). PAP was significantly correlated with age ($p<0.0001$, Spearman rank), with the most significant increase occurring in the upper quartile (age >58 years). Of the 5 individuals with mean PAP >25 mmHg, 3 had severe left ventricular disease and/or mitral valve pathology, and 2 had idiopathic pulmonary hypertension. Overall, there was no significant increase in PAP mean as a result of embolisation, even in patients with initial PAP mean in the upper quartile (>16 mmHg). In half of this group, embolisation led to a fall in PAP mean; the maximum rise was 4 mmHg in the same session, and 8 mmHg in sequential angiography sessions 3–80 (mean 26.7) months apart.
Conclusion: PAVM patients have higher PAP than previously predicted, increasing with age. PAVM embolisation does not lead to a consistent increase and may be undertaken with caution in the presence of pre-existing pulmonary hypertension.

Funding support: HHT patient donations

1. **Whyte**, *et al. J Appl Physiol* 1993;**75**:321–8.
2. **Trembath**, *et al. New Engl J Med* 2001;**345**:325–34.

P024 LONG TERM ADMINISTRATION OF INTRAVENOUS (IV) ILOPROST FOR PULMONARY ARTERIAL HYPERTENSION

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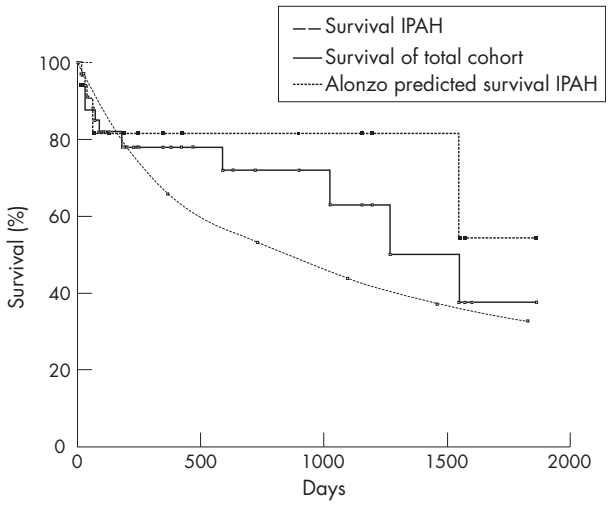
Introduction: IV Epoprostenol is considered gold standard therapy for pulmonary arterial hypertension (PAH), but is unstable and has a short half-life. In our centre, intravenous Iloprost, a synthetic PGI2 analogue with a longer half-life and better stability, is used in these patients.
Methods: A retrospective review of patients with PAH treated with IV Iloprost (Schering Health). The primary end point was survival as compared with that predicted by the D'Alonzo equation.[1] Secondary end points were change in six-minute walk distance and WHO class. All data expressed as mean (SD) unless stated. Changes in walk test and WHO class were analysed using *t* test for paired data (significance $p<0.05$).
Results: Thirty five patients (25 females), age 43 (SD 14) years, were treated with IV Iloprost between Nov 99 and May 06 for a median 242 days (range 2–1862). Treatment was generally well tolerated by 17



Abstract P024.

patients with idiopathic PAH, 7 CTEPH, 6 connective tissue disease associated PAH, 3 congenital heart disease associated PAH, 1 PAH secondary to pulmonary vasculitis, and 1 post-pneumonectomy. Haemodynamics prior to treatment: mean RA pressure 12 (7) mmHg, mean PAP 59 (17) mmHg, PCWP 12 (6) mmHg, CI 2.1 (0.7), and PVR 14 (5) Wood units. Treatment dose was 2.8 (1.2) ng/kg/min. Eleven patients died on treatment, 3 received lung transplantation, and 15 patients remain stable on treatment. Seven patients were transitioned to other therapies. Walk test improved from 254 (116) m to 317 (127) m, p=0.001. WHO class improved 3.5 (0.5) to 2.9 (0.8), p=0.0002.
Conclusion: Iloprost improves both survival and function in patients with PAH and can be used as an alternative to Epoprostenol in this patient population.

1. *Ann Intern Med* 1991;**115**:343–9.

P025 PHOSPHODIESTERASE TYPE 5 INHIBITOR AND THE SPECTRUM OF PULMONARY HYPERTENSION

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Background: The precise therapeutic role of phosphodiesterase type 5 inhibitor in the management of pulmonary hypertension remains to be fully elucidated.
Methods: An analysis was conducted in 353 patients from six studies evaluating the clinical efficacy of oral sildenafil therapy in pulmonary hypertension. Outcome measures of efficacy were the change in exercise capacity as measured by the total distance walked in six minutes and the change in cardiopulmonary haemodynamics as measured by the mean pulmonary artery pressure.
Results: Sildenafil significantly improved ($p<0.05$) the mean (standard error of mean) six minute walk distance and pulmonary artery pressure by 81 (16) m and 10 (2) mmHg respectively in patients with idiopathic pulmonary arterial hypertension and pulmonary hypertension associated with congenital heart disease, connective tissue disease, haemoglobinopathy, and high altitude.
Conclusion: Sildenafil improved exercise capacity and cardiopulmonary haemodynamics throughout the spectrum of pulmonary hypertension. Further studies are now required to evaluate whether survival is prolonged with the inhibition of phosphodiesterase type 5 in patients with pulmonary hypertension.

P026 A POTENTIAL ROLE FOR SILDENAFIL IN THE MANAGEMENT OF PULMONARY HYPERTENSION IN PATIENTS WITH PARENCHYMAL LUNG DISEASE

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Background: Sildenafil offers potential to treat patients with pulmonary hypertension by selectively inhibiting phosphodiesterase type five pathways in the lung. It is recommended for selected patients with pulmonary arterial hypertension but its role in the management of pulmonary hypertension associated with parenchymal lung disease is unclear.
Patients and Methods: Seven patients (68–86 years) with end stage chronic obstructive pulmonary disease (COPD, 4) and idiopathic pulmonary fibrosis (IPF, 3) were referred to our unit. All patients had a long term history of chronic lung disease and were on maximal appropriate therapy prescribed by their referring pulmonologist. Thromboembolic disease was excluded by pulmonary angiography and all patients had had high resolution thoracic CT scan. At assessment right heart catheterisation, 2D echocardiography and 6-minute walk test were performed prior to commencement of Sildenafil 50 mg tds. Their medication was otherwise unchanged. After eight weeks treatment right heart catheterisation, 2D echocardiography and 6-minute walk test were repeated.
Results: The pulmonary vascular resistance was reduced in six patients (from 13, 3, 3, 6.5, 3.5, and 10.5 wood units to 9.7, 2.5, 2.8, 4.4, 2.5, and 5.4 wood units respectively). Six minute walk test increased in six patients (from 110 m, 210 m, 80 m, 30 m, 210 m, and 80 m to 130 m, 312 m, 120 m, 82 m, 244 m, and 100 m respectively). One patient with COPD did not demonstrate a favourable response although their cardiac output increased on sildenafil therapy. 2D echocardiography showed a reduction in estimated PA pressure in six patients with an improvement in right ventricular systolic function in two COPD patients.
Conclusion: Our results suggest that Sildenafil may have a role for selected patients with COPD and IPF who have pulmonary hypertension.

P027 ACUTE HAEMODYNAMIC RESPONSES TO INHALED NITRIC OXIDE AND INTRAVENOUS SILDENAFIL IN DISTAL CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Introduction: Although surgery is the treatment of choice for chronic thromboembolic pulmonary hypertension (CTEPH), it is not appropriate for patients with inaccessible distal disease. These patients are traditionally managed supportively but may benefit from newer, more specific vasoactive therapies. This study examines the acute haemodynamic responses to inhaled nitric oxide (iNO) and intravenous sildenafil in this patient population.
Methods: Patients with de novo distal CTEPH or with persistent pulmonary hypertension post pulmonary endarterectomy were enrolled. At standard right heart catheterisation baseline measures of mean pulmonary artery pressure (mPAP), cardiac output (CO), pulmonary vascular resistance (PVR), blood pressure, and systemic vascular resistance (SVR) were recorded. iNO was then administered at 20 ppm for 10 minutes. After repeat measurements, iNO was discontinued with a subsequent washout period of at least 5 minutes. Sildenafil was then administered intravenously at two incremental doses (''sild1'' and ''sild2'', which have equivalent plasma levels to 25 mg and 50 mg orally) with further haemodynamic measurements during each infusion.
Results: Fourteen subjects (5/14 female, mean age 54.6 years (SD 15.1) were enrolled, with mean baseline measurements mPAP 45.9 mmHg (SD 9.3), CO 3.9 l/min (SD1.0), and PVR 10.2WU (SD4.6). Significant improvements in mPAP and PVR were demonstrated following iNO (-4.1 mmHg or -9.8% ($p<0.001$) and -1.4WU or -16.2% ($p=0.001$)), sild1 (-7.3 mmHg or -16.3% ($p<0.001$) and -2.6WU or -23.7% ($p<0.001$)), and sild2 (-8.6 mmHg or -18.9% ($p<0.001$) and -2.9WU or -27.1% ($p<0.001$)). The reduction in mPAP following sild2 was significantly greater than that following sild1 ($p=0.04$). Individual mPAP and CO responses to iNO correlated well with responses to sild1 ($r=0.86$ $p<0.001$ and $r=0.82$ $p<0.001$) and sild2 ($r=0.67$ $p=0.009$ and $r=0.61$ $p=0.02$). The PVR/SVR ratio, a measure of pulmonary selectivity, remained unchanged between administration of iNO, sild1, and sild2 (0.37 *v* 0.36 *v* 0.35 $p=0.289$).
Discussion: Although failing to meet formal positive haemodynamic response criteria, subjects displayed significant acute responses to both iNO and sildenafil, suggesting that increased vascular tone forms an important component of distal CTEPH. Individual responses to iNO and sildenafil correlated well, as would be expected given their common mechanism of action. Both iNO and sildenafil shared pulmonary selectivity, although sildenafil was associated with greater haemodynamic improvements than iNO. Incremental doses of sildenafil were associated with a dose dependent effect on mPAP.
Conclusions: Both nitric oxide and sildenafil lead to selective pulmonary vasodilatation in distal CTEPH.

P028 PULMONARY ARTERIAL PULSE PRESSURE AND MORTALITY IN PULMONARY ARTERIAL HYPERTENSION

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Objectives: Mean pulmonary artery pressure is an inconsistent predictor of mortality in pulmonary arterial hypertension (PAH) (Sitbon *et al, J Am Coll Cardiol* 2002). Systemic arterial pulse pressure is a powerful prognostic tool in conditions affecting the left ventricle (Franklin *et al, Circulation* 1999). We investigated the prognostic influence of pulmonary arterial pulse pressure (PAPP) in PAH.
Methods: Data for 67 patients with PAH (diagnosed January 1996–March 2004) were reviewed retrospectively. PAPP was correlated against cardiac index (CI) and α (a measure of pulmonary circulation distensibility) (Reeves *et al, Am J Physiol Lung Cell Mol Physiol* 2005). Linear Cox regression and Kaplan-Meier analyses were used to identify predictors of mortality.
Results: PAPP and α correlated powerfully ($r=-0.838$, $p<0.001$). PAPP and CI did not correlate suggesting a more complicated relationship between these two variables. CI, mixed venous O_2 (MVO_2) saturation and 6-minute walk test distance were the best predictors of mortality in a linear model. PAPP related to mortality in a bell-shaped fashion; 5-year mortality was 40%, 91% and 54% in patients with low, intermediate and

high PAPP, respectively. There was a trend towards lower CI and MVO_2 saturation in patients with intermediate PAPP and the highest mortality, although these differences did not reach statistical significance.
Conclusion: The bell-shaped relation between PAPP and survival that we found is compatible with the notion that disease progression in PAH is characterised by simultaneous, but perhaps staggered, reductions in pulmonary circulation distensibility and CI. In advanced disease, low distensibility and low CI may coexist, resulting in intermediate PAPP. To improve their predictive value, PAPP and CI should be reported simultaneously.

Pulmonary rehabilitation

P029 A ROLLING PROGRAMME FOR PULMONARY REHABILITATION: VIABLE OR NOT?

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We report a pilot audit to compare the efficacy of intermittent versus rolling pulmonary rehabilitation programmes (PRP).

We previously ran a fixed 7 week hospital based PRP course 4–5 times a year. 15 patients were initially assessed per course with an average of 5–6 patients completing it. Because of apparently high ''did not attend'' (DNA) rates, during 2005, we sent a questionnaire to 20 patients who failed to complete more than 50% of the course. Of the 75% who replied, the commonest reason (50%) for withdrawal was being unwell due to their chest condition. Since previous studies[1, 2] have shown that 21% of patients relapse within two weeks of an exacerbation, and early pulmonary rehabilitation after admission for an acute exacerbation of COPD is safe, from February 2006 we started a rolling programme to see if this would decrease waiting time for rehabilitation following an acute exacerbation and whether it might affect withdrawal rates during the course.
Conclusion: Although new patients enter a rolling program at different points, continuity has not been a problem. While the proportion of patients completing the programme and the mean number of sessions attended was the same, the rolling programme achieved a substantially reduced waiting time after exacerbations of COPD and may therefore be more effective in reducing readmission rates for subsequent exacerbations.

1. **Kim S**, *et al. Chest* 2004;**125**:473–81.
2. **Mann DC**, *et al. BMJ* 2004;**329**:1209–14.

P030 EDUCATION IN PULMONARY REHABILITATION: THE PATIENTS' PERSPECTIVE

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Introduction: There is limited research to direct the content and delivery of the educational component of pulmonary rehabilitation. Current guidelines (BTS, 2001) give no indication about which topics are essential for inclusion, nor the specific content and method of delivery. Importantly these proposed topics are not based on the patients' perspective.
Aims: To ascertain from the patients' perspective what should be included in the educational component of pulmonary rehabilitation (PR) and how this should be delivered.
Methods: A purposive sample of 32 patients with COPD were recruited from the regional respiratory centre at the Belfast City Hospital (8 mild, 20 moderate, 4 severe). Six focus groups were conducted (2 groups had attended PR, 2 non-PR groups, and 2 mixed groups). A structured schedule of topics was used to guide the discussion facilitated by an experienced moderator.
Data analysis: Focus groups were videotaped and analysed using a grounded approach. Results were verified by means of a follow up report which elicited participants' comments on the findings.
Results: The physical and psychosocial impact of COPD was described extensively. Patients reported considerable lifestyle adjustments and frustration as a result of their symptoms. Key topics identified by participants were: disease education (what is COPD and causes); management of breathlessness (practical strategies for activities of daily living and walking, pacing, and panic reduction); medication (how, when, and why to use medications); welfare and benefits system (disability entitlements, access to home aids, and appliances); exacerbation management (recognition of worsening of symptoms, when and where to seek help). There was ambivalence concerning the importance of disease progression and end of life issues. The majority of patients felt these along with a range of other topics should be included in supplementary information, which they could choose to access. Patients preferred a group format as practical demonstrations and peer support were considered important aspects of learning. The location could be hospital based or otherwise, as long as the sessions were delivered by a knowledgeable/credible individual.
Conclusion: This study has identified deficits in patients' knowledge, understanding, and management of their COPD. Health professionals should ensure that educational components are included in PR programmes which meet these needs, in a format that is acceptable to patients.

P031 BRISTOL COPD KNOWLEDGE QUESTIONNAIRE: EXPERIENCE WITH 100 PATIENTS ATTENDING AN OUTPATIENT PULMONARY REHABILITATION PROGRAM

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Introduction: The Bristol COPD Knowledge Questionnaire (BCKQ) is a new tool developed to measure knowledge of COPD in patients. It consists of 13 questions with 5 items offering a true/false/don't know choice. The 13 topic areas are epidemiology, aetiology, symptoms, breathlessness, phlegm, infections, exercise, smoking, vaccination, inhaled bronchodilators, antibiotics, oral steroids, and inhaled steroids. It has been shown to be valid and consistent with good test re-test reliability and responsiveness (*Chronic Respiratory Disease* 2006;**3**:1–7).
Methods: We have now administered the BCKQ to 100 patients before and after pulmonary rehabilitation to measure change in knowledge imparted by our program. 100 patients with COPD (mean (SD, range) % predicted FEV1 45.2 (17.7, 17–118)), mean age 67.9 (8.5, 49–85), 68 male, took part in an 8 week outpatient based PR program and completed the BCKQ before and after. The mean total score prior to PR was 51.4 (14.2, 8–85) % improving to 66.5 (12.6, 31–86) % following PR. Prior knowledge for the group was strongest in the areas of aetiology, exercise, and smoking. Specifically the effects of stopping smoking on risk of heart disease and decline of lung function together with the recommendation for yearly flu vaccination were the highest scoring items (all >95% correct). Prior knowledge was weakest concerning the topics of oral and inhaled steroids. Over 95% of patients believed that lung function improved following smoking cessation and with inhaled steroids.
Results: The greatest improvements in knowledge were seen in the topic areas of phlegm (mean improvement 25%), exercise and oral and inhaled steroids (all >20%). Least was learned regarding antibiotics (mean improvement 8%). Specifically the effects of dehydration on sputum clearance and the efficacy of spacer devices in reducing oral

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Program type/dates	Waiting times (weeks)	Started PRP (n)	Completed PRP (n)	Failed to complete (n)	Mean classes completed
Fixed program March–May 2005	9–36	11	5	6	12.4
May–July 2005	11–20	11	6	5	12
Rolling Program February–June 2006	3–6	11	6	5	12.8

thrush both showed at least 40% improvement in correct responses. Uncertainty was reduced as a result of education with the proportion of don't know responses reduced from 29 (16) % to 11 (9) %.
Conclusions: In this large group of patients there was no significant correlation found between improvements in knowledge and improvements in exercise performance or changes in health status measured with HAD, SEQ, and CRDQ. There was, however a significant ($p<0.001$) negative correlation between age and post education score suggesting there may be some truth in the contention that you can't teach an old dog new tricks.

The BCKQ has proved a useful tool in measuring the effects of the education component of our PR program and highlighting areas within the program that need revision or further emphasis.

P032 A PILOT STUDY TO COMPARE QIGONG EXERCISES WITH CONVENTIONAL EXERCISES IN PULMONARY REHABILITATION

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Background: Qigong (Tai Chi) is a low impact Chinese exercise known for its benefits in improving strength and flexibility in chronic conditions.[1] Qigong requires no specialist equipment, can be performed anywhere and is available in the community. Previous studies of Qigong have demonstrated improvements in cardiopulmonary function.[2] Pulmonary rehabilitation (PR) is a gold standard for patients with chronic obstructive pulmonary disease (COPD). There is no evidence of the use of Qigong as an exercise for PR and therefore investigated whether Qigong would benefit COPD patients as part of a PR programme.
Method: Twenty two patients were recruited for the eight week study (M=13, F=9), median age 66 years (range 55–81), Forced expiratory volume in 1 sec (FEV1) (% of predicted) median 39 (range 18–72) and were randomised to conventional PR or Qigong PR groups. Patients were stratified for disease severity using the Medical Research Council Dyspnoea (MRC) scale and FEV1%. Outcome measures used were incremental shuttle walk test (ISWT), BORG breathlessness score, chronic respiratory disease questionnaire-self reported (CRQ-SR), Hospital Anxiety and Depression Scale (HADS), endurance shuttle walking (ESW), and a patient satisfaction survey. Differences in mean data between and within groups were analysed using SPSS and significance was set at 95% ($p<0.05$)
Results: Fourteen patients completed the study. Both groups showed improvement from baseline with the biggest improvement in ESW ($p<0.036$ PR, $p<0.002$ Qigong PR). No significant differences were shown between the two groups (table).
Conclusion: Qigong exercises improve exercise tolerance and quality of life in most COPD patients on a PR programme.

1. **Thornton**, *et al*. Health benefits of tai chi exercise: improved balance and blood pressure in middle aged women. *Health Promot Int* 2004;**19**:33–8.
2. **Chao**, *et al*. The cardiorespiratory response and energy expenditure of tai-chi qui-gong. *Am J Chin Med* 2002;**30**:451–61.

P033 IS A PRACTICE INCREMENTAL SHUTTLE WALK TEST REALLY NECESSARY?

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Introduction: The incremental shuttle walk test (ISWT) is a commonly used outcome measure for pulmonary rehabilitation (PR). The distance walked in the ISWT can be used to calculate the speed of the endurance shuttle walk test (ESWT). The ESWT consists of 16 levels (1=1.5 kph, 16=6.0 kph). Singh *et al* (1992) advocate a practice walk (PISWT) but few centres do one. We set out to find out the following: (1) is a PISWT really necessary and (2) does a PISWT affect the level of ESWT?
Method: All patients attending PR perform a PISWT and an ISWT before the ESWT level is calculated. We present our data on the differences.
Results: 205 patients were assessed for PR between October 2002 and December 2005. We have PISWT and ISWT data on 184 patients. Table 1 shows the difference in distance walked between PISWT and ISWT. Table 2 shows the effect of PISWT on ESWT level.
Discussion: We have shown that there is a wide range in difference between PISWT and ISWT and the effect this has on ESWT can be very significant for an individual patient although not when taken as a whole.
Conclusion: A PISWT is necessary to gain an accurate ESWT level. An inaccurate ISWT at baseline could impact on apparent post PR outcome whether using the ISWT or ESWT as the outcome measure.

Abstract P033 Table 1 Comparison of PISWT and ISWT

	Difference (m)	% Difference
Mean	20	22
Median	20	10
Range	−55 to 340	−110 to 170

Abstract P033 Table 2 Effect of PISWT on ESWT level

Median change in level	0
Mean change in level	1
Range	−4 to 6

P034 COMPARING THE INCREMENTAL SHUTTLE WALK TEST AND ENDURANCE SHUTTLE WALK TEST AS AN OUTCOME MEASURE FOR PULMONARY REHABILITATION

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Introduction: The incremental shuttle walk test (ISWT) is a progressive walking test at an externally paced speed using a 10 m course. The endurance shuttle walk test (ESWT) is an endurance walk along the same course, at 85% VO_2 peak calculated from the ISWT (2nd walk). Since an ISWT needs to be performed to obtain the ESWT speed, more walks are required, making it more time consuming, and few centres therefore use it as an outcome measure. However, it has been reported as more sensitive to change than ISWT (Revill, 1999). The minimally clinically important change (MCIC) for the ISWT is 50 m but none is available for ESWT. We present data on the change in both walks following pulmonary rehabilitation (PR).
Method: Sixty three patients were assessed for PR between July 2005 and April 2006. ISWT & ESWT data were available for 41 patients. The change in both ISWT and ESWT was calculated post PR.
Results: Nineteen patients (45%) met the minimally clinically important change (MCIC) for ISWT.
Discussion: Most patients increased distance walked post PR, although less than half met the MCIC for the ISWT. The actual distances walked and the change in ESWT are much larger, giving participants greater evidence of their ability and their improvement, which we feel aids motivation. Even though it takes longer to perform we therefore believe

Abstract P032 Comparison between group means (SD) scores

Outcome measure	Qigong pre	Qigong post	Control pre	Control post	p Value
CRQ-SR	12.79 (4.33)	14.46 (4.93)	14.41 (5.34)	15.70 (4.12)	0.85
ISWT (m)	229 (45)	275 (51)	203 (149)	242 (136)	0.79
ESW (m)	180 (47)	448 (59)	201 (209)	426 (266)	0.67
HAD anxiety	9.8 (4.2)	11.1 (5.4)	9.1 (4.7)	9.5 (6.1)	0.71
HAD dep	9.6 (4.5)	7.7 (3.3)	7.2 (4,.8)	5.9 (3.3)	0.66

Abstract P034 Change in ISWT and ESWT post PR

	Metres		%	
n = 41	Mean (SD)	Median (range)	Mean (SD)	Median (range)
ESWT	404 (459)	275 (−830 to 1490	282 (548)	92.5 (−81 to 3233)
ISWT	52 (53)	40 (−50 to 180)	40 (60)	25 (−20 to 260)

the ESWT is a better outcome measure than the ISWT for PR, and find it a useful clinical tool.
Conclusion: In our DGH and community hospital based three site PR programme, we have confirmed the ESWT to be more sensitive to change than the ISWT. Moreover, greater walking distances and larger changes achieved potentially improves motivation.

P035 USE OF THE MODIFIED CANADIAN OCCUPATIONAL PERFORMANCE MEASURE IN PULMONARY REHABILITATION

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Introduction: The Canadian Occupational Performance Measure (COPM) is a tool for recording self-perception of function and has been used in COPD. A modified version of this tool was used for pragmatic reasons due to a period of restricted Occupational Therapy input to our pulmonary rehabilitation (PR) programme. We are interested in evaluating its validity and sensitivity. The Self Report Chronic Respiratory Questionnaire (CRQ-SR), a quality of life measure, is widely used within this client group. The CRQ-SR dyspnoea (D) component is very similar to the COPM Performance (P) component and the CRQ-SR mastery (M) component has some similarities to the COPM satisfaction (S) component. We present our audit data, having evaluated the change in both following PR.
Method: Fifty two patients enrolled in one of our PR programmes across three sites in North Surrey, completed the CRQ-SR and COPM pre and post PR. For the COPM, patients were asked to rate (0–10) performance (P) and satisfaction (S), for three chosen tasks important to them. The Minimal Clinically Important Change (MCIC) for both the dyspnoea and mastery components of the CRQ is 0.5 and for the COPM is 2.
Results: See table (n = 52).
Discussion: Our data suggest that COPM P may be more sensitive than CRQ-SR D, or that for some patients performance and dyspnoea are not as closely linked as we may assume. More patients achieve MCIC for both Satisfaction (COPM) and Mastery (CRQ-SR) than for either Performance (COPM) or Dyspnoea (CRQ-SR).
Conclusion: We need to further explore validity and sensitivity of the modified version of the COPM.

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% Achieving MCIC for COPM P	46
% Achieving MCIC for CRQ-SR D	38
% Achieving MCIC in both	25
% Not achieving MCIC in both	40
% Achieving MCIC for COPM S	54
% Achieving MCIC for CRQ-SR M	58
% Achieving MCIC in both	33
% Not achieving MCIC in both	15

P036 INFLUENCE OF PULMONARY REHABILITATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ON USE OF SECONDARY CARE RESOURCES

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We set out to assess the effect of our outpatient program of pulmonary rehabilitation on the subsequent use of healthcare resources in both primary and secondary care. A series of 6 week outpatient based programs of pulmonary rehabilitation were performed. The program has been described elsewhere (Finnerty JP *et al. Chest* 2001;**119**:1705–10). Data were analysed for patients taking part in six successive programs undertaken between February 2003 and March 2005, looking at all visits to GPs, number of hospital admissions with respiratory problems, and total days spent in hospital with respiratory problems in the 12 months before the 6 week program and the 12 months afterwards. The source of the data was the hospital information system (Meditech). Three patients died in the year after the program of CCF and were excluded from the analysis, and 41 patients had their data analysed. The mean number of GP visits before the program was 1.76 (SE 0.38) and after the program was 2.02 (0.6) (NS). Before the program, the mean number of hospital admissions was 0.90 (0.23), and after the program it was 0.68 (0.21) (NS). Before the program, the mean number of inpatient days with respiratory problems per patient was 8.78 (2.56), and after the program it was 3.44 (1.04) (NS). The number of visits to the physiotherapist was 1.39 (0.26) before, and 1.63 (0.58) after the program. The number of visits to our chest clinic was 2.20 (0.21) before and 2.07 (0.28) after the program (NS). The total number of hospital bed days with respiratory complaints in the year before the program was 360, and in the year after the program it was 141 (χ^2, $p<0.001$). We conclude that the number of inpatient days with respiratory complaints was significantly less after the program. This analysis cannot determine whether this was due to regression to the mean, or a true effect of the program.

P037 POST-TRAUMATIC STRESS DISORDER AND CHRONIC LUNG DISEASE: PREVALENCE AND CHANGES FOLLOWING PULMONARY REHABILITATION

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Background: Post-traumatic stress disorder (PTSD) is a common serious condition, but is often undetected. Main features include hyperarousal, avoidance behaviour and re-experiencing after a traumatic experience. It is treatable. Little is known about the prevalence in chronic diseases such as COPD and about the impact of PTSD on the symptoms and disability associated with COPD. It is possible that attacks of breathlessness or being given the diagnosis of a life threatening condition may cause PTSD in COPD patients and this may have a negative impact on their symptoms and behaviour.
Research Questions: (1) What is the prevalence of PTSD in patients with COPD referred to pulmonary rehabilitation (PR)? (2) Do PTSD symptom scores fall following PR? (3) What is the relation between PTSD symptom scores and changes in exercise tolerance and health status measures in patients with COPD?
Design: Cross sectional and longitudinal survey.
Participants: Patients with chronic lung disease attending PR programmes in Plymouth, Exeter, and East Devon.
Outcome Measures: The Posttraumatic Diagnostic Scale (PDS), Impact of Events scale (IES), the incremental shuttle walking test, Hospital Anxiety and Depression scale (HADS), and Chronic Respiratory Questionnaire (CRQ).
Methods: Questionnaires were completed at face to face interviews in the subject's home one week before commencing PR and at the end of the PR programme.
Results: 100 subjects took part, mean age 68 years (8.2); 65 male. Seventy per cent completed the PR programme. 192 traumatic experiences were reported by 74 subjects, 37 related to their lung disease. Their most traumatic experience was recorded, of which 24/74 (32%) were lung related. The prevalence of PTSD was 8% according to the PDS criteria. Those with PTSD reported worse health status than those without PTSD: mean CRQ total scores: 76 *v* 60, p = 0.02; mean HADS anxiety: 11.8 *v* 7.2, p = 0.01. After PR, exercise capacity and all CRDQ and HAD scales improved significantly in this cohort of patients, but PTSD symptom severity measured by PDS or IES did not change. Those with PTSD showed significantly greater improvements in CRQ mastery (median 6.5 *v* 3.0, p = 0.048); total CRQ (27.5 *v* 15, p = 0.033) and

HADS anxiety (−4.5 *v* −2, p=0.023), but not in other CRQ scales, HADS depression scale or shuttle test.
Conclusion: PTSD was present in a small minority of COPD patients referred for PR and was associated with poor health status. Those with PTSD improved more in anxiety and disease specific health status than those without PTSD. There is no evidence that PTSD symptoms are improved by rehabilitation, despite its positive effects on HAD scores, exercise and health status in this cohort.

P038 WHY DO PATIENTS DECLINE TO TAKE PART IN A RESEARCH PROJECT INVOLVING PULMONARY REHABILITATION?

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Background: 303 patients with chronic obstructive pulmonary disease (COPD) who had had a previous hospital admission for an exacerbation were thought to be suitable to take part in a randomised controlled trial of the effect of a comprehensive intermediate care package in preventing admission to hospital of elderly patients with the disease. 122 of these suitable patients consented to take part in the study but an identical number declined (40.3%) and there was no response from 59 (19.5%) Following the sending of an ethics committee approved recruitment letter, 39 of the 122 patients (32%) who had declined to take part in the study agreed to either a telephone or face-to-face interview which was recorded in all but one case. The interviews lasted a mean of 20.1 minutes. Following transcription, analysis was undertaken using the framework method (Ritchie and Spencer 1994).
Results: There was 86% congruence between two clinicians in identifying six framework themes from 10 transcripts. Subsequent analysis of all 39 transcripts confirmed the six initial themes with one additional minor theme. 19/39 (48.7%) patients reported location of the pulmonary rehabilitation class and travel to and from the class as a major obstacle, and 19/39 (48.7%) reported a perception that they would not benefit either because they perceived their condition to be too severe or felt they were on maximal therapy already. 15 of the 39 patients (38.5%) had competing commitments or demands and in 12/39 (30.8%) there was poor or negative understanding of the research study. In 11/39 cases (28.2%) past negative experiences either with exercise, previous research or healthcare staff led to decline to take part. In 10/39 (25.6%) of the cases the reason for declining to take part was influenced by the patients' perception that exercise would make them worse, and that they would not be able to commit to the intervention. A minor theme in a handful of cases concerned group work.
Conclusions: Non-participation in studies can lead to bias. Little is known about the decision making progress patients engage in when considering participation in a research trial that involves physical activity. In studies amongst those with COPD it appears that ease of access to the study venue, transport issues and other commitments interact with patients' perception of risk, benefit and cost. These factors are of equal or greater importance than items specifically related to taking part in a research project.
This study was funded by The Health Foundation.
*Dr Sridhar died on the 29 June 2006.

P039 BENCH-MARKING PULMONARY REHABILITATION: SHOULD THERE BE SOME STANDARDISATION?

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Introduction: The Trent Pulmonary Rehabilitation Consortium (TPRC) is a long standing special interest group, based within a largely industrial/former coalfield region of North/Central England. The total population of the area is 4 million and has a high proportion of COPD. We believe that the majority of pulmonary rehabilitation (PR) provided within the region is represented by the group.
Methods: A questionnaire regarding service provision across the region was piloted by a small number of group members to cover both hospital and community provision of PR. Questions were reformatted to assist clarity after this initial pilot. Subsequently all the group were invited to complete the questionnaire. Seventeen members completed the questionnaire. Responses came from 3 NHS Foundation Trusts, 8 Hospital Acute Trusts, and 9 Primary Care Trusts. Rehab leads were mostly physiotherapists, with 1 clinical scientist, 1 practice nurse and one with a nurse plus an audit lead. Sessions were usually twice weekly for a range of 5 to 8 weeks in duration. Venues ranged from Acute Hospital to Church Hall.
Results: Waiting lists varied from zero to more than six months. Outcome measures used by more than half of the centres were, in order of frequency, the incremental shuttle walking test, MRC breathlessness grade, Heart rate and SpO_2, BORG score, endurance shuttle walking test, and the Hospital Anxiety and Depression questionnaire. Many others were used by less than half of the respondees. Low levels of funding and wide variation in staffing level were evident. Five centres had access to a maintenance programme but only one thought it met the needs of PR graduates.
Discussion: The NICE clinical guideline on chronic obstructive pulmonary disease (COPD) recommends that PR should be available to all appropriate people with COPD. This will surely be reflected in the new national service framework (NSF) for COPD. Our region includes many areas of deprivation and high incidence of respiratory disease. Provision of PR is currently poor.
Conclusions: We recommend establishment of a national register and a core set of outcome measures. This will facilitate comparison between regions which will not only improve the quality of programmes but also provide data to underpin fair distribution of finite funding.

P040 BEST BUY FOR PULMONARY REHABILITATION: COMPARISON OF COMMUNITY AND HOSPITAL PROVISION. A REPORT OF THE COHORT STUDY OF PULMONARY REHABILITATION

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Introduction: This UK Health Technology Assessment Board funded study is a randomised controlled clinical trial comparing community versus hospital pulmonary rehabilitation sessions for patients suffering from chronic obstructive pulmonary disease (COPD). Individuals were randomly allocated into a 6-week programme taking place either in the community (intervention) or hospital (control) setting. We have reported clinical outcome elsewhere, here we report the interim cost effectiveness analysis of the two rehabilitation programmes.
Methods: Cost and effectiveness data were collected on 72 and 85 individuals in the community and hospital rehabilitation arms respectively. The cost of running each rehabilitation programme consisted of staff costs, hire of facilities and equipment. Approximately 8 individuals attended each session at a time. In addition costs were estimated for each individual by accounting for drug and heath service use (eg GP consultation, district nurse visits, etc). Effectiveness data were measured using the medical outcomes survey Short Form 36 item questionnaire (SF-36). The SF-36 scores were converted into a single preference based utility score (SF-6D) representing a Quality Adjusted Life Year (QALY). The ratio of the cost difference and the QALY difference between the two arms of the trial was calculated.
Results: For each session the community based rehabilitation programme cost £34.15 while the hospital based rehabilitation program costs £29.56 per patient. The mean incremental cost of a community based rehabilitation program compared to hospital rehabilitation was £45.45 (95% bootstrap CI −19.19 to 106.47) and the mean incremental effectiveness was −0.0013 (95% bootstrap CI −0.004 to 0.001) QALYs per patient. The point estimate of the incremental cost effectiveness ratio was thus negative (−35610 95% bootstrap CI −443221.2 to 394794.98). This indicates that the standard treatment (hospital rehabilitation) dominates.
Discussion: It must be borne in mind that these results are based only on the immediate effects after a programme of pulmonary rehabilitation has taken place. Data on longevity of effect (18 months) are still being collected. They do however question the prevalent assumption that all new pulmonary rehabilitation provision should be based in a community setting.

Respiratory physiology

P041 CAN PATIENT VERBAL RATINGS OF BREATHLESSNESS FACILITATE RAPID CLINICAL ASSESSMENTS?

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Background: Acute shortness of breath (SOB) is common and a potentially significant marker of cardiorespiratory disease. As a

subjective symptom that cannot be directly measured, rapid severity assessments and accurate site of care decisions can be difficult. This study investigated the validity of a verbal subjective rating scale for SOB and tested its ability to predict emergency department (ED) departure status for the acutely breathless patient.
Methods: This was a two-part prospective observational study conducted at a tertiary hospital: (1) tool validation, (2) predicting ED departure status. (1) A convenience sample of patients presenting for cardiac stress tests was used (n=48). Objective and subjective breathlessness parameters were collected before, during, and after exercise and included respiratory rate (RR), oxygen saturation (S_aO_2), heart rate (HR), blood pressure (BP), and verbal dyspnoea scores (VDS) for present dyspnoea; ''On a scale from 0–10, how bad is your SOB, with zero being no SOB and ten the worst SOB you can imagine?'' (2) A random sample of patients presenting to the ED with SOB was used (n=253). Subjective and objective breathlessness parameters were collected at initial presentation and 30 minutes later and included those considered for tool validation, plus VDS for the worst SOB during the current episode and arterial blood gasses (if applicable). Primary endpoints were ED departure status (home, emergency observation unit, inpatient ward) and inpatient length of stay (LOS).
Results: (1) Within-subjects, VDS were significantly correlated with RR (mean $r=0.95$), HR (mean $r=0.90$), and systolic-BP (mean $r=0.95$). Between-subjects, correlations were significant at all time points for RR only ($r=0.45$ to 0.65, $p<0.04$), indicating high individual variability in symptom perception. (2) Age and VDS at initial presentation were significant predictors of ED departure status (78.3% correct classification, $p<0.001$). VDS at initial presentation for present and worst dyspnoea were strong and significant correlates with inpatient LOS.
Conclusion: A verbal numerical SOB rating scale is a valid measure of breathlessness and in the acute care setting, may provide a useful strategy for streamlining initial assessments, patient prioritisation and site of care decisions.

P042 RESPIRATORY FUNCTION IN THE ARCTIC: INVESTIGATION OF RESPIRATORY ACCLIMATISATION AND THE ROLE OF THE HPA AXIS

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Background: Previous studies of cold acclimatisation and the acute cold response have all focused on small numbers of participants, the majority of whom are in military training.
Aims: To investigate acute and acclimatisation responses to the cold in young healthy civilians during a five week expedition to Svalbard in the Arctic, 400 miles south of the North Pole. The changes in salivary cortisol secretion were also studied during this time.
Methods: Sixty eight volunteers (39M: 29F) were assessed at baseline and in the fourth week to provide adequate time for acclimatisation. 13 subjects were also assessed on day 11 to investigate the acute response. Respiratory function was measured with a GP hand held portable spirometer within 12 hours of landing in Svalbard. We also measured urinary pH, glucose and protein, blood pressure, oxygen saturation, and resting pulse rate. During the expedition, the group was exposed to temperatures ranging from 5˚C to −20˚C (including wind-chill factor). Salivary cortisol level was measured at multiple time points over two days baseline and day 14 and again after the expedition. There was similar calorific intake (4000 kcal) across the group as well as activity—for example, trekking with packs and other forms of physical exercise such as ice climbing.
Results: Statistical analysis was performed using paired *t* tests. Comparison of the baseline (n=68) there was a small but statistically significant rise in FEV1 (mean base line 3.85 l, mean four week FEV1 3.93 l) ($p=0.02$) and systolic blood pressure (mean base line 117.7 mmHg, mean four week BP 113 mmHg ($p=0.042$) For those who underwent three measurements (n=13) there was a rise in FEV1 to 4.14 l on day 11 ($p=0.002$) followed by a fall in week four ($p=0.005$). Salivary cortisols were significantly elevated during the expedition compared to pre and post expedition measurements (mean pre-expedition 5.61 nmol/l mean during expedition 10.99 nmol/l, mean post expedition 5.85 nmol/l, $p=0.005$). No significant differences were found in diastolic blood pressure or between final and base line measurements for urinary pH, O2 saturation, and resting pulse.
Conclusion: This study did not demonstrate a decline in lung function during exposure to extreme cold weather indicating that acclimatisation in healthy young people from temperate regions exposed to arctic temperatures readily occurs. The small increase in FEV1 at day 11 and at the end of the expedition may be explained by due to increase plasma cortisol leading to reduced vagal tone.

P043 IS THE USE OF EARLOBE CAPILLARY BLOOD SAMPLES FOR ASSESSMENT OF BLOOD GAS TENSIONS SUFFICIENTLY RELIABLE TO ALLOW ITS USE IN ROUTINE CLINICAL PRACTICE?

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Background: Arterial blood gas (ABG) sampling is a routine investigation used to gain immediate information about a patient's gas exchange and metabolic status. There are potential risks and discomfort associated with this technique and for those patients in respiratory failure who require repeated sampling these factors increase. For many years there has been an alternative method available, arterialised capillary blood gas (CBG) sampling. This test is well tolerated and less invasive with scientific literature supporting its value, however it still remains under-used (Pitkin AD, *et al.* Arterialised earlobe blood gas analysis: an underused technique. *Thorax* 1994;**49**:364–6).
Aims: To assess the accuracy and reliability of CBG *v* ABG sampling within a busy clinical setting.
Methods: Patients requiring ABG sampling were consented to undergo simultaneous CBG earlobe sampling. All capillary samples were obtained by trained nursing staff according to rigorous standards, and all blood gases were taken by doctors using the Smiths ABG system. In addition a third sample (control) was derived by inserting blood obtained from an arterial sample into a capillary sample tube to control for any error introduced by this mode of delivery to the blood gas analyser. All samples were tested in the same analyser (Radiometer ABL77Sci).
Results: Fifty samples were obtained from 32 patients. There was a strong correlation between the CBG and ABG techniques for pH ($r=0.86$, $p<0.0001$), pCO_2 ($r=0.96$, $p<0.0001$), and pO_2 ($r=0.92$, $p<0.0001$). For all of these parameters similar levels of correlation were also noted when comparing ABG and CBG with the control sample. The mean absolute difference between ABG and CBG was −0.02 (standard deviation 0.03), 0.23 (0.55) kPa and 0.94 (1.26) kPa for pH, pCO_2 and pO_2 respectively. Analysis with Student's *t* test revealed that there were no significant differences between ABG and CBG for pH ($p=0.10$), pCO_2 ($p=0.54$) and pO_2 ($p=0.06$). The same was true when comparisons were made with the control sample.
Conclusions: We have shown that for pH and pCO_2 there is only a small mean absolute difference between ABG and CBG measurements with a strong correlation. For pO_2 this difference is larger, however the correlation remains strong, implying that it underestimates at a consistent level when compared to the true value. These results suggest that CBG sampling is a reliable and accurate technique and confirm its value in the management of respiratory failure patients on a busy medical ward. It is however important to remember the relative inaccuracy of the pO_2 when considering the absolute value.

P044 CARDIOPULMONARY EXERCISE TESTING IN THE INVESTIGATION OF UNEXPLAINED BREATHLESSNESS

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Cardiopulmonary exercise testing (CPET) is used to evaluate dyspnoea unexplained by or disproportionate to patients' cardiorespiratory function.[1] We report on 37 tests performed over 2 years in a district general hospital. Consultant respiratory or cardiac physicians referred patients after doing a careful clinical evaluation and appropriate investigations. 19 males and 18 females (mean (SD) age 63 (11) years, BMI 32 (7), FEV1 94 (20) % predicted) completed a maximal, symptom limited exercise test with a ramp protocol on a cycle ergometer. A respiratory physician and a clinical physiologist interpreted the results using Wasserman's flow charts.[2] Static lung volumes and gas transfer were measured in 24 patients each, 13 patients had neither measurement, 13 underwent echocardiography, and 7 had a VQ scan. Prior to CPET the following conditions potentially contributed to breathlessness: obesity (65%), airflow obstruction, or bronchial hyperreactivity (46%), restrictive defect or decreased gas transfer (16%), and cardiac disease (24%); more than one condition was present in 51%, one condition in 35% and none in 13.5%. Of 25 patients with cardiorespiratory disease, 18 (72%) had a normal peak oxygen uptake (VO_2), 4 (16%) a low VO_2 that was abnormal, and 3 (12%) a low VO_2 that was due to poor effort. Of 12 patients without apparent cardiorespiratory disease, 7 (58%) had a normal VO_2, and 5 (42%) a low VO_2 that was abnormal. The commonest reason for stopping was leg fatigue (55%) followed by dyspnoea (28%). At peak exercise the median (IQR) Borg score for leg fatigue was 5 (3–7) in those with cardiorespiratory disease and

4 (3–5.8) in those without apparent cardiorespiratory disease. For dyspnoea the scores were 4 (3.8–5) and 4 (3–7.3), respectively. In the group with cardiorespiratory disease, a new cause of dyspnoea was identified in 5 (20%) patients (3 had dysfunctional breathing, 2 a cardiac arrhythmia) whereas 17 (68%) had a normal response to exercise and 3 (12%) completed a submaximal test. In 12 subjects without apparent cardiorespiratory disease, a new cause of dyspnoea was found in 6 (5 had dysfunctional breathing, 1 had a chronic metabolic acidosis); 6 had a normal response to exercise. Thus, CPET demonstrated a normal ability to exercise in the majority of patients. This cannot be predicted from resting pulmonary and cardiac tests.[2] Those with dysfunctional breathing were given an explanation. No further testing was done in either group. Early use of CPET in the assessment of unexplained dyspnoea may provide reassurance about exercise capacity and reduce the overall number of investigations in these patients.

1. **Martinez F**, *et al*. Graded comprehensive cardiopulmonary exercise testing in the evaluation of dyspnoea unexplained by routine evaluation. *Chest* 1994;**105**:168–74.
2. **Wasserman K**, *et al*. Principles of interpretation: a flow chart approach. In: *Principles of exercise testing and interpretation*. Third edition. Lippincott Williams and Wilkins, 1999.

P045 CORRELATION OF THE TIMED WALK TEST WITH LUNG FUNCTION IN IDIOPATHIC PULMONARY FIBROSIS

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Introduction: Idiopathic pulmonary fibrosis (IPF) is a severe, often life-limiting disease. Simple reproducible measures of disease and functional status are needed. Exercise testing is increasingly used in IPF to assess disease severity. Tests available are the 6-minute walk test (6MWT), the shuttle walk test, and full cardiopulmonary exercise testing. However, these tests have limitations, for example the 6-minute walk test does not correlate with survival in IPF patients and the externally paced shuttle walk is not applicable to real life and IPF patients often underperform as they cannot keep up with external pacing. A recently reported test, the timed walk test (TWT) is a real world self-paced test which can be performed in any outpatient setting, and by patients with a wide range of disease severity.
Objective: To assess the TWT in 24 consecutive patients with IPF and whether it correlated with lung function parameters and baseline oxygenation.
Methods: The results of the TWT (distance walked, time walked, walk velocity (metres per second), degree of oxygen desaturation, oxygen desaturation per metre and per second) for 24 patients with IPF were correlated with lung function tests carried out at that time (diffusing capacity for carbon monoxide (DLCO), FVC, PO_2, TLC, FEV1/FVC). To make the test applicable to patients with a range of disease severity, and to reduce the effect of hypoxaemia on walk velocity, patients with oxygen saturations >88% on room air were exercised on room air and patients with resting oxygen saturations <88% were exercised with supplemental oxygen
Results: Using Spearman's rank test strong correlations were seen between the distance walked, walk velocity and the DLCO and PaO_2 at rest ($p<0.05$). Additional correlations were seen between the change in oxygen saturation per second and per metre and the DLCO ($p<0.05$).
Discussion: The parameters of the TWT reflect disease activity in IPF and this test is applicable to real-world situations, easily performed, even by those patients with severe disease. In addition this is the first report of the velocity of oxygen desaturation (per second and per metre) on the TWT correlating with DLCO. This is very helpful as DLCO is frequently impossible to measure in patients with severe IPF. We are proceeding to investigate whether the velocity of desaturation on the TWT correlates with survival in patients with IPF.

P046 CAN RESPIRATORY PATIENTS ACCURATELY ESTIMATE THEIR EXERCISE TOLERANCE?

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Introduction: Respiratory patients are frequently asked how far they can walk and this is often used as a measure of performance status. Anecdotally patients' estimations of exercise tolerance (distance walked to first stop) appears poor. We hypothesised that estimation of exercise tolerance would improve when given a visual prompt.
Methods: Patients undergoing a 6-minute walk test (6MWT) were asked to estimate a fixed distance (22 metres; a short corridor), as a measure of their distance perception. An estimation of exercise tolerance was made with and without a visual prompt (lengths of a 6MWT course). All values were converted to metres (m).
Results: Thirty patients had 6MWT, 14 male; mean (SD) age 66 (6) years, median (IQR) FEV1 1.10 (0.84 to 1.42) l. 23 had COPD and 7 had other respiratory conditions. Only 4 patients accurately estimated the fixed distance ($\pm$1 m), 18/30 were incorrect by >10 m. Median (IQR) estimated exercise tolerance for the whole group was 48 (19 to 87) m and with the visual prompt was 70 (40 to 200) m. 2/30 patients were excluded from further analysis as they did not stop during their 6MWT and had not reached their estimated distance within 6 minutes. Observed distance to first stop during the 6MWT was 140 (76 to 309) m. Only 1/28 accurately estimated their exercise tolerance ($\pm$5 m), median (IQR) error 55 (21 to 77) %. Five overestimated their exercise tolerance, but the majority (23/28; 82%) greatly underestimated how far they could walk. Inclusion of a visual prompt improved the estimation in 22/28 ($\chi^2=0.001$) but did not significantly improve the accuracy; error 43 (25 to 63) %.
Discussion: A combination of poor distance perception and inability to estimate exercise tolerance makes patients own estimation of exercise tolerance unreliable, even when a visual prompt is used. Patients' reports of exercise tolerance, without objective measures, should not be used as a reliable indicator of performance.

P047 RADIOLOGICAL AND CLINICAL FEATURES OF ALPHA-1-ANTITRYPSIN DEFICIENCY PATIENTS WITH DISCORDANT LUNG FUNCTION

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Introduction: Several distinct phenotypes of chronic obstructive pulmonary disease (COPD) exist (Sciurba. *Chest* 126;117S) which may relate to different underlying pathophysiological mechanisms, and be amenable to different therapeutic strategies. Alpha-1-antitrypsin deficiency (AATD) predisposes to COPD and the UK. AATD registry has collated radiological, clinical, and physiological data for more than PiZ 700 patients.
Aim: To examine the radiological features, paO_2, and quality of life in subjects with discordant lung function, to establish features that define these phenotypes.
Method: The database for the UK AATD registry was searched to find 10 patients with a normal (>80% predicted) forced expiratory volume in 1 second (FEV1) and an abnormal (<80% predicted) transfer factor corrected for alveolar volume (KCO) (group 1). 10 subjects with a normal KCO and abnormal FEV1 were identified (group 2). The voxel index (VI) was calculated for the upper zone (UZ) and lower zone (LZ) for each CT scan, using a threshold of −910 Hounsfield Units. Relative distribution of emphysema was determined by subtracting the LZ VI from the UZ VI. A positive result favoured lower zone predominance. In addition, St George's Respiratory Questionnaire (SGRQ) scores and paO_2 were compared between the two groups.
Results: Results are summarised in the table as mean (SD). There was no difference between the two groups for the extent of upper zone VI ($p=0.386$), although subjects from group 2 had a significantly greater lower zone VI than those from group 1, demonstrating greater lower zone emphysema ($p=0.021$). Relative distribution was therefore different between the two groups ($p<0.001$), with group 2 demonstrating lower zone predominance.
Conclusion: Subjects with abnormal FEV1 and normal KCO have predominant lower zone emphysema, lower paO_2, and worse SGRQ scores than those with an abnormal KCO and a normal FEV1. However, the latter group still have impaired SGRQ and paO_2 despite the normal FEV1.

Abstract P047

	Group 1 (n = 10)	Group 2 (n = 10)	p Value
FEV1 % Predicted	97.76 (16.4)	31.28 (5.6)	<0.001
KCO % Predicted	57.56 (6.6)	89.0 (7.4)	<0.001
Upper zone VI	33.84 (16.47)	28.14 (11.81)	0.386
Lower zone VI	38.03 (16.43)	54.94 (13.30)	0.021
PaO_2 (kPa)	9.93 (1.6)	8.45 (0.7)	0.020
SGRQ Total score	33.0 (16.6)	56.75 (15.3)	0.004

Surgical interventions in lung disease

P048 THE UTILITY OF OUTREACH LUNG BIOPSIES IN PERIPHERAL INTENSIVE CARE UNITS BY THORACIC SURGEONS FOR PATIENTS WITH RESPIRATORY FAILURE: A PRELIMINARY REPORT

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Objectives: Acute respiratory failure with rapid deterioration needing ventilatory support is a challenging condition to manage which can be caused by a variety of causes. Management is guided by microbiology, radiology, and bronchial washing, however it is not uncommon to need a histological or microbiological diagnosis from the lung tissue to guide treatment. Traditionally this involves transport of the patient to a centre with thoracic services for lung biopsy. We have recently avoided all the difficulties encountered in transferring a ventilated patient with organ support and the time delay by performing open lung biopsies in the intensive care units (ITU) in peripheral hospital. Postoperatively the patients were looked after by the intensivists and chest physicians with the thoracic surgeons available for any support.
Aim: The aim of the study was to review our results with the outreach lung biopsy practice for patients with acute respiratory failure in the ITU.
Methods: A prospective collected data from Jan 2004 to Dec 2005 was reviewed and analysed. The procedure was performed with single lumen endotracheal tube with two lung ventilation (two patients were on jet ventilation). All patients had bilateral infiltrates hence a non-targeted left lung biopsy was performed through a left antero medial minithoracotomy using versifier stapler. A single chest drain was placed in all cases. The procedure was performed in the ITU in six of the eight patients avoiding any shifts to the operating theatre.
Results: Eight patients who underwent open lung biopsy in that time frame in three referring hospitals two in the city of Birmingham and third one 50 miles away. There were five female patients and the age range was 24–65. None of the patients had any procedure related complications. The chest drains were removed within the first 48 hours. The diagnosis was established in all the patients and aided further decision making without the delay of the wait for an ITU bed in our centre.
Conclusions: Open lung biopsy can be safely performed through a minithoracotomy without single lung ventilation in the intensive care units in referring hospitals. This can be achieved by a team of visiting thoracic surgeon and the chest physician and intensivist at the local hospital. This practice avoids the undue delays in diagnosis due to lack of ITU beds and transports and benefits both the parent hospital and the tertiary centre.

P049 ORTHODEOXIA HINTS TOWARDS DIAGNOSIS OF ATRIAL SEPTAL DEFECTS AFTER PNEUMONECTOMY: REPORT OF THREE CASES AND A PROSPECTIVE STUDY

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Introduction: A rare cause of dyspnoea after pneumonectomy is right to left interatrial shunting due to atrial septal defect (ASD) that becomes significant only after surgery. These cases often provide a diagnostic mystery, but platypnoea and orthodeoxia-dyspnoea and significant oxygen desaturation on assuming an upright position are pathognomonic. We have encountered three cases of platypnoea and orthodeoxia secondary to interatrial shunting after pneumonectomy in our practice. We also performed a prospective study of post pneumonectomy patients aimed at determining whether simple, non-invasive methods can be used to identify the presence of a shunt.
Methods: Over a 21 month period (July 2004 to March 2006) we prospectively collected data for 25 patients (14 male and 11 female patients, median age of 64 (range 45 to 77) years) surviving a pneumonectomy (16 left and 9 right) in our unit. Between days 7 and 10 post surgery patients had oxygen saturation measurements taken in the lying (0˚), recumbent (45˚), and standing (90˚) positions; and a transthoracic echocardiogram was performed to exclude significant ASD.
Results: There was no evidence of orthodeoxia on the basis of oxygen saturations and no echocardiographic evidence of patent foramen ovale (PFO) or ASD. Using these methods of assessment, there was no evidence of undiagnosed right to left shunting.
Discussion: There were no false negatives in our study. Postural saturation measurement is an inexpensive, non-invasive, acceptable investigation that can be used to exclude interatrial shunting. We recommend it be performed in all patients with unexplained dyspnoea after pneumonectomy as atrial septal defects are eminently treatable conditions.

P050 SPREADING THE BENEFIT OF LUNG VOLUME REDUCTION SURGERY: ONE STAGE BILATERAL VERSUS A STAGED UNILATERAL APPROACH DETERMINED BY THE PATIENT

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Objective: Having demonstrated the comparative benefits of unilateral over bilateral video assisted thoracoscopic lung volume reduction surgery (VAT LVRS) it is now our policy to perform two-stage bilateral LVRS. The timing of the second operation is determined by the patients' perception of their symptoms. We wished to determine whether this policy would result in a more sustained improvement in postoperative benefits.
Patients/Methods: Since 1997 we have performed one-stage bilateral LVRS (group 1) in 26 patients: median age 58 (41–72) years and two-stage LVRS (group 2) in 7 patients:median age 59 (46–63) years. The median time between the two operations was 47 (14–71) months. Two further patients were turned down for their second stage procedure as their FEV1 and DLCO had fallen below selection criteria. The perioperative effects on pulmonary function and health status (Euroquol and SF 36) were recorded preoperatively and at 3, 6, and 12 months and thence annually for five years.
Results: In both groups FEV1 significantly improved (27% in group 1, 35% in Group 2) for 6 months but in group 2 a second significant improvement (32% from preoperative values) was seen at 4 years. After the initial improvement the subsequent decline was −27 (+/−74) ml/year in group 2 and −119 (+/−88) ml/year in group 1 ($p<0.01$). In both groups TLC and RV were significantly improved for 2 years (TLC −15% in group 1, −13% in group 2; RV −22% in group 1, −21% in group 2), but in group 2 further significant improvements (TLC −24%; RV −30% from preoperative values) were seen at 4 years. No significant improvements in Euroquol were seen in group 1 whereas significant changes were seen from 2–4 years post LVRS in group 2. There were significant changes up to 3 years in SF 36 scores in group 1, up to 4 years in Group 2.
Conclusion: Early results suggest a more prolonged surgical strategy determined by the patient can lead to a more sustained benefit. Patients need to be warned not to defer the second stage for too long as their physiology may have deteriorated to preclude further surgery.

P051 DO EXPANDABLE METALLIC AIRWAY STENTS HAVE A ROLE IN THE MANAGEMENT OF PATIENTS WITH BENIGN TRACHEOBRONCHIAL DISEASE?

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Background: With increasing availability, many centers are deploying expandable metallic stents to manage patients with diverse endobronchial pathologies. Although these devices have an important role in malignant disease their usefulness in benign large airway disorders is less defined.
Patients and Methods: Between 1997 and 2005, 31 patients aged (34–83 years) with benign large airway compromise secondary to tracheomalacia (7), post tracheostomy stricture (8), post tracheostomy rupture (2), post pneumonectomy bronchopleural fistula (2) and stricture post lung transplantation (3), lobectomy, tuberculosis, traumatic injury to right main bronchus (1 patient each) and external compression of the airway secondary to achalasia, multinodular goitre, aortic aneurysm, right brachiocephalic artery aneurysm, right interrupted aortic arch, and dissecting aneurysm (one patient each) who were medically unfit for formal surgical intervention were treated by Ultraflex stent deployment. The range of follow up was one week to 96 months. Stents were deployed under anaesthesia using rigid bronchoscopy.
Results: Complications included granulation tissue formation (11) treated with Nd Yag laser ablation; stent migration (1); stent removed, another deployed) metal fatigue (1); stent removal (1)); mucus plugging (2);

halitosis (6) difficult to treat despite antibiotics. 13 patients died from unrelated causes between one week and 15 months after stent deployment.
Conclusion: Endobronchial metallic stents should be considered only for selected patients with large airway compromise secondary to benign airway diseases for whom other medical comorbidities contraindicate formal airway surgery. Once deployed, they are difficult to remove, are associated with significant complications and require prospective bronchoscopic surveillance and often further therapeutic intervention.

P052 MESOTHELIOMA AND RADICAL SURGERY: THE MARS TRIAL

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Mesothelioma incidence continues to increase and will not fall again to present levels for about 15 years. Death rates in the UK are already higher than for malignant melanoma or cervical cancer. Over the last 30 years extrapleural pneumonectomy (EPP) has been offered by a limited number of centers internationally and they attract patients in hope of cure. EPP as sole therapy has generally been abandoned and is now performed within trimodality therapy. There have been no randomised clinical trials of EPP. The MARS feasibility pilot aims to recruit 50 patients. There are two stages to the trial. Patients who are eligible and consent are registered into the first phase during which they all receive three cycles of platinum based chemotherapy and are then restaged. Eligibility for randomisation is confirmed by the MARS MDM. After the second consent, patients are randomised to have or not have EPP. EPP is followed by radical radiotherapy. Outcomes to test feasibility are acceptability of the trial and tolerability of treatment. If feasibility is proven we will proceed to the full trial for which outcomes are survival and quality of life.

Eleven ''local'' centres are recruiting. There are two surgical centres and eight centres giving radical radiotherapy. By 28 July 2006, 93 mesothelioma patients were screened for eligibility. Of these, 46 (49%) were eligible and 37 (40%) have consented to the first phase. Eleven have been randomised, five of them to EPP.

All participating centres who responded to a recent questionnaire confirmed their continued support. The two phase consent has proved to be helpful in that both patients and teams have a two month period as fellow travelers on this difficult cancer journey before randomisation is called for. If half of the registered patients are subsequently randomised at the present rate the target should be met by September 2007.

On behalf of the MARS Trial Management Group.

P053 THE INTERRELATIONSHIP OF BODY MASS INDEX AND LUNG VOLUME REDUCTION SURGERY

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Objectives: Lung volume reduction surgery (LVRS) is thought to result in significant improvements in body mass index (BMI) in patients with severe emphysema. Patients with a higher BMI at the time of diagnosis of COPD are known to have better survival, and those with a low BMI prior to LVRS have significantly worse perioperative morbidity. We aimed to assess the influence of BMI on the outcome of LVRS in our own experience.
Methods: Complete preoperative BMI data were available in 99 of 116 patients who have undergone LVRS since 1995. These patients were placed in three categories: underweight (BMI $\leqslant$19 kg/m^2), normal (BMI 20–25 kg/m^2), and overweight (BMI $>$26 kg/m^2). The in-hospital course and perioperative change in BMI at 3, 6, 12, 24, and 36 months were recorded for each category and compared.
Results: Expressed as median (range). There were no significant differences in pre-op variables. There were significantly more post op ITU admissions among the patients in the lowest two BMI groups (10/23, 17/53, and 3/23 respectively, p=0.02), and significantly shorter hospital stay in overweight patients (16 days (5–79) *v* 17 days (6–111) *v* 13 days (6–25) respectively, p=0.02). There was no difference in survival between the three groups (p=0.6). BMI increased significantly in the underweight and decreased significantly in the overweight.
Conclusions: LVRS and BMI are interrelated. Future work is needed to explore the roles of changing energy requirements and exercise capacity in this relationship.

Abstract P053

	Pre op BMI kg/m^2	BMI change at 3 months	BMI change at 6 months	BMI change at 12 months	BMI change at 2 years	BMI change at 3 years
Underweight, n=23	18.08 (13.89 to 19.84)	*+4.06 (−1.1 to +14.4)	*+4.37 (−0.6 to +14.4)	*+6.05 (+2.7 to +13.2)	*+5.10 (−0.8 to +12.9)	*+2.71 (−1.3 to +5.8)
Normal, n=53	23.08 (20.05 to 25.83)	−0.65 (−8.8 to +12.9)	+0.4 (−10.1 to +11.5)	+0.94 (−7.4 to +12.8)	+1.02 (−10 to +13)	+2.08 (−7.6 to +15.4)
Overweight, n=23	28.63 (26.3 to 33.56)	*−1.65 (−10.7 to +0.4)	*−3.4 (−9.6 to +0.4)	*−1.0 (−8.8 to +2.5)	*−1.4 (−8.2 to +4.6)	*−5.2 (−8.6 to −1.2)

*Denotes a significant change from pre-op, p<0.05.

Abstract P054

Mass range	30–60 g	60–120 g	>120 g
Change in %pred FEV1	5.25 (p=0.289)	7.37 (p=0.002)	5.22 (p=0.175)
Change in %pred RV/TLC	−8.42 (p=0.491)	−14 (p=0.008)	−25 (p=0.107)
Change in %pred DLCO	0.75 (p=0.787)	1.11 (p=0.821)	−1.6 (p=0.959)

P054 DOES THE WEIGHT OF LUNG RESECTED INFLUENCE THE OUTCOME OF LUNG VOLUME REDUCTION SURGERY?

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Background: Lung volume reduction surgery (LVRS) has been shown to be of benefit in improving the respiratory function, but it remains more of an ''art'' than a ''science''. We wished to determine whether an optimum resected weight of lung could be derived for this operation.
Methods: A retrospective review of prospectively collected data of 58 cases of LVRS of the upper lobes, performed in our centre by a single surgeon between 1997 and 2005, was performed. Standard selection criteria were applied. LVRS was performed using buttressed stapling. Extent of resection was determined by estimating functionless target areas. Median weight of resected lung was 90 g (range 39–170 g). Patient were divided into four quartiles based on lung mass resected (30–60, 60–90, 90–120, and >120 g), and comparison was made between the first and fourth quartiles and the second and third quartiles in terms of improvement in perioperative FEV1, RV/TLC ratio, and DLCO at a median of 8 months (6–12 months).
Results: A statistically significant peri-operative improvement in FEV1 and RV/TLC ratio was seen in the quartiles closest to the median but not in the first and fourth quartiles. There was no statistically proven improvement in DLCO in our study.
Conclusion: Inadequate or overzealous resection has a detrimental effect on outcome of lung volume reduction surgery.

P055 THE ABILITY OF SUBJECTS WITH CHEST INJURIES TO PROVIDE BREATH SAMPLES USING LION SL 400 BREATH ALCOHOL TESTING DEVICE: A STUDY USING POST-THORACIC SURGERY MODELS TO MIMIC CHEST INJURIES

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Objectives: Police in the UK are using roadside alcohol testing from1967, which is now mandatory, if stopped with a suspicion of drink driving. Drivers are initially tested for alcohol impairment at the roadside with a screening device. Various investigators have addressed the impact of co-morbid respiratory illnesses and the minimum lung function requirements to activate various breath tests at various stages.[1–3] We postulated that subjects with significant chest trauma may not have any difficulty in providing an adequate breathalyser sample.
Aim: The study was aimed to investigate if chest injury patients can activate the Alcometer using the thoracic surgical patients as the chest trauma model.
Methods: A prospective self controlled study of twenty patients undergoing thoracic surgical procedures in Birmingham Heartlands Hospital was performed between August 2005 to Dec 2005 with LREC and R & D approval. A Lion Alcometer SL400 was used which is a microprocessor controlled, multifiltering infrared spectrometer similar to the ones used by the UK police. The device has two functions firstly as a spirometer in measuring the forced expiratory volume and peak flow to actually trigger the device and micro filtering infrared spectrometer, which analyses the sample of breath for evidence of alcohol. We tested the first parameter testing the patient's ability to activate the device without alcohol (dry activation). The ability of the subjects to activate the device preoperatively and postoperatively was analysed.
Results: Twenty patients who underwent thoracotomy for various procedures were recruited. The mean age was 69.3 years (37–83 years) with 17 males in the study. The mean pre-op was FEV1 the mean pre-op PEFR were 1.96 l (range 1.16–2.46 l) and −265 l/min (range 126–429 l/min) respectively. The mean postoperative FEV1 was 1.09 l (range 0.34–2.2 l) and post-op PEFR was 165 l/min (range 36–492 l/min). Twelve patients had thoracic epidural for pain relief, with the rest having intrathecal morphine followed by morphine infusion. All the patients were able to activate the device preoperatively with varying FEV1s. Only two patients were able to activate the device post-operatively (10%). The two patients who activated the device were male patients who underwent decortications.
Conclusions: Patients following thoracotomies cannot generate the breath to activate the Lion Alcometer SL400. We hypothesise this will be case with patients with chest injuries.

1. **Briggs JE**, Patel H, Butterfield K, *et al.* The effects of chronic obstructive airways disease on the ability to drive and to use a roadside alcometer. *Respir Med* 1990;**84**:43–6.
2. **Gomm PJ**, Osselton MD, Broster CG, *et al.* Study into the ability of patients with impaired lung function to use breath alcohol testing devices. *Med Sci Law* 1991;**31**:221–5.
3. **Honeybourne D**, Moore AJ, Butterfield AK, *et al.* A study to investigate the ability of subjects with chronic lung disease to provide evidential breath samples using the Lion Intoxilyser 6000 UK breath alcohol device. *Respir Med* 2000;**94**:684–8.

Inflammation and cell responses in asthma

P056 PRO AND ANTI-APOPTOTIC ACTIONS OF RESPIRATORY SYNCYTIAL VIRUS ON PRODUCTIVELY INFECTED DENDRITIC CELLS

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Introduction: Respiratory syncytial virus (RSV) causes annual epidemics of respiratory disease affecting the whole community. Individuals are re-infected throughout life. This re-infection does not appear to be due to antigenic shift or multiple subtypes of the virus. An alternative explanation is that the virus is able to interfere with the development of effective memory responses. Dendritic cells (DCs) are present on mucosal surfaces and prime naïve T-cells and stimulate both the primary and secondary immune response. Due to their location and function DCs are vulnerable targets of viral intervention. The aim of this study was to investigate the interaction between human monocyte-derived DCs (MoDCs) and RSV.
Methods: Monocytes were isolated from human buffy coat by magnetic negative selection seeded at a density of 1×10^6 cells/ml cultured in serum free X-Vivo 20 media supplemented with GM-CSF and IL-4. On day 6–8 of culture MoDCs were challenged with 1×10^4–1×10^6 pfu/ml purified GPF expressing RSV (rg-RSV). Productive infection of MoDCs was determined using fluorescent microscopy to monitor plaque formation of HeLa cells cultured with infected MoDCs and/or supernatant. Viral replication and viability of MoDCs was monitored by fluorescent microscopy and flow cytometry.
Results: The results of this study demonstrate that RSV infects MoDCs in a dose dependent manner. The virus is able to replicate within the MoDCs and be released productively to infect other cells. In addition, MoDCs infected with low titres of RSV showed prolonged survival and delayed onset of apoptosis compared to unchallenged control cells. However, at high viral titres both apoptosis and necrosis of infected cells was significantly higher than unchallenged control cells. These effects on cell viablilty were detected as early as 4 hours post infection.
Discussion: These data suggest that RSV can act in several ways. The virus delays MoDC apoptosis to allow optimal viral replication. However, this effect is dependent on viral load, suggesting that once a threshold level of virus is reach within the infected cells they will rapidly die by apoptosis or necrosis and release virus. In addition, RSV induced cell death may stop presentation of viral antigens to T-cells and therefore prevent the initiation of an appropriate immune response.
These data were previously presented at the ATS.

P057 ITRACONAZOLE-MEDIATED INHIBITION OF CALCIUM ENTRY INTO CHEMOATTRACTANT-ACTIVATED HUMAN NEUTROPHILS IS DUE TO INTERFERENCE WITH PRODUCTION OF LEUKOTRIENE B4

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Itraconazole inhibits the influx of Ca^{2+} into chemoattractant-activated neutrophils, which may be a useful secondary anti-inflammatory property of this anti-mycotic. The current study was designed to identify the mechanisms by which itraconazole (0.1–5 mM) antagonises Ca^{2+} uptake by activated human neutrophils, focusing primarily on the effects of this agent on 5′-lipoxygenase (5-LO) and phospholipase A_2 (PLA_2) activities in cells activated with either the chemoattractant platelet-activating factor (PAF, 200 nM) or the Ca^{2+} ionophore, A23187 (1 mM). The activities of 5-LO and PLA_2 in activated neutrophils were measured according to the magnitudes of generation of leukotriene B_4 (LTB_4) and arachidonic acid (AA) using immunoassay and radiometric procedures respectively, while cytosolic Ca^{2+} concentrations were determined by a spectrofluorimetric procedure using the Ca^{2+}-sensitive dye, fura-2/AM. Activation of neutrophils with PAF was accompanied by a sustained elevation in cytosolic Ca^{2+} which was associated with increased generation of arachidonic acid and LTB_4, all of which were attenuated by itraconazole (mean reductions of 68%, 63% and 93% respectively, all with a p value of <0.05 by comparison with the drug-free control system). However, only LTB_4 production was inhibited by the anti-mycotic in cells activated with A23187, compatible with a selective affect of this agent on 5-LO. These anti-inflammatory effects of itraconazole on PAF-activated neutrophils were mimicked by LY255283 (1 mM), MK 886 (0.5 mM), and pyrollidine-1 (2.5 mM), an antagonist of LTB_4 receptors and selective inhibitors of 5-LO and cytosolic PLA_2 respectively. Taken together these observations suggest that itraconazole functions primarily as an inhibitor of 5-LO and that the inhibitory effects of this agent on Ca^{2+} influx and PLA_2 activity in chemoattractant-activated neutrophils are consequent to decreased production of LTB_4. This may be a useful secondary activity of itraconazole in the treatment and prophylaxis of allergic bronchopulmonary aspergillosis and chronic granulomatous disease respectively.

P058 PATTERN OF AIRWAY INFLAMMATION IN ACUTE SEVERE ASTHMA

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Introduction: Sputum cell count as a measure of airway inflammation has been used to guide treatment response in patients with asthma. There are very few studies looking at airway inflammation in acute severe asthma. We investigated the pattern of airway inflammation in patients with acute severe asthma.
Methods: Patients admitted to Norfolk and Norwich University Hospital between October 2004 and February 2006 with acute severe asthma were invited to participate. Patients' demographics, history, medical treatment, and spirometry were documented. Sputum cell counts and peripheral blood counts were analysed. Patients were classified as eosinophilic ($\geq$3% sputum eosinophils) or non-eosinophilic ($<$3% sputum eosinophils). Patients were classified as atopic if RASTwas positive to one or more aeroallergens. Blood eosinophilia was defined as $>0.4\times10^9$/l. The characteristics of sputum eosinophilic and non-eosinophilic groups were compared using the Student's *t* test, χ^2 test, and Mann-Whitney U test with $p<0.05$ being considered statistically significant.
Results: Ninety two patients consented to the study and 69 (46F) successfully produced sputum samples and were analysed in the study.
Conclusion: (1) Patients with eosinophilic airway inflammation were younger than those with non-eosinophilic airway inflammation. (2) Peripheral blood eosinophilia only occurred in patients with eosinophilic airway inflammation. (3) Flu-like symptoms, atopic status, and smoking history did not differ significantly between patients with eosinophilic and non-eosinophilic airway inflammation.

P059 PORTABLE EXHALED NITRIC OXIDE MEASUREMENT: COMPARISON WITH THE GOLD-STANDARD TECHNIQUE

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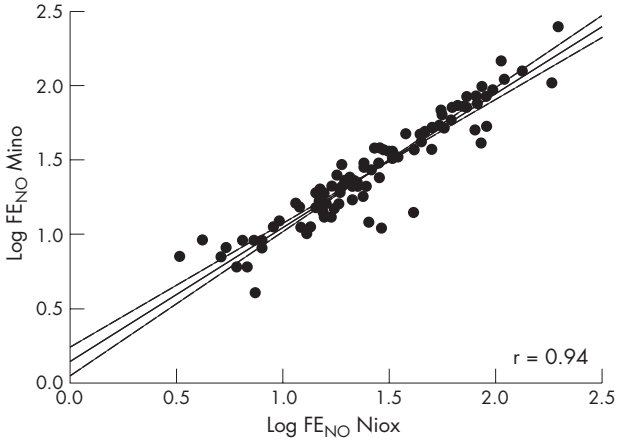
Background: Measurement of fractional exhaled nitric oxide (FE_{NO}) can assist in the diagnosis of asthma, and may also act as a useful surrogate inflammatory marker on which to base treatment decisions in asthma management algorithms. Until recently this technique was confined to research facilities and secondary care institutions. A portable nitric oxide analyser (NIOX MINO) has been developed, but few data exist comparing this with established larger laboratory based analysers (NIOX).
Methods: 101 asthmatic patients and 50 healthy volunteers had simultaneous FE_{NO} measurements undertaken using a NIOX and MINO.
Results: In both asthmatics (fig) and healthy volunteers there was a good correlation between the measurements obtained using each device ($r=0.94$ and $r=0.96$ respectively). Altman-Bland plots confirmed the agreement between the devices.
Conclusion: FE_{NO} obtained using a portable device correlate well with those obtained using an established laboratory analyser. This may facilitate measurement of asthmatic airway inflammation in primary care.



Abstract P059 Correlation between log FE_{NO} MINO versus NIOX in asthmatics.

Abstract P058

	Eosinophilic	Non-eosinophilic	
n	36 (21F)	33 (25F)	
Mean age (SD)	42.8 (15.9)	51.9 (17.1)	p=0.02*
Flu-like symptoms (n)	18	17	χ^2=0.01 (NS)
Median pack years (range)	4.5 (0–52)	7.5 (0–36)	p=0.27
Atopic (n)	21	16	χ^2=0.67 (NS)
Blood eosinophilia (n)	13	0	

NS, not significant; F, female patients.

P060 T CELL RECRUITMENT TO THE HUMAN ASTHMATIC AIRWAYS IS DEPENDENT ON CC CHEMOKINE RECEPTOR 4

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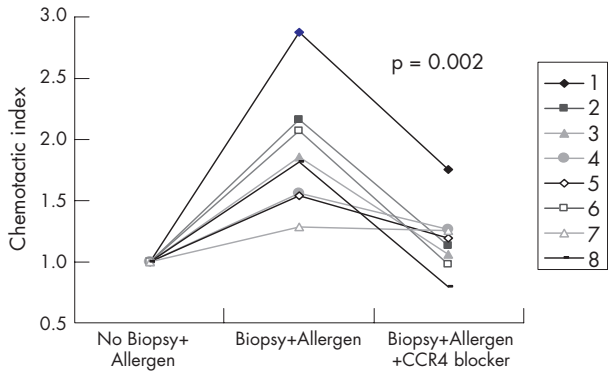
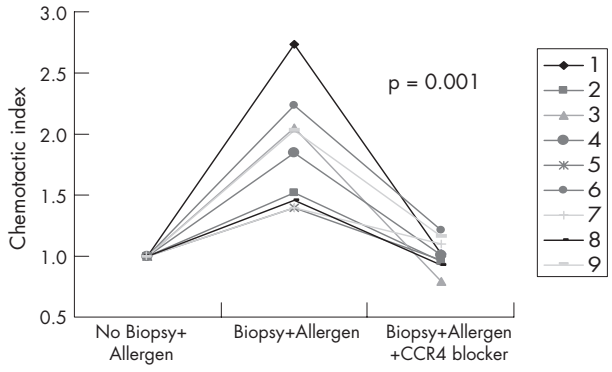
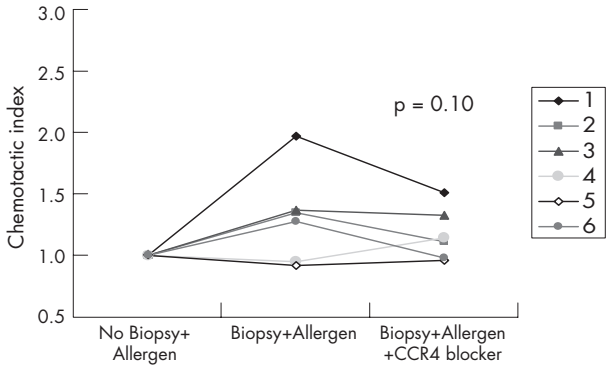
Airway inflammation and remodelling in response to chronic exposure to environmental airborne allergens are pathological hallmarks of asthma.[1] Activated Th2 type T cells, whose numbers are increased in asthmatic airways, play an important role in perpetuating these chronic inflammatory changes.[2] The central mechanisms governing the accumulation of these T cells in human asthmatics airways are not fully elucidated. Work to date has identified increased T cell chemotactic activity in the asthmatic airways.[3] While many chemokines and their receptors are likely to be involved in this process, we have addressed the critical question of specificity of the chemotactic activity. We have shown that in asthmatic subjects the proportion of CCR4 expressing blood T cells is increased in relation to disease severity. These T cells are also seen in significantly greater numbers in the subjects' airways, obtained by dispersion of bronchial tissue and DTE (dithioerythritol) treatment of sputum, compared to the blood suggesting selective recruitment to the airways. We have shown that when human asthmatic subject's bronchial biopsies are challenged with allergen (*Dermatophagoides pteronyssinus*) ex vivo for 24 hours, the supernatant generated increased chemotactic activity to corresponding subject's memory CD45RO+ T cells as demonstrated by using 96 well chemotaxis plates and subsequent 4 colour FACS analysis of migrated cells. This increased T cell chemotaxis is significantly reduced by a specific CC chemokine receptor 4 antagonist (figs 1–4). Detailed phenotypic analysis of migrated memory T cells showed that this effect was seen for both Th2 and Th1 type T cells as shown by expression of CCR4 and CXCR3 respectively. Overall these finding indicate that T cell recruitment to the human asthmatic airways is strongly CCR4 dependent.



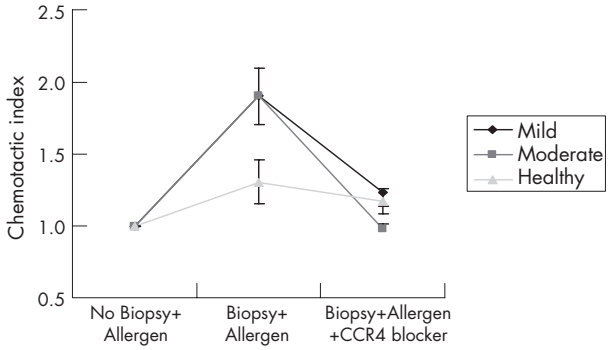
Abstract P060 Figure 1 Show the peak chemotactic indices of memory T cells to allergen challenged human bronchial biopsies with and without a specific CC-chemokine receptor antagonist in 8 mild asthmatics.



Abstract P060 Figure 2 Nine moderate asthmatics.



Abstract P060 Figure 3 Six healthy volunteers.



Abstract P060 Figure 4 Mean chemotactic indices + SEM in the above groups.

1. Kay AB. *N Engl J Med* 2001;**344**:30.
2. Robinson DS, *et al. N Engl J Med* 1992;**326**:298.
3. Hidi R, *et al. J Immunol* 2000;**164**:412.

P061 BRONCHOALVEOLAR LAVAGE AND FIBROBLAST ACTIVITY IN ASTHMA

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Introduction: Asthma is associated with chronic structural airway changes associated with alterations in the extracellular matrix composition. Airway fibroblasts are integral to such changes and increased numbers of transformed fibroblasts are evident within the airway wall in asthma. We have investigated the net and contributory mitogenic activity within bronchoalveolar lavage (BAL) recovered from asthmatics and healthy airways, using primary cultured airway fibroblasts from both asthmatics and non-asthmatics.
Methods: Primary cultures of fibroblasts were grown from endobronchial biopsies taken from healthy and asthmatic volunteers. BAL fluid from healthy or asthmatic donors was used to challenge the fibroblasts over 24 hours. Broad spectrum and specific inhibitors were pre-incubated with the fibroblasts before addition of stimuli. Fibroblasts mitogenesis was assessed using the [^{3}H]-thymidine incorporation assay.
Results: Bronchoalveolar lavage from asthmatics (n=8) exerted significantly greater mitogenic activity than BAL from healthy control subjects (n=8) on both asthmatic and non-asthmatic primary airway fibroblasts ($p \leqslant 0.05$). The non-asthmatic fibroblasts demonstrated greater mitogenic activity, independent of the stimuli, than the asthmatic airway fibroblasts ($p \leqslant 0.0001$). When healthy and asthmatic fibroblasts were pre-incubated with 100 ng/ml Pertussis toxin (G-protein coupled receptor inhibitor) before challenge with healthy or asthmatic BAL, there was a significant inhibition of fibroblast thymidine incorporation ($p \leqslant 0.028$). Thymidine incorporation was also significantly inhibited after pre-incubation with wortmannin (phosphatidylinositol-3-kinase (PI3-K) inhibitor) ($p \leqslant 0.026$), SU5402 (basic fibroblast growth factor (bFGF) inhibitor) ($p \leqslant 0.028$), AG1478 (epidermal growth factor [EGF] inhibitor) ($p \leqslant 0.028$), and PD123-319 (angiotensin II inhibitor) ($p \leqslant 0.028$). Intracellular MAPK inhibitors U0126 (MEK 1/2),

SB203580 (p38) and JNKI1 (JNK) have also been used, and they show that U0126 inhibits fibroblast thymidine incorporation, however this is preliminary data and no significance can be attributed.
Discussion: The use of pertussis toxin has identified the involvement of G-protein coupled receptors in BAL induced mitogenic responses. Subsequent use of more specific inhibitors against bFGF, EGF, angiotensin II, MEK 1/2, JNK, p38 PI3-K indicated the relevance of both MEK 1/2 and PI3-K mediated pathways and the individual factors bFGF, EGF and angiotensin II to the BAL-induced fibroblast mitogenic response in asthma. The individual factors in BAL and their relative contribution are still being evaluated.

P062 ST2 GENE KNOCKOUT ATTENUATES ALLERGIC AIRWAY INFLAMMATION

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Introduction: Asthma is a common allergic airways disease, in which T helper type 2 (Th2) cells play a central role, and mast cells and eosinophils are important effector cells. The membrane receptor ST2L is found on Th2 cells (Xu D *et al*, *J Exp Med* 1998) and on mast cells, and is important in both Th2 differentiation and effector responses. Interleukin (IL)-33 binds to ST2L and results in production of Th2 cytokines in vivo (Schmitz J *et al*, *Immunity* 2005). Therefore, we hypothesised that ST2 gene knockout (ST2-/-) would result in attenuation of allergic airways disease through reduced Th2 cytokine production.
Methods: Wildtype (ST2+/+) and ST2-/- BALB/c mice were sensitised with ovalbumin (OVA) and alum intraperitoneally on day 1. Allergic airways disease was induced by intranasal challenge with OVA on days 9, 10, and 11, and mice culled 24 hours later. Bronchoalveolar fluid (BALF) cell counts were performed on cytospins. Cytokines from BALF and draining lymph node (DLN) cells restimulated with OVA were measured by enzyme-linked immunosorbant assay (ELISA). Lungs were fixed in formalin before processing and H&E staining.
Results: ST2-/- mice had significantly reduced total BALF cell and eosinophil counts compared to WT mice (fig A). There was also reduced eosinophil accumulation around the airways (fig B, C). Both BALF and DLN cytokine production (IL-4, -5, -13, and IFNγ) were similar in the two groups, with only BALF IL-5 showing a significant reduction (WT 126 pg/ml (SEM 17.3), ST2KO 62 pg/ml (SEM 37), $p=0.01$).
Conclusion: ST2-/- attenuates allergic airways disease, as measured by airways eosinophilia, but this cannot be wholly explained by reduced Th2 cytokine production.

P063 THE CHEMOKINE RECEPTORS CCR8 AND CRTH2 ARE PREFERENTIALLY EXPRESSED ON PERIPHERAL BLOOD TH2 LYMPHOCYTES IN ASTHMA AND NORMAL SUBJECTS

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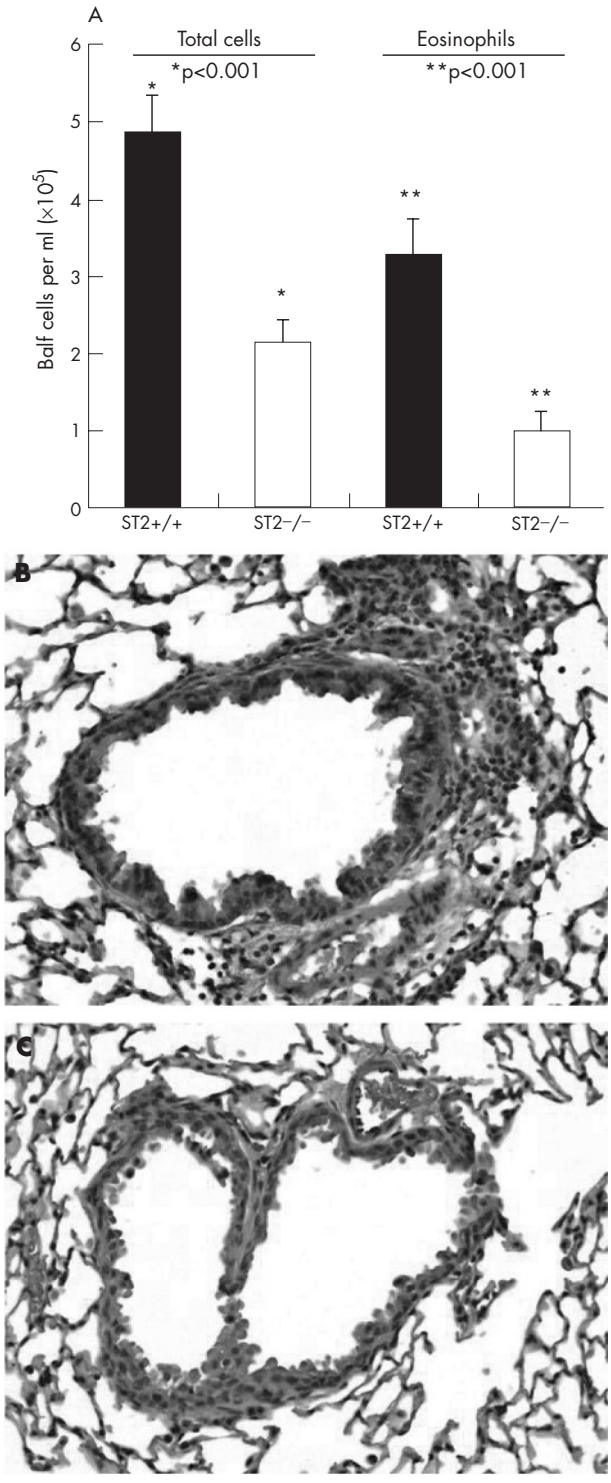
Cytokines secreted by T_H2 cells could account for most of the pathophysiology seen in the asthmatic airway. Chemokines and their receptors could play key roles in the recruitment of T_H2 cells into the asthmatic lung. CCR3, CCR4, CCR8, and CRTh2 are receptors shown to be associated with T_H2 cells. Recently CCR3 and CCR4 were shown to be preferentially expressed on T_H2 cells in human asthmatics. CRTh2 a chemokine receptor homologue and CCR8 have been shown in both in vitro and animal studies to be expressed preferentially on T_H2 cells. We have used flow cytometry to study the possible involvement of CRTh2 and CCR8 and their association with CCR3 and CCR4 in T_H2 cell recruitment to the lung in asthmatics. We have found that 3.1% (SEM 0.4) and 4.1% (SEM 0.4) of the $CD3^+$ T cells to be $CCR8^+$ in normal and asthma subjects respectively. CRTh2 expression was seen in 1.2% (SEM 0.4) and 2.7% (SEM 0.7) of the CD3+ T cells in normal and asthma subjects respectively. The percentages of IL-4 and IFN-γ secreting $CD3^+$ T cells following stimulation with phorbol-myristate-acetate and calcium ionophore were 1.1 (SEM 0.1) and 8.1 (SEM 1.5) respectively. There were significantly more ($p<0.01$) IL-4 secreting $CD3^+$ T cells also expressing CCR8 (29%; SEM 4.3) or CRTh2 (26%; SEM 4.5) than there were IFN-γ secreting cells also expressing CCR8 (4.7%; SEM 1.7) or CRTh2 (2.4; SEM 0.5). Approximately 50% of IL-4 producing $CD3^+$ T cells were identifiable using CCR8 and CRTh2. All $CCR8^+$ cells were $CCR4^+$ and $CCR3^-$. Majority of $CRTh2^+$ cells were also $CCR4^+$ (~70%). Both CCR8 and CRTh2 appear significantly enriched on T_H2 cells and could play a role in the selective recruitment of these cells to the asthmatic lung.



Abstract P062 ST2-/- mice have attenuated airway inflammation. OVA-specific airways inflammation was induced as described in ST2+/+ and ST2-/- mice. Total cell numbers in the BALF were counted, and the number of eosinophils determined by differential counts on cytospins. 5 μm lung sections were stained with H&E and examined by light microscopy using a x20 objective lens. (A) BALF total cell counts and eosinophil counts are reduced in ST2-/- mice. (B) ST2+/+ mice have a florid airway inflammatory response. (C) ST2-/- mice have much reduced airway inflammation.

Obstructive sleep apnoea

P064 THE UNDERSTANDING AND COMPREHENSIBILITY OF PICTOGRAMS USED IN A NEW SCREENING TOOL FOR SLEEPINESS AND OBSTRUCTIVE SLEEP APNOEA SYNDROME

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Background: The diagnosis of sleepiness is key to the assessment of those with obstructive sleep apnoea syndrome (OSAS). We have previously translated the Epworth Sleepiness Score (ESS) into pictograms and found good agreement between the traditional ESS and the pictorial ESS if words were included, but without words the agreement was less good. We found no significant difference in overall scores when we pictorially depicted question eight as a driver or a passenger.[1] This led us to question whether all the eight questions in the ESS were useful in evaluating sleepiness and whether we could reduce the number of questions and add some pictorial screening questions to devise a new tool for assessing OSAS.
Methods: With the aid of a medical artist we developed pictorial representations of four of the original ESS questions: (1) sitting and reading, (2) watching TV, (3) sitting quietly after lunch, and (4) as a passenger in a car and four new pictograms to depict body size, neck size, witnessed apnoea, and blood pressure. Using established methods of testing for comprehensibility of pictograms, we measured the *Guessability* and *Translucency* of these new pictograms in two groups attending our outpatient department: those attending for assessment or treatment of OSAS and those attending for non-sleep related respiratory disorders (controls).[2] Translucency scores were ranked from 1 to 7, with a score of 1 representing no relationship and 7 a very strong relationship between pictogram and words.
Results: A total of 64 patients have been studied so far, 33 in the sleep group and 30 in the control (non-sleep) group. Comprehensibility of each of the images has been reasonable amongst both groups of patients and in translucency testing a mean score of 5 or more was recorded for all images other than witnessed apnoea (mean 4.64). Witnessed apnoea is a difficult image to portray pictorially and it was only marginally better understood by those with OSAS compared to controls.
Conclusion: With the exception of one image we believe we now have a reasonable tool for use with those with potentially reduced literacy and the new scale is now to be evaluated against other methods of assessing sleepiness and used for screening.

1. Ghiassi R, Murphy K, Partridge MR, *et al.* Driving and the Epworth Sleepiness Scale. *Am J Respir Crit Care Med* 2004;**169**:687.
2. Houts P, Witmer J, Egeth H, *et al. Pat Educ Counsel* 2001;**43**:231–242.

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P065 PREVALENCE AND CLINICAL CHARCTERISTICS OF OBESITY HYPOVENTILATION SYNDROME PRESENTING TO A UK SLEEP CLINIC

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Background: The size of the nation is increasing, 21% of both men and women in England have a body mass index >30 kg/m^2.[1] With our increasing obesity will come an epidemic of health related problems including sleep disordered breathing.
Aims: To determine the prevalence of obesity hypoventilation syndrome (OHVS) and which clinical or physiological characteristics distinguish it from obstructive sleep apnoea (OSA), in patients presenting to a general sleep clinic with snoring and or daytime hypersomnolence.
Methods: Retrospective review of Salford Royal Hospital's sleep clinic oximetry and polysomography (embelletta) studies June 04–July 06. OSA defined as Apnoea Hyponoea Index (respiratory disturbance index, RDI >5). OHVS defined as daytime hypercapnia or diagnostic oximetry trace (oxygen saturation <88% for >5 consecutive minutes).
Results: 368 completed studies (151 oximetry, 217 polysomography) performed of which 159 were normal, 150 confirmed OSA, 34 OHVS (22 high CO_2 and 12 characteristic oximetry trace) and 25 revealed alveolar hypoventilation other causes (neurological, copd).

Abstract P065

	OSA	OHVS	p Value
BMI kg/m^2	36.3	44.1	<0.001
Neck circumference cm	44.2	47.5	<0.001
Epworth score _/24	12.4	12.6	NS
Snore time (minutes)	21.9	22.2	NS
RDI (events per hour)	26.8	34.7	NS

Conclusion: OHVS was diagnosed in 16.3% in all positive sleep studies perform in our clinic (9.2% of all studies performed). They can be identified by their physical parameters but not by their snoring or somnolence indices. Provision for planning of future non-invasive ventilatory and sleep services will need to estimate the evolving trends.

1. Health survey for England 2000 (Department of Health)

P066 A DISTRICT GENERAL HOSPITAL SLEEP SERVICE BASED ON HOME OXIMETRY 1998–2006

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In 1998 a dedicated investigation and treatment service for patients with sleep-related breathing disorders was commissioned for residents of Dorset (pop. 701 000) with its own funding stream. Patients undergo initial assessment by Respiratory Specialist Nurse (band 6) which includes history, Epworth score and examination. Patients undergo overnight oximetry in their own home and return to the consultant clinic. If a trial of CPAP is deemed necessary this is provided at the first consultant visit. Patients given a trial of CPAP are seen again within 6 weeks. At the 6 week assessment the decision is made as to whether to continue with the CPAP treatment or not. Those who have become established on CPAP successfully are then followed up at 2 yearly intervals with compliance check, machine service, mask change, etc. Humidification and full face masks are available to those who do not tolerate nasal CPAP over the first 6 weeks. Telephone support is available at all times for new and established patients. Those found to have non-respiratory sleep disorders are followed up in a separate clinic if necessary.

Between 1998 and May 2006, 2035 patients have been seen in the clinic. 1142 (56%) have had a trial of CPAP of whom 682 (34%) have remained longterm users (CPAP usage greater than 4 hours per night). 56 patients established on CPAP prior to the inception of this service and subsequently followed up have been excluded from the analysis.

Mean compliance of those established on CPAP is 5.6 hours per night. The dropout rate after 2 years is 4.5% and the mean reduction in Epworth score is 5. Trend analysis suggests that this fall is maintained in later years.

The cost of the service is made up of 1 consultant PA, 1 full time respiratory nurse specialist (37.5 hours per week), A&C support (25 hours per week), equipment including CPAP machines, replacement masks as necessary, computing and oximetry. Budget for the first year was £56,000 and for 2005–06 £110,000. The total cost of the service over 7.5 years is £750,000.

Using this model it has been possible to screen over 2000 patients for sleep related breathing disorders and establish 682 on nasal CPAP at an approximate cost of £375 per patient.

P067 LONG TERM CHANGES IN QUALITY OF LIFE AND SLEEPINESS IN SNORERS AND SLEEP APNOEA PATIENTS

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Background: Current guidelines recommend treatment for sleep apnoea hypopnoea syndrome (SAHS) only if the respiratory disturbance index (RDI) is >10 with excessive daytime sleepiness.[1] Many heavy snorers may progress to SAHS and a few may have worse daytime sleepiness or quality of life, despite a lower RDI. We looked at long-term symptoms in both SAHS and snoring patients.
Methods: A prospective, longitudinal cross sectional study within a sleep disorders breathing clinic of a UK district general hospital. 102 consecutive attenders with daytime somnolence and snoring were

investigated at baseline with overnight limited sleep studies and completed the Epworth Sleepiness Scale (ESS) and SF36. In accordance with local policy at the time, those with and ESS >10 and an apnoea hypopnoea index (AHI) >5 were started on continuous positive airways Pressure (CPAP) as first line treatment. Those with an AHI <5 were referred to ENT and/or advised to lose weight. Groups were similar in terms of age and gender ($p>0.05$) but the SAHS group had a higher mean body mass index (BMI) ($p<0.01$). All subjects were mailed the ESS and SF-36 after a mean period of 7.9 (SD 0.7) years.
Results: Two patients from each group died. 46 from the 98 (47%) living subjects responded to the follow up questionnaire. Of these, 25 were diagnosed at baseline as snorers (AHI <5) and 21 were diagnosed with SAHS (AHI >5). The SAHS group reported a significant improvement in ESS at follow up ($p<0.01$, effect size 0.76) with a trend towards improvement in 4/8 of the SF36 dimensions (NS). 13/21 SAHS patients reported using CPAP for >4 hours per night. Snorers showed a deterioration in mean (SD) ESS from a normal (9.3 (4.9)) to an abnormal level (10.5 (6.1)) of sleepiness (NS) and deteriorations in 7/8 of the SF36 quality of life dimensions ($p<0.05$, effect sizes from 0.47 to 0.84).
Conclusions: On an intention to treat basis, subjective levels of daytime sleepiness and maintenance of quality of life improved in SAHS patients over a prolonged period despite only moderate compliance with CPAP and often having mild disease. Snoring patients reported significant deterioration in quality of life and a trend towards worsening daytime sleepiness. Snoring patients may need to be offered treatment and/or follow up visits to ensure that there is no progression of their condition. Further studies are warranted to prospectively study snoring patients to determine their long term outcome.

1. **Scottish Intercollegiate Guidelines Network/BTS Guideline**. June 2003.

P068 VERY HIGH PREVALENCE OF SLEEP APNOEA SYMPTOMS IN PATIENTS WHO HAVE UNDERGONE ELECTIVE CARDIOVERSION FOR ATRIAL FIBRILLATION

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Introduction: Recurrent hypoxia from undiagnosed sleep apnoea syndrome (SAS) may be an independent cause of relapsed atrial fibrillation (AF) following cardioversion (DC). We used the Berlin Sleep Questionnaire to estimate the prevalence of SAS in patients who had who had relapsed back into AF following successful DC, against those who remained in sinus rhythm (SR).
Methods: Cross sectional, observational study with LREC approval. The questionnaire was mailed to a random sample of 143 (still living) patients who had undergone electrical DC for AF between 2000 and 2005. None had known SAS. Possible confounders on AF were noted. Failed DC was defined as being back in AF at 3 months (cardiology) review or the need for repeat DC up to the end of 2005.
Results: 49% (n = 70) responded. Responders were similar (p = NS) to non-responders in baseline characteristics (see below). 54% (38/70) of all responders had a Berlin Score of ''medium to high risk'' for SAHS. The table compares Berlin scores in the sub-groups of responders who were otherwise also matched for confounders for AF (age, gender, smoking status, weight, blood pressure at DC, duration of AF, presence of valvular heart disease, left atrial size, DC energy required (joules), and initial DC success rates).
Conclusions: The risk of SAS, as estimated using the Berlin Sleep Qnr, is similar in those whose AF relapsed to those who remained in SR. However, we were surprised by the background potential of undiagnosed SAS in these patients undergoing elective DC. At least 27% (38/143) scored ''Medium to High risk'' and so fulfilled the Berlin Sleep Qnr criteria for sleep studies. A prospective study, objectively screening people for SAS prior to DC would clarify this.

Abstract P068

	High risk SAHS	Medium risk SAHS	Low risk SAHS
Failed DC (n = 49)	17%	37%	47%
Successful DC (n = 21)	20%	34%	47%
p Value (χ^2)	0.76	0.58	0.99

P069 INVESTIGATING TIME WITH SIGNIFICANT NOCTURNAL DESATURATION AGAINST SLEEP APNOEA MARKERS POSSIBLY PREDICTING SLEEP RELATED PULMONARY HYPERTENSION

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Background: Although thought to correlate with the magnitude of gas exchange abnormalities, pulmonary hypertension (PH) associated with hypoventilation syndromes was initially considered rare in the absence of daytime hypoxaemia; additionally, it had been suggested that the severity of nocturnal events assessed as the apnoea/hypopnoea index (AHI) do not appear to be the determining factor with more in favour of the severity of obesity and possibly coexistent respiratory disease. A recent study (*Eur Soc Cardiol* 2006), however, has again shown that severe obstructive sleep apnoea (OSA) is independently associated with pulmonary hypertension in direct relationship with disease severity and presence of diastolic dysfunction and importantly that continuous positive airway pressure therapy (CPAP) reduces the pulmonary systolic pressure levels.
Aims: We aimed to study if there are any correlation of time with significant nocturnal desaturation against sleep apnoea markers and its potential value as a predictor for developing significant pulmonary hypertension.
Methods and Results: We have therefore investigated patients newly diagnosed with any grade of sleep apnoea with the aim of identifying the prevalence, severity, and distribution of associated nocturnal hypoxia (as a potential surrogate marker for developing pulmonary hypertension). Mean (SD, range) age for the 156 successive patients diagnosed on overnight polysomnography was 52.1 (12.6, 19–81) years. Of these, 28.7% had mild disease (AHI 5 to 14), 43.3% had moderate disease (AHI 15 to 29), and 27.4% had severe disease (AHI 30 and above). Arbitrarily taking a threshold at oxygen saturation of <90% for >10% of the time, 105 (66.9%) remained above this and 51 (32.5%) below; these two groups then differed statistically (both $p<0.001$) considering age (49.6 *v* 57.2 years) and AHI (20.8 *v* 33.8) but not with Epworth score or BMI. Regression analysis similarly showed a poorly fitted model.
Conclusions: (1) Highlight the distribution of sleep apnoea patients with the potential if left untreated of developing significant pulmonary hypertension and (2) recognise that the magnitude of the amount of hypoxia correlates poorly with Epworth scores.

Diagnostic methods in tuberculosis

P070 INCORRECT DIAGNOSES OF TUBERCULOSIS USING LIQUID CULTURE MEDIUM: LESSONS TO BE LEARNT

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Introduction: A positive culture of *Mycobacterium tuberculosis* (*Mtb*) is normally taken as evidence of active disease. Liquid culture medium has revolutionised the diagnosis by providing rapid culture results (median in our laboratory nine days, range 3–16 days). However, the high sensitivity of the test may occasionally result in adverse clinical consequences.
Background: When setting up cultures for mycobacterium on 25 October 2005, a vial of antibiotic/growth supplement became contaminated with a splash of fluid containing *Mtb*. Subsequently, 11 patient samples, acquired between September and October 2005, became falsely culture positive, with a genotype identical to the contaminating species. We have looked at the clinical effects.
Methods: Eleven sets of notes were reviewed. Patient age, sex, consultant, date and type of sample, smear result, and date of culture report were recorded. Information regarding subsequent TB treatment included reason for treatment, duration of therapy and reported side effects. Information given to the patient, documentation, HIV testing, and contact tracing were also recorded. Complaint and communication issues were noted.
Results: Eleven patients (aged 21 to 78 years; 6 male). Five tests were requested by respiratory consultants, two by infectious diseases, one by thoracic surgery and three by other departments. Four sputum samples, two BAL fluid, one spinal abscess fluid, two pleural fluid and two soft tissue biopsy samples were affected. All smears were negative. Five patients were treated for TB with standard therapy, six were not. One patient developed significant treatment side effects. One patient subsequently died of undiagnosed pulmonary embolus. One patient

had an HIV test after the false positive TB result. Two patients had contact tracing performed (one extensive due to a large family). Of the five treated for TB, three were treated on the basis of the contaminated result only, the other two also had a high clinical suspicion for TB. When the result was found to be a contaminant, three patients had their unnecessary treatment stopped, after 8 days, 20 days, and 21 days. In all five patients treated, events were recorded in the notes, but discussion was recorded in only two. Of the six patients in the untreated group, four were not treated because TB was clinically unlikely and in two the positive result appeared not to have been noticed by the clinician, having been filed unsigned or not recorded in notes. Four patients were told of the contaminated result, two were not. There are no recorded complaints from any of the 11 patients.
Conclusion: Contamination of antibiotic/growth medium had significant clinical impact. The laboratory has now changed the processing method. Clinicians should be aware that the high sensitivity of liquid culture may occasionally cause confusion and results should be interpreted by a clinician experienced in tuberculosis.

P071 THE USE OF T-SPOT-TB TO ESTIMATE TB REACTIVITY RATES AMONG HEALTHCARE WORKERS ATTENDING THE BTS WINTER CONFERENCE 2005

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Introduction: T-SPOT *TB* is a diagnostic assay which enumerates T cells specific for antigens secreted by *Mycobacterium tuberculosis* but not by *Mycobacterium bovis* bacille Calmette-Guerin (BCG) strain or the majority of non-tuberculous *Mycobacteria*. The test is intended as an aid to the diagnosis of both active and latent forms of tuberculosis (TB) and is recommended for use in the detection of latent TB infection within the most recent NICE Guidelines. It has been extensively validated and is establishing widespread use in diverse clinical settings such as preventative TB screening amongst immunocompromised patient groups, contact tracing and occupation health related TB screening.
Methods: At the BTS Winter meeting 2005 a survey of healthcare professionals was undertaken to estimate the latent TB infection rate amongst this cohort using the T-SPOT *TB* assay. A brief medical history was taken from a total of 44 consenting volunteers attending the meeting, including age (range 21–78 years), gender (50:50 male:female), country of birth, ethnicity, BCG status, history of previous skin testing, previous diagnosis of active TB, and estimated years of exposure to TB infected patients. An 8 ml blood sample was drawn and sent for analysis by T-SPOT.*TB*.

Of the 6/44 (13.6%) that tested positive for latent TB, all 6 had a previous positive skin test and 5/6 (83.3%) recorded extensive occupational exposure to active TB cases. Within the full cohort 36/44 had both a T-SPOT *TB* result and recorded a skin test result.
Results: None (0/36) of the samples were T-SPOT *TB* positive but skin test negative; none of the cohort reported any current immunosuppressive therapy or condition. Of the 14/36 (38.9%) of samples that were T-SPOT *TB* negative but skin test positive, 12/14 (86.0%) reported as being BCG vaccinated, 1/14 (7.1%) reported as receiving 6 skin tests.
Conclusions: T-SPOT *TB*, in comparison to the skin test, offers the potential to more accurately detect latent TB infection in healthcare workers particularly in a setting of BCG vaccination, placement of repeated skin tests and exposure to TB patients.

Abstract P071

	T-SPOT +ve	T-SPOT −ve	
TST +ve	6	14	55.5%
TST −ve	0	16	44.5%
	16.7%	83.3%	

P072 WHICH PATIENTS WITH TUBERCULOSIS ACCEPT AN HIV TEST?

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Background: Colleagues from north London, UK observed that many tuberculosis (TB) patients were not being offered an HIV test. Furthermore, they observed a particular problem for patients diagnosed in out-patient clinics compared with those diagnosed on the wards.(Dart, *et al. Thorax* 2006) Here we report results of HIV test offering and acceptance at a south London hospital.
Methods: All patients diagnosed with TB at Kings College Hospital after 2001 and before 2006 were eligible for inclusion. Patients were identified from our database that included fields for whether an HIV test had been offered, whether it had been accepted and the result. The place of diagnosis and ethnic group was also recorded. HIV tests are offered with supportive counseling on the ward and by trained TB nurses in clinic. TB nurses undertake regular reviews of who has been offered an HIV test, an activity supported by computer generated lists.
Results: Of 422 TB patients, 395 (93.6%) were offered a test, 294 (69.7%) accepted and 85 (20.1%) of all TB patients tested HIV positive.
Conclusions: Our methods result in more than 90% of patients being offered an HIV test. Fewer patients accept a test, but test acceptance appears to reflect the underlying epidemiology of HIV infection. Clinician pressure may be a significant factor in the acceptance of HIV tests by TB patients.

P073 THE CLINICAL SPECTRUM OF ADULT TUBERCULOSIS: A UK PROSPECTIVE STUDY

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Background: Clinicians may not consider a diagnosis of tuberculosis (TB) unless a patient has systemic symptoms such as fever, sweats, and

Abstract P072 HIV testing for patients with tuberculosis aged >15 and ⩽65 years at Kings College Hospital diagnosed between 2002 and 2005

	Offered test	Accepted test	HIV positive
Place of diagnosis			
Outpatients	242/262 (92%)	170/262 (65%)	36/167 (22%)
Inpatients	151/159 (95%)	122/159 (77%)	48/121 (40%)
	p=0.2*	p=0.007	p=0.001
Ethnic group†			
White	45/55 (82%)	35/55 (64%)	6/35 (18%)
South Asian	31/33 (94%)	15/33 (46%)	0/14 (0%)
Black Caribbean	40/42 (95%)	31/42 (74%)	7/30 (23%)
Black African	228/236 (97%)	183/236 (78%)	63/181 (35%)
	p=0.001	p=0.001	p=0.01
Age categories (years)			
>15 to ⩽25	76/82 (93%)	53/82 (65%)	6/53 (11%)
>25 to ⩽45	245/258 (95%)	189/258 (73%)	68/187 (36%)
>45 to ⩽65	72/81 (89%)	50/81 (62%)	10/48 (21%)
	p=0.155	p=0.085	p=0.001

Abstract P073

Site of TB	No fevers	No sweats	No weight loss	No fevers/sweats/weight loss
Pulmonary (n = 82)	27 (33%)	30 (37%)	30 (37%)	17 (21%)
Lymph node (n = 31)	19 (61%)	18 (58%)	19 (61%)	12 (39%)
Other (n = 12)	5 (42%)	7 (58%)	6 (50%)	5 (42%)
Miliary (n = 5)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total (n = 130)	51 (39%)	55 (38%)	55 (38%)	34 (26%)

weight loss; together with abnormal inflammatory blood markers. We sought to investigate whether this wisdom remained true in our ethnically diverse, metropolitan population.
Methods: Baseline demographic data and symptoms were documented for all individuals enrolled in a prospective study of paradoxical reactions. Baseline blood tests were obtained including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and lactate dehydrogenase (LDH).
Results: Symptoms were recorded for 156 individuals diagnosed with active TB, of whom 50% were female; 28% HIV infected; 59% had pulmonary TB; 54% were of black-African ethnicity, 21% Asian, and 19% Caucasian. They had a median age of 33 years (range 18–79). 130/156 (83%) were TB culture positive. Pre-diagnosis, no fever was reported in 67/156 (43%); no sweats in 66/156 (42%); and no weight loss in 72/156 (46%). All three were not present in 48/156 (31%). To exclude the possibility that those without symptoms were largely TB culture negative and therefore incorrectly diagnosed, we reviewed the culture positive cases (n = 130), as shown in the table. Of these subjects, 17% had a normal baseline CRP, 25% a normal ESR and 64% a normal range LDH. Commonly noted abnormalities were low albumin in 42%, anaemia in 54%, hyponatraemia in 30% and lymphopenia in 22%. No difference in total lymphocyte count was seen according to HIV status.
Conclusions: All forms of active TB frequently present without ''typical'' systemic symptoms or abnormal blood inflammatory markers. This finding has implications for the prompt diagnosis of TB; as well as the prevention of ongoing transmission of infection through early treatment.

P074 DIAGNOSTIC PATHWAYS IN CERVICAL TUBERCULOUS LYMPHADENITIS (CERVICAL TUBERCULOUS)

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Introduction: We examined the pathways by which the diagnosis of cervical TB was established in this hospital which serves a population with very high rates of TB (>60/100 000).
Methods: In 3 years (2003–05) 74 adults (⩾18 years) were treated for the condition. The largest ethnic group was Bangladeshi (43%) followed by Somali (21%). 40 were female and 34 male; mean age was 33.7 years (range 18–71 years). 89% were born outside the UK. Numerous specialities were involved in performing diagnostic procedures: most (60%) were done in the ENT department, but other specialists involved included radiologists, maxillofacial and general surgeons, and general physicians.
Results: Fifteen patients had a node biopsy as their first investigation (9 excisional, 6 ultrasound-guided core biopsies). Only 10/15 had microbiological samples sent, of which 9/10 were culture positive. All 15 were examined histologically, which was suggestive of TB in 13/15. Two samples with negative histology grew TB on culture. 59 patients had fine needle aspiration (FNA) as their first investigation, 32 of which were ultrasound guided. 41/59 were sent for TB culture (69%) and 25 of these 41 (61%) grew TB. 53/59 were examined cytologically. Granulomas suggestive of TB were seen in 26/53, of which 9 were also culture positive. No useful diagnostic information was obtained from 15 of the FNAs. Eight of these patients went on to biopsy, as well as 3 who had cytology suggestive of TB and one who later grew TB from the FNA. Of these 12 who had biopsy as a second line investigation, 6/11 sent for microbiology grew TB and 9/11 examined had suggestive histology. The 3 biopsies with negative or no histology grew TB on culture.
Discussion: Our investigation is of patients treated for TB, not of all those presenting with cervical lymphadenopathy, and must be interpreted with that reservation in mind. However, it does demonstrate an unsystematic approach to the investigation of nodes eventually treated for TB, with different clinical teams involved and no clear protocol for investigation. There were variations in the diagnostic investigation performed, and samples were often not sent for microbiological analysis despite a heavy local workload and experience of TB. The situation appears similarly unsatisfactory elsewhere in the UK.[1] Recent NICE guidelines give no helpful advice, and we believe the BTS should consider investigating this matter and producing recommendations for the investigation of suspected cervical TB.

1. **Tsikoudas A**. *J Otorhinolaryngol Relat Spec* 2003;**65**:261–5.

P075 DIRECT PCR EXAMINATION FOR *MYCOBACTERIUM TUBERCULOSIS* IN RESPIRATORY SAMPLES CAN BE COST EFFECTIVE

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Introduction: Identification of *M tuberculosis* (MTB) by direct polymerase chain reaction (PCR) from respiratory samples is not routinely recommended.[1] However, in view of the low specificity of tuberculin skin tests (TSTs) and the high cost of interferon-gamma (IFN-y) blood assays, direct PCR may have an important role in areas of high prevalence of environmental mycobacterial infection (EMI).
Aim: To compare the cost of direct PCR with the cost of unnecessary TB contact procedures in patients found to have EMI on culture.
Methods: All direct PCRs performed on smear-positive patients between 2004 and 2006 were reviewed and compared with culture results. Unit costs for PCR, chest *x* ray, TST, and IFN-y were estimated at £50, £11, £10, and £30 respectively. The costing model assumed at least four contacts per EMI index case[2] and a TST specificity of 50%.
Results: Smear-positive sputa from 131 patients underwent direct PCR testing and were further evaluated. 89 patients grew MTB and 42 (32%) had EMI. Sensitivity, specificity, positive and negative predictive values for direct PCR versus MTB culture were 99%, 95%, 98%, and 98% respectively. Total cost of all PCRs performed amounted to £6550. The cost of contact procedures for PCR-negative/MTB culture-negative index cases was estimated at £7760 (excluding health visitor and medical staff time).
Conclusions: Direct PCR testing of smear-positive patients is cost-effective if there is a high prevalence of EMI.

1. Roy Coll Phys, 2006.
2. *Eur Resp J* 2000;**16**:976–9.

Clinical aspects of COPD

P076 THE PATIENT AT THE CENTRE OF THEIR CARE: AN IT BASED PACKAGE FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PRIMARY CARE

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Background: New guidelines for chronic obstructive pulmonary disease (COPD) encourage early accurate diagnosis using spirometry and effective strategies at all stages of the disease. Despite financial incentives, primary care is often over-burdened and many practices find it difficult to provide COPD services.
Methods: An electronic assessment and management package devised for visiting nurses in Plymouth and North Devon, UK was used in 14 practices in Plymouth and 2 in North Devon. COPD disease registers were checked for coding errors and patients able to attend the surgery were invited. Clinical and spirometry data were entered by the nurse, patients then completed the Clinical COPD questionnaire, the MRC dyspnoea scale and the Lung Information Needs Questionnaire on the computer. The software package collated and interpreted the data, producing reports for both patients and GPs, including recommendations for management as per NICE guidelines. Individual information

needs were addressed by the nurse who provided British Lung Foundation leaflets, advice and action plans.
Results: Of 631 patients invited, 584 were seen. COPD was confirmed in 375/534 (70%) who underwent spirometry. COPD severity grading was 188/375 (50%) mild, 152/375 (41%) moderate, and 35/375 (9%) severe. Treatment according to NICE guidelines was assessed in 237 patients, 51 (21%) were on the correct drug treatment, and these tended to have mild disease. Eight patients had undergone pulmonary rehabilitation, but it was recommended in 102 patients. Oxygen assessment criteria were met by only 7/375 (2%). Multiple regression analysis showed main determinants of health status (total CCQ score) were MRC dyspnoea scale ($p<0.001$), frequency of exacerbation ($p<0.001$), lung function ($p<0.001$), and smoking status ($p<0.001$). The system proved popular with patients and primary care staff, especially the reports.
Conclusion: There is room for improvement in primary care diagnosis and treatment. IT based systems have considerable potential to help patients and support healthcare professionals. The data collected provide insights into treatment and patient centred outcomes and may provide useful markers for demonstrating quality of care.

P077 ''VOLUME RESPONSE'' TO BRONCHODILATORS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE IS RELATED BOTH TO FLOW LIMITATION AND EMPHYSEMA PHENOTYPE

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Introduction: Chronic obstructive pulmonary disease (COPD) is a heterogeneous condition with diagnosis and treatment determined primarily by clinical features and spirometry. However, different clinical, physiological, radiological, pathological, and inflammatory phenotypes exist and may allow individualised management and targeting of therapy. We hypothesised that both tidal flow limitation (TFL) and degree of emphysema are likely to represent overlapping phenotypes and will both influence response to bronchodilators.
Methods: We studied 31 subjects with moderate to severe COPD (FEV1: 1.29 (0.64)l, 47 (20)% predicted; FEV1/FVC: 0.52 (0.12)). Subjects completed lung function testing and assessment of TFL, using the forced oscillation technique, before and after 5 mg salbutamol. Emphysema phenotype (EP) was graded on a 0–15 scale based on DLCO, visual high resolution CT emphysema score and proportion of lung parenchyma at <-910Hu on HRCT. The 9 flow limited (FL) subjects had marginally higher emphysema scores than 22 non-FL (NFL) subjects: FL 8.2 (0.5) *v* NFL 7.3 (0.5); NS.
Results: FL subjects were more obstructed and hyperinflated than NFL subjects: FEV1 0.92 *v* 1.43 l; $p<0.01$, FEV1/FVC 0.43 *v* 0.55; $p<0.01$, RV 4.8 *v* 4.03 l; $p=0.13$. After the bronchodilator each group showed a similar, small improvement in FEV1 but FL subjects showed a greater volume response: ΔFVC 0.67 *v* 0.3 l; $p=0.01$, ΔSVC 0.52 *v* 0.15 l; $p<0.04$, ΔRV -0.48 *v* -0.2 l; NS. Subjects were split into two groups about the median emphysema score. Those with more emphysema (EP score 9.2 *v* 5.9) had worse lung function: FEV1 0.96 *v* 1.62L; $p=0.002$, FEV1/FVC 0.44 *v* 0.56; 0.004, IC 1.75 *v* 2.1 l; $p=0.13$, RV 4.57 *v* 3.87 l; $p=0.13$. Higher emphysema score was also associated with volume, not flow response to salbutamol: ΔFEV1/FVC -0.03 *v* 0.01; $p<0.01$, ΔFVC 0.48 *v* 0.27 l; $p=0.07$, ΔSVC 0.3 *v* 0.13 l; $p=0.13$, ΔRV -0.43 *v* $+0.04$; $p<0.01$.
Conclusions: Bronchodilator responsiveness, in particular ''volume response'' is influenced both by flow limitation and extent of emphysema, which appear to be overlapping physiological COPD phenotypes. In patients with more severe airflow obstruction, resting flow limitation and more extensive emphysema it is important that change in FEV1 is not used to gauge response to bronchodilator therapy.

P078 RELATION BETWEEN LUNG FUNCTION AND FRUIT CONSUMPTION IN SMOKING AND NON-SMOKING MEN IN NORTHERN IRELAND

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Background: Fruit consumption may have a protective effect on lung function. We tested the hypothesis that individuals with higher fruit consumption would have a better percent predicted FEV1 (FEV1%). We were also interested in the interaction with smoking history.
Methods: 10 600 French and Northern Irish men aged 50 to 59 years were recruited mainly at their place of work from 1991 to 1994 as part of the Prospective Epidemiological Study of Myocardial Infarction (PRIME). This involved a food frequency questionnaire and physical measurements including lung function by spirometry. We present a cross sectional analysis of the 1779 Northern Irish men for whom a valid spirometry trace and food frequency questionnaire had been obtained at baseline.
Results: The men had a mean age of 55 years and 32% had never smoked. The mean fruit consumption per day was one piece. The table shows that there was a significant increase in FEV1% with fruit consumption in the smokers of on average 3.66 per unit of fruit consumed but in the former and never-smokers this increase in FEV1% was only 0.9.and 0.03 per unit of fruit consumed, respectively. This difference in association between the three groups was significant ($p=0.04$). After adjustment for confounders (including education, BMI, alcohol intake, waist-hip ratio, age, physical activity, vitamin supplement use, cholesterol, height, and social status) made little difference to these findings.
Conclusions: There is a positive association between fruit consumption and lung function in smoking middle-aged men in Northern Ireland. Fruit consumption has more benefit with respect to lung function in smokers than non-smokers in this population.

P079 LUNG FUNCTION IN MID-LIFE IS A BETTER PREDICTOR OF ARTERIAL STIFFNESS THAN LATER LUNG FUNCTION: RESULTS FROM THE CAERPHILLY PROSPECTIVE STUDY

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Background: Low FEV1 and increased arterial stiffness have been shown to predict increased cardiovascular mortality over and above smoking status. We have examined whether poor lung function increases arterial stiffness in the Caerphilly Prospective Study (CaPS).
Methods: 2959 men (aged 49–67 years) were recruited between 1979 and 1988 (phases I and II). Between 2003–05, they were re-examined (phase V) to obtain measures of arterial stiffness (median follow up period 18.6 years; n=825). FEV1 and FVC data were available at baseline (n=2767) and phase V (n=1099). Arterial stiffness, was measured using applanation tonometry (SphygmoCor) to estimate aortic pulse wave velocity (APWV).
Results: At baseline, mean (SD) FEV1 was 2.77 (0.73) litres, FEV1% predicted 84.4 (20.2)%, with 462 (17%) exhibiting airways obstruction. At phase V, FEV1 was 2.25 (0.64) litres, FEV1 % predicted 82.7 (21.4)%, 583 (53%) subjects had airways obstruction. APWV was 11.5 (2.8) m/sec. Both FEV1 and FVC were inversely related to APWV, though FVC was a stronger predictor. For a one standard deviation

Abstract P078 Average increase in FEV_1% per piece of fruit consumed daily by smoking status

		Unadjusted		Adjusted	
Smoking status	n	Increase (95% CI)	p Value	Increase (95% CI)	p Value
Never	571	0.03 (−1.50, 1.50)	0.97	−0.69 (−2.16, 0.78)	0.36
Former	628	0.90 (−0.75, 2.60)	0.28	1.23 (−0.47, 2.93)	0.15
Current	580	3.66 (1.55, 5.70)	0.001	2.60 (0.51, 4.79)	0.02
Test for interaction		p=0.025		p=0.03	

decrease in FEV1 and FVC, APWV increased by 0.44 (95% CI 0.21 to 0.66, p<0.0001) m/sec and 0.55 (95% CI 0.34 to 0.77, p<0.0001) m/sec respectively adjusted for age, height, heart rate and mean arterial pressure. This was stronger than the association of APWV with serum lipids. Lung function at baseline was a stronger predictor than at follow-up. Neither FEV1/FVC ratio nor the rate of decline in FEV1 was associated with APWV. Subjects with GOLD III/IV had an increase in APWV of 1.29 (95% CI 0.48 to 2.10, p=0.002) m/sec.
Conclusions: Arterial stiffness was more strongly related to lung function measured over two decades earlier than current lung function. The development of lung function and arterial elasticity may share a common mechanism in early life. Alternatively, the determinants of lung function may have an adverse effect on arterial stiffness, which then tracks across the life course. This is one potential mechanism that may link COPD with cardiovascular disease

P080 CARDIOVASCULAR AND BONE DISEASE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Osteoporosis is associated with an increased risk of cardiovascular disease, both of which pertain to chronic obstructive pulmonary disease (COPD). We hypothesised that increased arterial stiffness, an indicator of cardiovascular risk, and osteoporosis would be associated in COPD.
Methods: Seventy five clinically stable patients and 42 age and sex matched healthy smokers (HS), both free of cardiovascular disease, underwent spirometry; dual energy x-ray absorptiometry; venous sampling for IL-6, TNFα soluble receptors (sr) I&II; and determination of augmentation index (AIx) and aortic pulse wave velocity (APWV) (Sphygmocor) as measures of arterial stiffness. Arterialised capillary pO_2 was determined in patients.
Results: Patients had a mean (SD) FEV1 56.7 (21.1) % predicted compared with 107.6 (15.9) % predicted in the HS. The AIx, APWV and inflammatory mediators were greater in patients compared with HS. Bone mineral density at the lumbar spine and hip were less in patients than HS, p<0.01 with osteoporosis more common in the patients. APWV was related to age (r=0.63, p<0.0001), Log_{10} IL-6(r=0.31, p<0.01), Log_{10} TNFα srI (r=0.27, p<0.05) and inversely with FEV1 (r=−0.43, p<0.01) and pO_2 (r=−0.34, p<0.01) in the patient group. Patients with osteoporosis of the hip had a greater APWV (13.1 (1.8) m/s) than those without (11.2 (2.7) m/s), p<0.05.
Conclusions: Increased arterial stiffness was related to airways obstruction, the presence of osteoporosis, systemic inflammation and hypoxaemia, and may explain the excess risk of cardiovascular disease in COPD. The association of increased arterial stiffness and osteoporosis suggests premature aging occurs in COPD.
Supported by GlaxoSmithKline.

Abstract P080

	HS (n=42)	Patients (n=75)
AIx	25.9±6.2	30.1±8.2*
APWV (m/s)	8.95±1.7	11.4±2.7**
IL-6 (pg/ml)	1.29±1.58	2.11±1.84**

*p<0.01, **p<0.0001.

P081 BONE THINNING: PREVALENT IN COPD BUT EARLY DETECTION ALLOWS TREATMENT OPPORTUNITY BEFORE VERTEBRAL FRACTURE OCCURS

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Introduction: Bone thinning (osteopenia and osteoporosis) predisposes to vertebral and long bone fractures. We have previously reported a high prevalence of bone thinning in COPD patients (GOLD 1-IV), compared to healthy subjects (HS).[1] We explored the prevalence of vertebral fractures in COPD patients.
Methods: We performed instant vertebral morphometric assessment (IVA) in patients with a spectrum of severity of airways obstruction (n=43), aged 67.5 (9.4) years, 26 male. None were or had been on oral maintenance corticosteroids. IVA incorporates lateral thoracic and lumbar views at the same time as the DEXA assessment of bone mineral density (BMD) (Hologic Discovery) to examine presence of vertebral fractures and grade severity. We also studied 24 gender matched HS: 62.7 (6.9) years. From the BMD, a gender specific T score is calculated.
Results: Osteoporosis (T score <−2.5) was present in 30% patients (8% HS) and osteopenia (−2.5< T score<−1) in 41% patients (23% HS), p=0.004. The presence of vertebral fractures was similar in both groups, p=0.91. Vertebral fractures were present in 8 (19%) patients (severity of fracture—6 mild, 1 moderate, 1 severe) 5 male; 6 of whom had a FEV1 <50% predicted. In 2 patients there was >1 vertebral fracture. In HS, there were 4 (17%) with vertebral fractures (all mild severity fracture, all male). The upper thoracic vertebrae (above T4) were not clearly visible. Using logistic regression with presence of vertebral fracture being the dependent; age, BMD lumbar spine, gender and FEV1% predicted were inputted as variables. Only FEV1% predicted was a significant variable, p=0.023.
Discussion: This study reinforces the need to identify osteoporosis in patients with COPD, where prevalence is increased as there is a therapeutic opportunity before vertebral fracture occurs.

1. Bolton CE, *et al. AJ RCCM* 2004.

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P082 OUTDOOR ACTIVITY AND DEPRESSION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Loss of independence in chronic obstructive pulmonary disease (COPD) is associated with increased disease severity, reduced quality of life, and increased anxiety (Okubadejo *et al. Eur Respir J* 1997;**10**:1572–5). We have studied the relationship between the amount of time spent outdoors and depression in patients with COPD.
Methods: We studied 96 patients (57 male) with COPD from May to July 2006; mean age 70.3 years (SD 8.4), FEV1 1.21 l (0.61), FEV1 % predicted 47.4% (20.2), BMI 26.2 kg/m^2 (6.3) and smoking history 47.7 pack years (30.1). All patients completed a Center for Epidemiologic Studies Depression scale (CED-20) when clinically stable. Over the study period 43 patients completed a St. George's Respiratory Questionnaire (SGRQ) and 55 patients returned diary cards on which they recorded the hours spent outdoors each day. SGRQ scores, average hours outside and lung function were related to the CED-20.
Results: We found a relationship between higher Total scores on the SGRQ (that is, lower quality of life) and increased depression (r=0.46; p=0.002). Higher Activity and Impact domains of the SGRQ were associated with higher CED-20 scores (r=0.44; p=0.004 and r=0.43; p=0.004, respectively). However, there was no statistically significant relationship between the Symptom scores on the SGRQ and depression (r=0.24; p=0.12). CED-20 scores correlated inversely with the amount of time spent outside indicating greater depression in the more housebound patients (r=−0.28; p=0.04). There was no relationship between FEV1 or FEV1 % predicted and depression (r=0.01; p=0.93, and r=0.14; p=0.18 respectively).
Conclusions: This study suggests that higher CED-20 scores in COPD are related to reduced outdoor activity and health related quality of life. We did not find a direct relationship between depression and FEV1. These findings suggest the importance of identifying depressive symptoms in COPD patients, in particular when undergoing exercise training, so that optimal benefits can be achieved on outdoor activities.

P083 EDUCATION FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IS VARIABLE AND POORLY TARGETED: SELF-MANAGEMENT AND EXERCISE ARE NEGLECTED

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Background: To manage their disease, patients with chronic obstructive pulmonary disease (COPD) may need to modify their behaviour as

Abstract P083

Domain	Adequately met score =0–1	Fully met score =0
Disease knowledge	103/340 (30%)	26/340 (8%)
Medicines	284/339 (84%)	155/337 (46%)
Self-management	26/337 (8%)	100/337 (3%)
Smoking	317/339 (94%)	228/339 (67%)
Exercise	99/340 (29%)	41/340 (12%)
Diet	153/339 (45%)	20/339 (6%)

smoking, exercise, medication and self management can all impact on outcomes. We examined the information needs of patients in Devon recruited in primary care using the Lung Information Needs Questionnaire (LINQ). There are six domains (disease knowledge, medicines knowledge, self-management, smoking, exercise, and diet).
Methods: An electronic assessment and management package was devised for use by visiting nurses in 16 practices in Devon, UK. In a comprehensive assessment, data collected included spirometry, clinical data and questionnaires: LINQ, Clinical COPD questionnaire, MRC dyspnoea scale.
Results: Data were obtained from 375 patients with confirmed COPD and LINQ was completed by 340. The domain score disease knowledge was correlated with disease severity—those with more severe disease had been given more information: Pearson coefficients with FEV1% expected were 0.22, $p<0.001$; MRC dyspnoea scale −0.20, $p=0.001$; total CCQ score −0.26, $p<0.001$.

In some areas information needs were well met—in current smokers 93% had been advised to stop smoking and 80% had been given practical help such as nicotine therapy. Only 7% were confused about their medication and 93% tried to take their medication exactly as prescribed. However, written action plans were given to 56/335 (17%), and were provided less often to those most at need, only 2/25 (8%) with A&E attendances and 4/25 (16%) of those admitted in the last year. Only 5/24 (21%) with hospital admissions knew when to call an ambulance. For exercise, 29% had information needs adequately met, but for the most breathless (MRC grade 4 and 5) the figure was only 20%. For diet, those with low BMI (<20) are at greatest risk, of these 55% had been told nothing about diet.
Conclusions: Education for patients with COPD is important to the patients and may affect outcomes. In this study, it appears that smoking and medicines information needs are well met, but self-management and exercise are poorly focused on those with greatest need.

P084 RANDOMISED CONTROLLED TRIAL OF NURSE-LED BREATHLESSNESS INTERVENTION TO IMPROVE THE MANAGEMENT OF BREATHLESSNESS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AT A DISTRICT GENERAL HOSPITAL

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Introduction: We report a single centre, prospective, randomised control trial, involving 51 patients with confirmed chronic obstructive pulmonary disease (COPD), in whom therapy had been optimised and breathlessness remained a predominate symptom. Patients were assigned to receive either four 30-minute consecutive weekly sessions in the clinic, with interventions consisting of strategies to manage breathing control, psychosocial support and relaxation techniques, or routine care in a COPD nurse specialist clinic.
Measurements: Primary outcomes were dyspnoea, emotional function, fatigue, and mastery, as measured by the self-reported Chronic Respiratory Questionnaire (CRQ-SR). FEV1, functional status, exercise capacity by shuttle walk, Borg scores, and oxygen saturation, at baseline, 1 and 6 month post intervention were also measured.
Results: Borg scores on exertion decreased within both groups at one month., whereas paradoxically, Borg scores at rest increased within both groups. Other results are shown in the table.
Conclusion: The breathlessness intervention was associated with a small improvement in dyspnoea and fatigue (CRQ-SR) at 1 month, and in dyspnoea at 6 months, compared to conventional treatment, but the results were not statistically significant. There was no change in FEV1 or shuttle walk distance. The breathlessness intervention was popular with patients and warrants a larger multicentered, better powered study, to assess its benefits.

P085 ICATS CHRONIC OBSTRUCTIVE PULMONARY DISEASE REFERRAL TRIAGE AND CLINIC OUTCOMES AUDIT

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At last year's winter BTS meeting we presented an audit of the first three months of the Stockport COPD ICATS (Tier 2) service. We now present an audit of the activity of the Stockport COPD Tier 2/ICATS clinic in the first year of its existence. The multidisciplinary team consists of a GPwSI, Specialist nurses, physiotherapist, pharmacist and respiratory physiologist. The clinic runs once a week in the PCT's recently opened ICATS centre.

All GP referral letters to the Respiratory service are triaged by the team. If Choose and Book is used by the GP, the default position is for an ICATS triage. The team decides to either continue with a secondary care referral or send an appointment for the ICATS clinic. (Criteria for ICATS include Known COPD, age >40, current or ex-smoker, diagnostic uncertainty)

Between April 2005 and April 2006 392 letters were triaged. 118 (36%) were felt to be suitable for ICATS review, 211 (64%) continued to secondary care. 90 patients were seen in the ICATS clinic (the remaining 28 are yet to be seen or have failed to attend their first appointment and have been sent a second). Of the 90 patients seen: 52 (58%) were seen once, assessed, and returned to their GP's care with a treatment plan and reference to national and local guidelines. 26 (29%) were seen between 2 and 3 times, pending results of simple investigations etc before being discharged to their GP's care as above. Seven (8%) were referred on to secondary care respiratory physicians; (2 with ?bronchiectasis, 2 with haemoptysis, 1 with rapid weight loss, 1 with Alpha-1 Anti-trypsin deficiency, 1 with abnormal CXR). Five (6%) were referred to non-respiratory secondary care; (3 to cardiology with aortic valve disease, unstable angina, heart failure; 2 to ENT with post-nasal drip).

Thus, 87% of the patients triaged to ICATS were managed successfully by the multidisciplinary team in the ICATS setting.

Abstract P084

	Baseline mean (SD)		Change mean (SD) 1 month			Change mean (SD) 6 month		
	Contr (n=26)	Treat (n=25)	Contr (n=22)	Treat (n 22)	p Value	Contr (n 25)	Treat (n 24)	p Value
CRQ Dy	2.33 (0.85)	2.15 (1.01)	0.68 (1.04)	0.88 (1.24)	0.56	0.22 (1.06)	0.55 (1.16)	0.30
CRQ Em	4.02 (1.03)	3.79 (1.49)	0.70 (1.29)	0.73 (1.00)	0.92	0.02 (1.11)	0.20 (1.00)	0.55
CRQFa	3.33 (1.15)	3.27 (1.07)	0.26 (0.99)	0.49 (1.16)	0.49	−0.15 (1.15)	0.03 (1.03)	0.56
CRQ Ma	3.75 (1.18)	3.95 (1.53)	0.83 (1.24)	0.77 (1.18)	0.88	0.29 (1.21)	0.36 (1.09)	0.82
FEV1 l	1.05 (0.54)	1.23 (0.60)	0.11 (0.27)	−0.09 (0.23)	0.02	0.01 (1.21)	−0.01 (1.09)	0.81
SWT (m)	167.50 (131.03)	202.80 (128.24)	31.43 (71.52)	29.47 (46.48)	0.92	8.95 (67.98)	−5.00 (45.85)	0.44

P086 VARIATION OF MOODS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND EFFECTS OF LONG TERM ANTIDEPRESSANTS TREATMENT ON MOODS

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Background: Anxiety and depression has a significant impact on hospital admissions in a number of elderly chronic obstructive airways disease (COPD) patients. We are currently conducting the SOMIC study to assess variation of moods in COPD patients from stable state and the time of hospital admission with exacerbations. We are also trying to review the effects of long term antidepressants on moods in COPD.
Methods: Hospital Anxiety and Depression Scoring methods (HADS) was used to assess level of anxiety and depression in 79 COPD patients above 60 years of age during hospital admission with an exacerbation, initially within 3 days of admission repeated again at the time of discharge and then in a stable state. Scores of 8–10 were considered moderately anxious or depressed above that value to have severe form of mood changes. Score variations from 0–21. We specifically looked at a small group of patients who were already taking antidepressant treatment for a longer time period before entering the study. The aim of the exercise was to review any useful impact of the treatment on moods in these patients. As long term compliance with antidepressants for COPD patients has noted to be not very good and difficult as reported from previously published trials.
Results: A total of 79 COPD patients' moods were assessed. They had a mean age of 72 years (SD 7.3, range 60–93 years) and 54 male patients (68%). 71(90%) patients had a strong smoking history. Mean depression scores at admissions were noted to be: 7.7 (4.0), 7.1 (4.3), 7.5 (4.7) Mean anxiety was 8.6 (4.3), 6.9 (4.9), 6.4 (4.5) Among these patients, five patients (7%) were on long term antidepressant treatment and their individual Depression scoring on HADS scale were: 11, 7, 13, 10, 12 respectively with a mean HAD score of 10.6 and their mean time on antidepressant treatment was around 13 months. The above HAD score values suggests that severe depression in COPD patient may not show improvement with long term usage of antidepressants in severe forms of depression.
Conclusion: There is some evidence to suggest anxiety was slightly higher at admission but decreased at discharge and in the outpatients. Depression on the other hand remained constant over the three time periods. Long term antidepressants treatment in severe depression may not improve depression levels in COPD patients. As the number of COPD patients on long term antidepressants were low in the study so it is difficult to draw any conclusions but certainly trials with larger numbers of patients on long term antidepressant treatments are needed to assess this further.

P087 DOES THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH PROVIDE AN APPROPRIATE MODEL FOR IDENTIFYING OUTCOME MEASURES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE?

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Introduction: The World Health Organization's International Classification of Functioning, Disability and Health (ICF) provides a common framework for health outcome measurement (Cieza A, *et al. J Rehabil Med* 2004). This study aims to investigate whether the ICF specific core sets for obstructive pulmonary diseases (ICF OPD) (Stucki A, *et al. J Rehabil Med* 2004) aids in the identification of outcome measures to assess the effect of pursed lip breathing (PLB) in stable COPD.

Abstract P087

ICF Category	ICF OPD area (number)	Symptom areas of COPD potentially affected by PLB
Function	Respiratory (b440)	DH and RR (1)
	Emotional (b152)	Anxiety (2)
	Exercise tolerance (b455)	Exercise capacity (3a)
Activities	Carrying out daily routine (d230)	Breathlessness (4)
	Walking (d450)	Exercise capacity (3b)
Environment (Barrier −) (Facilitator +)	Air quality (-) (e260)	Symptom mastery (5)
	Products and substances for personal consumption (+) (e110)	Pattern of medication usage (6)

Method: Search of the literature identified 17 preclinical studies, 3 clinical trials, and 6 reviews relating to PLB. Grade B evidence suggests that PLB reduces respiratory rate (RR), increases tidal volume and improves arterial blood gases in COPD (Dechman G, Wilson CR. *Phys Ther* 2004). PLB may also reduce breathlessness through reduction in dynamic hyperinflation (DH) and/or improvement in mastery of symptoms. These findings were applied to the ICF OPD to generate outcome measures for a clinical study of PLB in stable COPD.
Results: Six discrete symptom areas of COPD, potentially remediable by PLB, were identified (numbered in table). Appropriate outcome measures were then defined: change in inspiratory capacity and RR on exercise (1), Hospital Anxiety and Depression Scale (2), Chronic Respiratory Disease Questionnaire (3a, 4, 5), endurance shuttle walk test (3b), medication usage (6).
Conclusion: The ICF OPD proved a useful tool for identifying a broad and comprehensive range of outcome measures for studying PLB in COPD. Use of the ICF OPD at the design stage of a clinical trial may improve the potential for identifying positive clinical benefits of an intervention, which might otherwise be missed

P088 IMPACT OF THE FIRST NATIONAL CHRONIC OBSTRUCTIVE PULMONARY DISEASE AUDIT ON A BUSY DISTRICT GENERAL HOSPITAL

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The Royal College of Physicians carried out a national audit of chronic obstructive pulmonary disease (COPD) in 2003. It involved all 238 acute NHS hospitals in the UK. It collected demographic and clinical information about patients hospitalised with an exacerbation of COPD. Readmission rates and 90 day mortality were also collected. The audit provided a snap shot of COPD care in the UK and allowed NHS trusts to compare themselves against this National standard. Our hospital, a 620 bedded busy district general hospital (DGH) contributed 39 patients to the previous audit. The outcomes of the audit were used to support the continuing development of our assisted discharge team. We were disappointed that the use of NIV was relatively low and this has been addressed through further education within the trust. We repeated the audit to review the effectiveness of our COPD services and changes made since the previous audit.

The audit was done using the Royal College COPD audit collection tool as in 2003. We studied 38 consecutive admissions with COPD exacerbations from January 2006. Patients were identified from

Abstract P088

	2006	2003	National data 2003
Mean age at admission (years)	75	72	71
How many had previous admissions	13%	26%	64%
How many were readmitted (90 days)	5%	5%	27%
How many are still alive	92%	87%	84%
Seen by respiratory consultant/nurse	63%	46%	70%
Median hospital stay	6 days	7 days	6 days
Ventilatory support for pH <7.35	100%	63%	37%

discharge coding information. 56 possible patients were identified, 18 were excluded as their admission was not due to COPD.

We demonstrated a low readmission rate in 2003 and this was confirmed again in the current audit. The low readmission level is maintained in spite of a relatively elderly population of which 60% have significant comorbidity. There also has been an improvement in mortality and reduction in median hospital stay by 1 day. All 8 patients with respiratory acidosis received NIV. In 2003 this figure was only 63%.

We conclude that the first National COPD audit was very helpful in supporting and guiding development of COPD services. Repeating the audit has helped us assessing the impact of further changes and is a very useful tool to demonstrate the effectiveness of supported discharge teams in COPD. In times when ineffective services are at risk of being cut it is timely to be able to demonstrate and continue to demonstrate that a service works.

P089 EVALUATION OF AN INNOVATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE CARE IN AN INNER LONDON HOSPITAL: RESULTS OF A QUALITATIVE STUDY

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Introduction: Recent systematic reviews have suggested that early discharge schemes are safe for selected patients with chronic obstructive pulmonary disease (COPD). However there is little information on patients' understanding, perceptions or experiences of this new model of care. Here we present findings from the first qualitative evaluation of a respiratory supported early discharge scheme (REDS) for COPD patients from patient's and hospital staff perspective.
Aim: To explore patients' experiences and staff's views of a recently introduced SED scheme at one inner London hospital and to identify important features that could facilitate the wider implementation of supported early discharge in COPD.
Intervention: REDS was set up with external short term funding. It involved planned discharge of COPD patients from hospital within 3.5 days of admission with follow up at home (for example: inhaler technique) by trained respiratory nurses visiting daily for the first 3 days and then for a further two weeks depending on patients needs.
Methods: Qualitative study using semi-structured in-depth interviews with a maximum diversity sample of COPD patients admitted to the hospital with breathing problems, including those exposed and not exposed to the REDS scheme and hospital staff about the SED service was carried out. A grounded theory approach was used to analyse data from the interviews. A process of open coding was used to identify concepts, their properties and dimensions from the data. The 'constant comparison method' was used to refine emerging conceptual categories through comparison and searching for deviant cases. An interim analysis was undertaken where subsequent interviews could be informed by the findings of earlier ones. Nudist N6, a computer software package was used to organise the data.
Results: Forty interviews were conducted. Many patients were suffering from anxiety and/or depression. Most patients perceived that they did not have a real choice to stay in hospital. Front line staff felt that the main purpose was to keep people in their homes. Patient discharge (transport and medication pick-up) was rarely smooth or quick. Some patients found REDS nurse visits helpful, many felt that nurse visits did not bring anything new or different to their care and were not sure why the nurses were visiting. According to the staff, the SED scheme was to keep patients in the community but there was little awareness by the GPs of this service.
Conclusion: Partly because of a lack of clear objectives, ''on the ground'' supported early discharge is not working as well as could be hoped. Patients do not appear to welcome or understand this new model of care

P090 AN EVALUATION OF RELATIONSHIPS BETWEEN FATIGUE AND DEPRESSION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Subjective fatigue has recently been identified as a one of the diversified symptoms in chronic obstructive pulmonary disease (COPD). Although, little is known about potential relationships between fatigue and depression
Methods: Eleven patients with stable COPD (7 male; age 70(54–82)yrs); mean (SD) FEV1 0.85 (0.22) l, % predicted FEV1 34.9 (14.0) % , FEV1/FVC 44.9 (14.9) l, completed the Multidimensional Fatigue Inventory 20 (MFI 20), five subscale questionnaire. Depression was assessed using Hospital Anxiety and Depression Scale (HADS) (depression subscale). Higher scores reflect higher depression and fatigue in both cases. Relationships between depression and fatigue were tested using Spearman's correlation.
Results: There was a wide range of scores in MFI 20 (28–83) and HADS depression (2–12), mean (SD) MFI 20 total score 67 (16.4) and HADS depression 6.6 (3.6). There was a significant correlation between depression and total MFI 20 score, and ''General Fatigue'', ''Reduced Motivation'', and ''Mental Fatigue'' subscales of MFI 20 (table).
Conclusion: These early data suggest that in COPD patients, reduced motivation, mental fatigue, and general fatigue are strongly associated with higher levels of depression. Physical fatigue and reduced activity, however, show no association supporting the idea that fatigue is a multicomponent construct that may have varied causes.

We gratefully acknowledge the support of GlaxoSmithKline.

P091 AN OBSERVATIONAL STUDY OF PRESCRIBING FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN PRIMARY CARE

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Introduction: In South Devon there are in excess of 15 000 GP consultations and 1000 hospital admissions for chronic obstructive pulmonary disease (COPD) each year. Torbay respiratory department has attempted to rationalise COPD prescribing by establishing local guidelines for primary care management based on the recent NICE guidelines and by developing an accurate register of patients with COPD in primary care. An observational study was undertaken to examine the management of patients with COPD in primary care in the Torbay region.
Methods: We analysed data on all patients registered with COPD from five local GP practices who provided information for the Torbay COPD primary care register.
Results: In five GP practices covering 34 372 patients, 661 were diagnosed with COPD (1.9%). 53% male and mean age 70 years. 369 (56%) were treated with inhaled corticosteroids (ICS). 83% of whom were prescribed beclomethasone (BDP), with an average dose of 876 μg/d (BDP or equivalent range 100 to 4000 μg/d). 11% of patients were on combination ICS/long acting beta agonists (LABA). Very high doses of ICS were predominantly related to the use of fluticasone (FP) 32/369 (9%) (avg 2000 μg/d of BDP or equiv). 337 were prescribed salbutamol, 111 were prescribed atrovent and 159 prescribed combivent. Only 67 (10%) were prescribed tiotropium and 178 (27%) were prescribed a LABA. Eight (1%) were on home Oxygen and 65 (10%) were treated with oral prednisolone. 46 (7%) were prescribed nebulisers and 35 (5%) were taking a theophylline. 15% were on no treatment.
Conclusions: This study suggests that GPs are largely adhering to local prescribing policy. The high number of patients (56%) on ICS is greater than expected. Patients on FP (5%) were prescribed much higher doses

Abstract P090 Relation between depression (HADS depression) and fatigue dimensions (MFI 20) (Spearman's Rho)

	MFI 20 Total score	MFI 20 General fatigue	MFI 20 Physical fatigue	MFI 20 Reduced activity	MFI 20 Reduced motivation	MFI 20 Mental fatigue
HADS	0.77**	0.67*	0.40	0.09	0.72*	0.75**

*Correlation significant at the 0.05 level.
**Correlation significant at the 0.01 level.

which may be associated with a greater risk of systemic adverse effects in a vulnerable patient population who are often elderly, relatively immobile and with significant comorbidities. The risk:benefit profile for ICS is likely to be worse in this group. Currently a lower proportion of patients are treated with tiotropium than we would expect and this mitigates in favour of more education in primary care. We aim to expand the COPD database to incorporate all GP practices in the Torbay Care Trust and include spirometric data. This will provide an accurate and contemporary register of patients with COPD in primary care thereby allowing assessment of outcomes on different treatment regimes.

Clinical features of COPD exacerbations

P092 APPETITE CONTROLLING GUT HORMONE RELEASE DURING ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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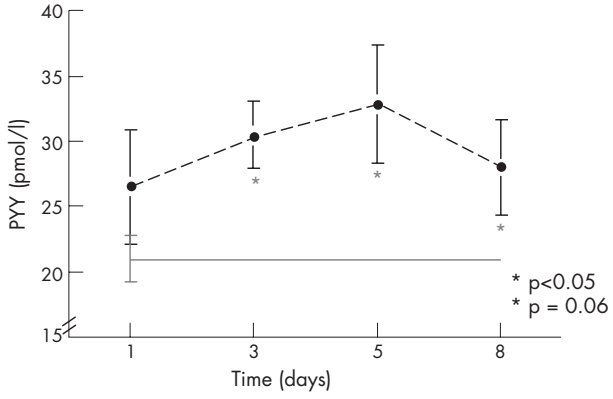
Introduction: Chronic obstructive pulmonary disease (COPD) patients with acute exacerbation suffer from an impaired energy balance due to a decreased dietary intake (Vermeeren *et al.* 1997), leading to weight loss and increased risk of malnutrition (Ergun *et al.* 2003). Nutritional support of patients during exacerbations is often difficult due to appetite loss. Cytokines have been shown to increase during this time (Schols *et al.* 1996) and may influence this appetite loss. Ghrelin and PYY are peptides released from the gut which stimulate and inhibited appetite respectively. The aim of this study was to investigate how these gut hormones change during an acute exacerbation of COPD and secondarily, to establish the relationship between gut hormones and cytokines.
Methods: Ten patients with acute exacerbation of COPD (mean (SEM): 74.5 (2.4) yrs, BMI 24.6 (1.6) kg/m^2, 4 male) underwent fasting blood sampling on days 1, 3, 5, and 8 of hospital admission to measure plasma concentrations of ghrelin, PYY, IL-1β, IL-6, and IL-8. Changes in food intake, biochemical and anthropometric markers of nutritional status were recorded. A comparison was made to 10 matched healthy controls (75.0 (2.9) years, BMI 25.3 (1.6) kg/m^2).
Results: Compared to healthy subjects, COPD patients exhibited a higher PYY level during the stay (day 3; 30.5 (2.6) pmol/l, $p<0.05$, day 5; 32.9 (4.6) pmol/l, $p<0.05$, day 8; 28.0 (3.7) pmol/l, $p=0.06$ *v* 20.7 (1.8) pmol/l) (see fig). There was no significant difference in ghrelin concentrations between patients and control subjects on day 1, 3, 5, and 8. All measured cytokines were significantly higher in patients with COPD compared to the normal range of theses cytokines, however no correlation between either PYY or ghrelin and any cytokine was found, but this is most likely due to a small sample size. Patients took half of their energy requirement on day 3. Anthropometric and biochemical indices pointed to deterioration during exacerbation ($p<0.05$).



Abstract P092 Pattern of fasting plasma PYY (mean (SEM)) during acute exacerbation of COPD patients compared with healthy age and body mass index matched control group.

Conclusions: These data suggest PYY concentrations are elevated in COPD exacerbations but ghrelin remains unaltered. PYY inhibits appetite and so this may explain the suppressed appetite commonly seen in this group of patients. Cytokines, IL-1ß, IL-6, and IL-8, all increase during acute exacerbation of COPD and may contribute to alterations in metabolic status during inflammatory stress in this disease. Further research is needed to establish whether increases in cytokines are related to increased PYY.

P093 CHEST RADIOGRAPH IN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: The chest radiograph is an important diagnostic tool and is performed routinely in most patients with exacerbation of chronic obstructive pulmonary disease (COPD). This study was performed to determine the prevalence and pattern of clinically significant abnormalities on the CXR and their impact on mortality in patients with exacerbation of COPD.
Patients and Methods: Retrospective study of 324 patients admitted with diagnosis of exacerbation of COPD to the medical assessment unit of Aberdeen Royal Infirmary between April 2004 and September 2005. Patients who had concomitant diagnosis of congestive cardiac failure, required intubation or noninvasive ventilation at admission or had mortality within 48 hours of admission were excluded. Only the first CXR (portable/departmental) performed at admission was considered. Clinically significant abnormalities were defined as presence of consolidation/patchy infiltrates, pulmonary oedema, pneumothorax and previously undiagnosed mass lesion. Data about the patients and reports of the CXRs were obtained from the computerized database.
Results: Mean age of patients was 66.2 years (SD 16.4); 173 (53.4%) were males. CXR was performed at admission in 311 patients (96%). Clinically significant abnormalities were noted in 125 patients (40.2%). These were infective (consolidation/patchy opacities) in 90 (28%), pulmonary oedema in 28 (9.0%) and previously undiagnosed mass lesion in 7 patients (2.2%). All the seven patients with mass lesion were evaluated with CT thorax and lung cancer was confirmed in 4 patients. Pulmonary oedema was clinically not suspected in 19/28 patients (67.8%). Chest radiograph was reported as normal in 37 patients (11.8%). Chronic changes related to COPD were found in 149 patients (48.0%). Mortality at 7 days was 4% (13/324) and all these deaths occurred in patients with infective changes on the CXR ($p<0.001$).
Conclusions: This study reveals high yield of clinically significant abnormalities on the CXR in patients with exacerbation of COPD. CXR helps in diagnosing coexisting pulmonary oedema, when it is clinically not suspected. There is significantly higher mortality in patients who have radiological evidence of infection in this group of patients.

P094 DIFFERENCES BETWEEN SMOKERS AND EX-SMOKERS IN SEVERITY AND MECHANISMS OF INFECTIOUS EXACERBATIONS

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Background: Exposure to cigarette smoke can influence an array of inflammatory and defense mechanisms in the lungs, including those to viral and/or bacterial infections. Following a pilot study of current smokers and ex-smokers (>1 year abstinence) which noted that current smokers had more severe COPD exacerbations, we embarked on a properly powered study to test the hypothesis that current smoking, compared with ex-smoking, leads to more severe and prolonged infectious exacerbations of COPD, with a greater degree of inflammation within the airways which is due to reduced neutrophil responses to the infectious agents.
Methods: We have so far assessed the first 25 (9 ex-smokers) of the planned 60 total patients to be recruited admitted to Southampton General Hospital with acute infectious exacerbations of COPD. Exacerbation was defined by the following symptoms for at least 2 consecutive days: 2 or more of 3 major symptoms (increase in dyspnoea, sputum purulence or sputum volume) or any 1 major symptom together with any 1 of the following minor symptoms: increased nasal discharge, wheeze, sore throat, cough or fever. Other causes of dyspnoea/admission (eg cardiac failure, inability to cope and pneumonia) were excluded. Throughout the exacerbation FEV1, FVC, and IC were measured by handheld spirometer from day 1 to 7. Neutrophil activation markers were analysed in peripheral blood and sputum.

Abstract P094

	Mean (l)	SEM	Significance p value
FEV1 Current smokers	0.057	0.027	0.003
FEV1 Ex smokers	0.370	0.083	
FVC Current smokers	0.096	0.041	0.007
FVC Ex smokers	0.267	0.059	
IC Current smokers	−0.005	0.047	0.002
IC Ex smokers	0.333	0.075	

Results: Ex-smokers recovered more quickly than current smokers (see table for mean (SEM) increase in spirometry from admission to day 7) and required fewer hospital days than current smokers. Using flow cytometry, we observed increased expression of adhesion molecule CD11b and decreased expression of activation marker CD66b in sputum of smokers; in blood the opposite profile was observed. This suggests increased recruitment of neutrophils in smokers but their reduced state of activation.
Conclusion: Current smoking is a risk factor for more severe exacerbations, requiring longer to recover and prolonged hospitalization. This might result from inadequate neutrophil defenses.
S Bourne was funded by the Ministry of Defense.

P095 EXACERBATION FREQUENCY AND DECLINE IN FEV1 IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH AND WITHOUT DIABETES

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Introduction: In chronic obstructive pulmonary disease (COPD), faster FEV1 decline is also associated with higher levels of airway and systemic inflammatory markers. Hyperglycemia can promote inflammation leading to higher levels of TNFa, CRP, and oxidative stress. Whether in COPD patients, the presence of diabetes hastens lung function decline is unknown.
Methods: We examined 219 COPD patients enrolled in the London COPD cohort. Patient characteristics were recorded at recruitment and FEV1 measured every 3 months. The study took place over 10 years, with the average patient recording data for 3.09 years (range 1.0–9.73).
Results: 4.6% (10/219) of patients had a history of diabetes. The diabetic patients were on average 19.3 kg heavier ($p=0.0015$) with a BMI of 33.0 kg/m^2 (SD 4.32) and were taking a lower beclomethasone equivalent daily dose of inhaled steroids (200 μg (IQR 0–750) vs 1000 μg (IQR 500–1600; $p=0.0197$). They had a higher FEV1 at recruitment 1.61 l compared to 1.11 l ($p=0.0016$) but no significant difference was seen in their annual exacerbation rate (1.98 (IQR 0.61–3.19) per year compared to 2.30 (1.03–3.59) per year; $p=0.718$) or whether they smoked or not (2/10 compared with 77/205; $p=0.261$). The diabetics were more likely to have a history of ischaemic heart disease 40% (4/10) compared with 16% (33/206) ($p=0.049$). Generalised least squares random effects models (4433 observations on 212 patients) with adjustment for whether FEV1 was recorded at exacerbation or not, current smoking status and its effect on decline and FEV1 at recruitment, showed that FEV1 fell by 27.7 ml per year (95% CI 31.5 to 23.9) in non-diabetic patients ($p<0.0001$). In diabetics, FEV1 fell by 7.0 ml per year which was not significantly different from the non-diabetics. ($p=0.152$). For both groups, FEV1 declined faster in smokers by 6.2 ml/year ($p=0.044$). FEV1 as % predicted was also not different between diabetics and non-diabetics ($p=0.134$).
Conclusion: This study has shown that diabetic COPD patients have a similar rate of FEV1 decline as non-diabetic COPD patients.

P096 PAYMENT BY RESULTS, THE TARIFF AND VIRTUAL EARLY SUPPORTED DISCHARGE

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Acute admissions for chronic obstructive pulmonary disease (COPD) exacerbations account for over 1 million bed days per annum in the UK, with estimated direct costs of over £490 million.[1] Early supported discharge (ESD) is possible in selected patients with no adverse effects on outcome.[2] Under Payment by Results, the Department of Health's National Tariff for each uncomplicated COPD admission >48 hours is £1709 and £342 (20%) for each admission <48 hours. The local tariffs, corrected for Market Forces Factors, are £1925 and £385 respectively.
Methods: A prospective ESD feasibility study was performed as part of the business planning process to develop this service. Two Respiratory Specialist Nurses working 9am–5pm, Monday–Friday described a ''virtual'' ESD scheme to 100 consecutive COPD patients admitted with an exacerbation from 1 October 2004. Standard exclusion criteria were used to identify those requiring a conventional admission. In those patients who were potentially agreeable to ESD, the time-point at which hospital staff, the patient, and any relatives felt they would cope at home with an ESD and at which all the eligibility criteria were met, was taken as the virtual discharge date. The difference between the actual discharge date and virtual discharge date was calculated for each of the patients who met the criteria for ESD.
Results: Thirty admissions (30%) met the criteria for virtual ESD between days 1 and 7 of their admission, saving 88 virtual bed days. With current local admission rates, this equates to 752 bed days per annum ESD would also have reduced length of stay of 8 admissions (8%) from >48 to <48 hours, hence saving our local Primary Care Trust at least £105,348 per year (2006/7 tariff). Wider potential benefits would include reduced bed occupancy and reduced admissions.
Conclusion: The Tariff and Payment by Results can be used as powerful levers to develop business cases for new services.

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2. **Cotton MM**, *et al*. *Thorax* 2000;**55**:902–6.

P097 ANXIETY AND DEPRESSION IN READMISSIONS TO HOSPITAL WITH ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Readmission is common following hospitalisation due to an exacerbation of chronic obstructive pulmonary disease (COPD). Some studies have shown depression to be a risk factor for readmission (Amagro *et al. Respiration* 2006;**73**:311–17) while others have not (Gudmundsson *et al. Eur Respir J* 2005;**26**:414–19). We set out to examine if depression and anxiety as measured by the Hospital Anxiety and Depression score (HAD) was a risk factor for both readmission and for rapid readmission, that is, >3 months. A significant score being anxiety or depression score > or =8. Data were prospectively collected on 51 random patients admitted to our hospital with an exacerbation of COPD, any subsequent admissions in the one to three years of follow up were noted from the patients records and the computerised patient administration system. Patients had a mean (SD) age of 69 (9) years, mean FEV1 of 37 (13) % predicted and a mean HAD score of 15(7). Thirty three patients were male and 35 of the patients had been admitted before. Thirty three of the patients were readmitted but a significant depression score was not any more common in these compared to those who were not readmitted, 17 out of 33 versus 7 out of 18, $\chi^2=0.74$, $p>0.2$. Nor was anxiety more common in patients who were subsequently readmitted, 17 of 33 versus 8 of 18, $\chi^2=0.23$, $p>0.5$. When we looked at rapid readmission, 10 out of 15 who were rapidly readmitted were depressed versus 14 out of 36 in the group not rapidly readmitted, $\chi^2=3.28$, $p=0.07$. Looking at anxiety, 8 of 15 were anxious versus 17 of 36 in those not rapidly readmitted, $\chi^2=0.15$, $p>0.5$. In summary we did not find a relationship between anxiety or depression and readmission to hospital with an exacerbation of COPD. However there was a relationship, though not quite statistically significant between depression and rapid readmission. Suggesting that depression plays a part in why some patients are rapidly readmitted to hospital but is not important as far as readmissions after three months.

P098 REDUCING CHRONIC OBSTRUCTIVE PULMONARY DISEASE WINTER ADMISSIONS BY PRE-EMPTIVE PATIENT REVIEW AND PROVISION OF EMERGENCY MEDICATIONS

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Introduction: In 2005, the Kingston chronic obstructive pulmonary disease (COPD) Working Group devised a strategy to reduce the number of COPD admissions in the coming winter months. We developed a model of care for all 1352 registered COPD patients in Kingston Primary Care Trust (PCT). This consisted of an individual Autumn review of each patient in General Practice. A personalised self

treatment plan was drawn up. In addition each patient was dispensed with an emergency supply of antibiotics and steroids with clear guidance when to start the medications and who to contact in case of an exacerbation. This model of care was drawn up into a Service Level Agreement and offered to GPs as an enhanced service.
Results: 1115 patients (82%) were reviewed and given emergency medication and a personalised self treatment plan by the end of November 2005. We looked at the number of COPD emergency admissions of Kingston PCT patients into Kingston Hospital over the winter months in 2005/6 and compared with the previous winter, 2004/5. There was a 25% reduction in COPD emergency admissions when comparing the October to February periods. The data also showed a 40% reduction in length of stay when comparing the same time periods.
Discussion: We demonstrated a significant reduction in COPD admissions and an even greater reduction in COPD bed days in Kingston Hospital. The personalised patient review and care plan, in conjunction with medications to treat exacerbations early, were instrumental in this change. There were high levels of patient satisfaction and positive reports from Practice nurses and GPs. We appreciate that external factors, including environmental condtions, could confound the outcomes but we have shown that this patient centred approach is feasible and can provide significant benefits.

P099 A QUESTIONNAIRE SURVEY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH READMISSIONS AND PROLONGED LENGTH OF STAY

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Acute exacerbations of chronic obstructive pulmonary disease (COPD) result in patient readmission and prolonged hospital stay, contributing to the progressive deterioration of patients, increased mortality, and the high cost of care. In England and Wales 900 000 COPD patients are diagnosed with COPD (*Thorax* 2004; **59**(Suppl I):1–232) and Milton Keynes alone has a predicted 3750–6250 COPD patients with 488 exacerbations/year.

Preliminary data from the Milton Keynes COPD readmission audit (August 2003–August 2004) show 449 patients admitted to hospital with 31% (143/449) being readmitted. The total length of stay was 3592 days (average stay: 8 days). In an audit of the 449 COPD admissions 100 patients received a questionnaire focusing on quality of life (chronic management, acute care and social circumstances), 64 replies were received and 44 patients contributed to the audit.

Median age of patients was 77 years, 59% had mobility problems and 27% continued to smoke. Over 60% of patients had been diagnosed with COPD for more than 4 years and 36% had 5 or more exacerbations per year. In all, 61% of patients were unable to cope with exacerbations at home, and 60% had no access to pulmonary rehabilitation.

Over a quarter of the patients audited were not on long acting bronchodilators and appropriate oxygen use remained an issue. Major factors associated with readmission were number of exacerbations per year, exercise tolerance, mobility, albumin levels and ability to cope at home. Major factors leading to prolonged length of stay were age, living alone, lack of independence, impaired mobility and stairs at home.

Patients with COPD need to be well supported in the community with greater involvement of many health care professionals.

P100 THE EPIDEMIOLOGY OF SCOTTISH HOSPITAL ADMISSIONS DUE TO CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Exacerbations of chronic obstructive pulmonary disease (COPD) represent a major burden to healthcare services. This study aims to determine the extent of this burden in the Royal Infirmary of Edinburgh (RIE) compared with the rest of Scotland.
Methods: Data on number of patients, deaths, hospital admissions and bed days for COPD and all other conditions requiring hospital admission were obtained from the Information Services Department Scotland for April 2000–March 2005 for RIE and Scotland and analysed using the two-tailed independent samples *t* test.
Results: 651 (60) and 8995 (616) COPD patients/year are admitted to RIE and rest of Scotland respectively accounting for 1.3–2.0% of the annual hospital patient burden. Compared to hospitals in the rest of Scotland, COPD in RIE accounted for a higher percentage of admissions ($p=0.005$), readmissions ($p=0.013$), and deaths ($p=0.038$), but a lower percentage of in-hospital COPD deaths ($p<0.0005$). There was no significant difference observed in percentage bed days. Data from general practice registers show that prevalence of COPD in the community is 1.5% in Lothian and 1.8% in Scotland.
Conclusions: COPD is associated with longer-than-average hospital admissions, readmission and high mortality compared with all other causes of acute hospital admissions. Better characterisation of COPD patients, particularly frequent exacerbators should aid development of cost-effective management strategies to reduce exacerbations and hospital admissions.

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P101 FIRST NORTHERN IRELAND CHRONIC OBSTRUCTIVE PULMONARY DISORDER EARLY DISCHARGE SCHEME: A ONE YEAR REVIEW

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Background: Early discharge schemes have been shown to be effective in reducing admission lengths for chronic obstructive pulmonary disease (COPD) patients. It is unclear whether such schemes can reduce hospital readmissions. The Royal Victoria Hospital respiratory early discharge scheme (REDS) commenced in June 2005. REDS patients, following discharge, have follow up visits from the community team (nursing and physiotherapy) for up to two weeks. Patients can then self-refer to the community team thereafter.
Aims: (1) To evaluate the efficacy and safety of the scheme in its first year of operation, with particular reference to length of stay (LoS). (2) To consider if entry onto the scheme helped reduce subsequent admission rates of COPD patients.
Methods: Data were obtained from medical records on all COPD patients admitted between 01/06/2005 and 31/05/2006. LoS (trimmed at 30 days) were compared between REDS and non-REDS patients. Of the 407 admissions, case notes of 282 were available for more detailed assessment. The following were recorded: if patients were assessed for REDS, accepted for REDS and if not, why not. The following data on REDS patients were obtained from the community team: adverse events, readmissions while on REDS, self-referrals to the scheme and if this resulted in further hospital admission.
Results: There were 407 COPD admissions. Of the 282 reviewed in detail, 69 were not assessed for REDS. Of the 213 assessed, reasons for exclusion from REDS included: residing outside the community team catchment area (44), requiring NIV (14), further investigation (12), medically fit for discharge (11), rehabilitation (10), social issues (10), and patient refusal (6). The remainder had various comorbid reasons. REDS patients ($n=39$) had no adverse events and had a significantly shorter LoS (median (interquartile range)) compared to non-REDS patients ($n=368$) (3 (2–4) *v* 7 (4–13), $p<0.001$). There were 7 readmissions whilst on REDS and 3 patients required GP visits. There were 25 subsequent self-referrals to the community team with no resultant admissions to hospital compared with 32 readmissions from 11 REDS patients who did not avail of self-referral.
Conclusion: The review of the first year of the first respiratory early discharge scheme in Northern Ireland showed that it is safe and effective, facilitating a reduced length of stay. Patients were keen and willing to self-refer thereafter and this possibly prevented subsequent hospital admissions.

P102 CHARACTERISTICS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS ACCEPTED ONTO AN EARLY DISCHARGE SCHEME

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We have been collecting data prospectively on patients accepted onto our chronic obstructive pulmonary disease (COPD) early discharge scheme since the beginning of 2005. We ask that the team complete, workload permitting, large datasets on every patient they accept onto the scheme and every 10th patient they do not accept (this latter group is much bigger and has no further contact with the team following an initial assessment and education session). These data are allowing us to characterise more precisely the population we accept for early discharge and we present some of our initial findings within this abstract. We also attempt to contrast some of the data on patients accepted for early

Abstract P102 Table 1

Characteristic	Accepted group	Not accepted
Admission heart rate	88	90
Admission respiratory rate	21	22.4
Admission systolic BP	131.3	128.4
Admission saturation (%)	93	92.7
FEV1during admission (%pred)	33.5	32.5
Body mass index (kg/m^2)	24.3	22.9
Usual walking distance (m)	131	125
Usual MRC dyspnoea score	3	3.07
Exacerbations per annum	2.84	2.54
Admissions in last 12 months	1.39	1.48
Oedema (%)	34.6	38.8
Known to have angina (%)	18	11

Abstract P102 Table 2

Readmission data (retrospective analysis from Trust IHS)	Accepted	Not acc
28-day readmission rates, all causes of readmission	19.1%	23.6%
28-day readmission rates, due to exacerbation	11.7%	9.8%

discharge (209) with those from a smaller sample (40) of the group who have not been discharged on the scheme.

Both groups consist of patients with severe disease who exacerbate frequently. There appears to be no difference emerging between the accepted and not-accepted groups, suggesting we are not merely discharging the ''simpler'' patients early, or that patients remaining in hospital have more severe exacerbations. 28-day readmission rates are interesting. While the accepted group appears to have a lower all-cause readmission rate, this is not true of those readmitted with further COPD exacerbation—both groups have low readmission rates and, while this may reflect difficulties in coding diagnoses on IHS, we note that the team deliver an education package to all COPD cases they assess, irrespective of acceptance onto our scheme.

P103 MANAGEMENT OF ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN THE EMERGENCY DEPARTMENT: A COMPLETED AUDIT ON THE INTRODUCTION OF A PATHWAY

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Introduction: Acute exacerbation of chronic obstructive pulmonary disease (COPD) is a common medical emergency presenting in Accident and Emergency (A&E) departments. This audit was designed to identify the deficiencies in the current practice in management of these patients in the Emergency department, and then re-audit to assess whether the introduction of a pathway was effective in improving practice.

Methods: The latest guideline in management of COPD (Management of COPD in adults in primary and secondary care, National Institute of Clinical Excellence, 2004) was taken as the standard. 72 patients admitted through the Emergency department of the Countess of Chester Hospital with a final discharge diagnosis of ''COPD'' were audited. Audit parameters included: patient profile, diagnosis status (known COPD or not), current home treatment for COPD, initial assessment—full set of observations and arterial blood gas (ABG) measurements, oxygen and nebuliser therapy, use of steroids and antibiotics, investigations requested, reassessment and outcome from A&E.

The initial audit was on 34 admissions between 3/7/05 and 28/9/05. An emergency medicine multidisciplinary pathway for acute exacerbation of COPD was then introduced in the A&E department of Countess of Chester in February 2006. It incorporated guidelines for initial oxygen therapy, ABG measurements, drug therapy, criteria for medical admission and indications for non invasive ventilation. The re-audit was done on 38 admissions between 27/4/06 and 19/6/06.

Outcomes: Performing initial ABG measurements: 25/34 patients (74%) in 2005 versus 35/38 patients (92%) in 2006 audit. Time interval between arrival in A&E and ABG measurements: median 76 minutes in 2005 versus 65 minutes in 2006. Documenting initial oxygen therapy: 15/34 (44%) in 2005 versus 31/38 (82%) in 2006. Initial nebuliser therapy: 26/34 (76%) in 2005 versus 36/38 (95%) in 2006. Investigations: Chest radiograph, full blood count and urea and electrolytes: 30/34 (88%) in 2005 versus 38/38 (100%) in 2006. Prescription of steroids: 14/34 (41%) in 2005 versus 18/38 (47%) in 2006. Medical admission from A&E: 23/34 (67%) in 2005 versus 37/38 (97%) in 2006

Conclusion: This audit identified the key areas for improvement in managing acute exacerbation of COPD in emergency departments. The use of a multidisciplinary pathway proved useful in improving practice in the emergency department setting.

P104 SYMPTOMS AND EXACERBATIONS IN A CHRONIC OBSTRUCTIVE PULMONARY DISEASE POPULATION ASSESSED FOR EARLY DISCHARGE

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We have been asking chronic obstructive pulmonary disease (COPD) patients about their usual symptoms as an addendum to their assessment for early discharge. We have also asked how patients have managed their exacerbations in the last 12 months (that is, themselves using medications at home, via their general practitioner or by coming to hospital). We have recorded data in 209 patients and exacerbation management in 169. Our database shows that this group of hospitalised patients has significant disease (% predicted FEV1 34%) and exacerbates frequently (2.84 per annum). 74% tended to receive antibiotics and steroids for exacerbation, 19% received antibiotics alone, and 7% steroids alone.

Thus, in this group of patients with severe disease, breathlessness and cough were the major reported symptoms to occur regularly but sleep disturbance and tiredness were also prominent. It is important to

Abstract P104 Table 2 Patient management of exacerbations over last year

Method of management	Self	GP	Hospital
Number of patients	15	73	81
Number of exacerbations	35	170	302

Abstract P104 Table 1 Symptoms reported: figures represent percentages of the 209 patients

Dyspnoea	100 Daily			
Cough	43 Daily	28 Occasional	10 Never	19 If unwell
Sputum volume	73 Teaspoon	12 Eggcupful	6 Tbspoon	9 Minimal
Sputum colour	38 Clear	36 White	12 Yellow	14 Other
Wheeze	11 Always	25 Occasional	41 Exertion	23 Never
Tight chest	11 Always	25 Occasional	41 Exertion	23 Never
Tiredness	31 Always	25 Occasional	44 Never	
Somnolence	6 Always	22 Occasional	72 Never	
Headache	13 Always	25 Occasional	62 Never	
Sleep quality	46 Good	54 Disturbed		

consider factors other than breathlessness and cough when assessing COPD patients, therefore. Notably, only 9% of patients tended to manage exacerbations themselves, 43% referred to their GP and 48% to hospital. One would perhaps expect our selected to group to have a high rate of hospital-managed exacerbations, but the data suggest there is also room for significant improvement to occur in the amount of self-management. We have now altered our behaviour to increase the number of COPD self-management plans we give to our patients, in the hope this may lead to a reduction in the number of admissions and also allow improved management of non-dyspnoea symptoms.

Management of chronic cough

P105 COUGH FREQUENCY DISTRIBUTION IN PATIENTS WITH CHRONIC COUGH USING AN AUTOMATED 24 HOUR AMBULATORY COUGH MONITOR

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The Leicester Cough Monitor (LCM) is a 24-hour cough monitor that automatically detects cough sounds recorded in an ambulatory setting. We have previously shown that automatic cough frequency measurement is valid and reproducible over 6 hours in patients with chronic cough. We now report our experience of ambulatory cough monitoring over 24 hours. 19 patients, (mean (SEM) age 58 (3.8) years, 11(58%) females) undergoing investigation of their unexplained dry chronic cough at a specialist cough clinic, underwent 24 hour cough monitoring. Each patient completed a symptom diary indicating timing of meals and bedtime, and time of worst symptoms. Cough count per hour ranged from 0–307. Pattern of coughing was predominantly daytime, with an even distribution between morning, afternoon and evening. One patient had mainly nocturnal cough, 3 had a biphasic distribution with a morning peak and then another peak either late afternoon or evening. Mean cough count/hour ranged from a low of 2.47 (3am) to a high of 22.42 (11pm). Mean cough counts/hour were calculated for several time frames (see table). The postprandial period was defined as the 2 hours following the end of each meal. Night-time was time from patient going to bed until they arose. Paired *t* tests were used to compare the mean cough counts/hour among the various time frames.

There were significantly less cough counts/hour at night compared with the daytime (mean difference −14.8, 95% CI −25.9 to −3.8; p=0.01); but no difference between the postprandial period and daytime (mean difference 0.6, 95% CI −3.1 to 4.3; p=0.7). There were no significant differences in mean cough count/hour between mornings, afternoons or evenings, although there was a trend for a lower morning cough frequency compared to the afternoon. Our data suggest that cough predominantly occurs during the daytime in patients with chronic cough. Cough frequency is not significantly different in the post prandial period.

Abstract P105

Time period	Mean cough count/hour	Minimum	Maximum	SEM
24 hours	13.5	3.8	61	2.9
Daytime	18.6	4.2	89.1	5.4
In bed	3.8	0	9	0.8
Postprandial	20.4	5	113	26.4

P106 OESOPHAGEAL IMPEDANCE-PH MONITORING IN GASTRO-OESOPHAGEAL REFLUX INDUCED COUGH

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Introduction: Gastro-oesophageal reflux disease is one of the commonest causes of chronic cough. 24 hour oesophageal ph monitoring is considered the gold standard for acid reflux disease, however this investigation does not determine the extent of non-acid reflux which we suggest plays a significant role in reflux induced cough

Methods: Twelve patients with a clinical diagnosis of chronic cough due to gastro-oesophageal reflux and a negative 24 hour esophageal ph monitoring underwent oesophageal impedance-ph monitoring using a nine channel combined multichannel intraluminal impedance and manometry catheter (Sandhill Scientific). Coughing bouts were identified by an event marker. The mean number of episodes of coughing was 26.7 (21) over 24 hours. A mean total of 46.6 (30.1) reflux episodes were detected. Of these 16.3 (11) were related to acid reflux compared to 30.3 (33.1) episodes that were non acid reflux events. In order to relate cough with the reflux, the reflux events occurring up to 5 minutes prior to cough was considered significant. Of the coughs recorded, 10% were acid related and 14.7% non-acid related events. Reflux occurred frequently in the 60 minutes immediately post prandial. A mean of 21.6 (16.4) episodes occurred with 57.6% being non-acid events.

Discussion: This study demonstrates in patients with negative ph monitoring, gastro-oesophageal reflux does occur. Non-acid reflux events occur more frequently than acid reflux and may be responsible for a significant amount of gastro-oesophageal reflux induced cough. The use of oesophageal impedance-ph monitoring rather than the conventional ph monitoring alone may increase the sensitivity of oesophageal monitoring in the diagnosis of reflux induced cough.

This poster was presented at the American Thoracic Society meeting in San Diego, May 2006.

P107 BRONCHOSCOPIC ABNORMALITIES IN UNEXPLAINED CHRONIC COUGH

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Background: Flexible bronchoscopy is not routinely recommended for the investigation of chronic cough. Diagnostic protocols advocate sequential investigations and trials of treatment for asthma-like syndromes, post nasal drip, and gastro-oesophageal reflux disease.[1] Where this strategy fails to elucidate the diagnosis, a number of further investigations are suggested. In such selected patients flexible bronchoscopy may be more diagnostically useful.

Methods: The NWLRC runs a specialist cough clinic seeing patients from the North West region. We have reviewed the bronchoscopic findings in consecutive new referrals to this clinic over an 18 month period. Patients with unexplained cough despite investigation and treatment trials (chest *x* ray, pulmonary function, methacholine challenge, ENT examination, and empirical reflux treatment) were bronchoscoped.

Results: Between January 2005 and June 2006, 154 new referrals were seen (47 referrals from general practitioners and 107 tertiary referrals). 73 bronchoscopies were carried out, of these 8 (11%) had a diagnosis made based on findings from inspection and biopsy. These included tracheopathia osteochrondroplastica (TPO) (4 cases), tracheomalacia (1 case), elongated uvula touching the vocal cords (2 cases) and endobronchial amyloidosis (1 case). TPO patients all had early changes with the typical appearance of nodules mainly on the tracheal cartilage rings but not causing significant airway obstruction. CT scans showed no other abnormalities.

Conclusions: TPO is thought to be a rare condition but 54% of sufferers complain of cough as a symptom.[2] In selected patients with chronic cough, in whom initial investigative protocols and treatment trials have been unsuccessful, flexible bronchoscopy is indicated and may reveal pathology potentially contributing to cough.

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P108 CORRELATION BETWEEN AIRWAY WALL AREA OF THE APICAL SEGMENTAL BRONCHUS WITH DISTAL AIRWAY WALL THICKENING IN NON-ASTHMATIC EOSINOPHILIC BRONCHITIS

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Introduction: Limited CT of the apical segmental bronchus (ASB) right upper lobe has been validated as a measure of airway wall remodeling in asthma and chronic obstructive pulmonary disease (COPD). Airway wall area of the ASB has been shown to correlate inversely with post

bronchodilator (BD) FEV1. To date no study has examined whether airway wall thickening of the ASB in non-asthmatic eosinophilic bronchitis (EB) correlates with distal airway wall thickening. Furthermore the correlation of thickening of the ASB and distal airways with post BD lung function has not been assessed.
Methods: Twelve patients with EB (according to the ACCP criteria) were recruited. Patients had a mean (range) age of 57 (36–69) with disease duration of 9 (5–18) years and post BD FEV1 of 108 (81–139)% of predicted. All participants took a 2 week course of oral prednisolone 0.5 mg/kg followed by limited CT (120 kv, 50 mas, 16×0.75 mm collimation, pixel area 0.323 mm^2) scanning of the right upper lobe to capture the ASB. Airway wall dimensions of the ASB were measured by ray casting using the full width half maximum method (Harvey Coxson VA) by a blinded and unblinded observer. The mean of measurements taken from the origin to the division point of the ASB was corrected for body surface area (BSA). Distal airways ranging from 4–15 mm^2 in the right upper lobe, corresponding to 4–8th generation airways, were measured using the same technique and the mean airway wall dimensions were corrected for BSA. We have previously validated ray casting using an airway phantom model and generated second order polynomial equations describing the relationship of wall area and luminal area %error according to airway size. ASB and distal airway measurements were corrected using the polynomial equations.
Results: The mean (SEM wall area (WA), Lumen area (LA) and total area (TA) of the ASB were 19.4 (1.3), 13.6 (2.9), and 33.0 (3.8) mm^2/m^2 respectively. There was a good correlation between observers of the ASB measurement ($r^2=0.9$). Both the TA and %WA of the ASB correlate well with the TA and %WA of smaller airways in EB ($r^2=0.457$, $p=0.0158$ and $r^2=0.6073$, $p=0.0028$, respectively). These observations are consistent with COPD with a near identical intercept and gradient (Nakano *et al.* 2000, AJRCCM, 162, 1102–1108). Interestingly, there was no significant correlation between any airways and post BD FEV_1 before correction with the polynomial equations. However, there was a significant correlation between TA of distal airways and post BD FEV1 (% predicted) after correction ($r^2=0.3374$, $p=0.0476$).
Conclusion: This study demonstrates that airway wall geometry of the ASB correlates with distal airways in EB, and that distal airway (generations 4–8) geometry correlates significantly with post BD FEV1 in patients with normal lung function.

P109 WHAT IS THE MINIMAL IMPORTANT DIFFERENCE FOR THE LEICESTER COUGH QUESTIONNAIRE?

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The Leicester Cough Questionnaire (LCQ) is a self-completed cough specific health status measure that has been shown to be valid, reproducible and responsive (Birring SS, *et al. Thorax* 2003;**58**:339–43). The purpose of this study was to determine the LCQ minimal important difference (MID), which is the smallest change in health status or quality of life (QOL) that is considered to be clinically meaningful. 53 patients with chronic cough (mean (SEM) age 56 (2) years, 30 (57%) females, duration of cough 5 (1.2) years) completed the LCQ during investigation of their cough in a specialist cough clinic and completed a repeat LCQ and four Global Rating of Change Questionnaires (GRCQ: overall QOL, physical, psychological, and social domains) >2 months after the first visit. The GRCQ is a 15-point scale widely used to assess the MID of health related questionnaires and is scored between +7 (great deal better) to −7 (great deal worse). The MID is the mean change in LCQ score for patients scoring GRCQ −3/−2/2/3 (2 = little, 3 = somewhat better/(-)worse). The LCQ total score range is 3–21 and domain scores (physical, psychological and social) range from 1–7. A higher LCQ score indicates a better QOL. The MID for the total LCQ score was 1.3; it was 0.4 for domain scores (table).

In conclusion, we propose a change in LCQ total health status score of 1.3 is the minimal important difference. This data should aid interpretation of LCQ scores and help those designing clinical trials for patients with cough.

P110 IMPROVEMENT IN HEALTH STATUS FOLLOWING OUTPATIENT CHEST PHYSIOTHERAPY FOR PATIENTS WITH REFRACTORY CHRONIC COUGH

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Chronic cough is a common condition that often results in significant physical and psychological morbidity. Troublesome cough persists in up to 30% of patients referred to specialist cough clinics despite extensive investigations and treatment trials. Pharmacological therapies for refractory cough are largely ineffective and have significant side effects. Chest physiotherapy is occasionally prescribed for patients with refractory cough but its efficacy has not been formally evaluated. We assessed health related quality of life (QOL) in 23 patients with stable chronic cough (mean age (SEM) 60 (2) years, 13 (57%) females, mean duration of cough 13 (2) years) at baseline and >2 months after outpatient based chest physiotherapy. All patients were investigated using a standardised diagnostic algorithm. The causes of cough were: idiopathic chronic cough (16), cough variant asthma (2), pulmonary fibrosis (2), rhinitis (1), gastro-oesophageal reflux (1), and eosinophilic bronchitis (1). Health status was assessed using the Leicester Cough Questionnaire (LCQ), which is a well validated 19-item self-administered questionnaire for patients with chronic cough (total score range 3–21; higher scores indicate better QOL). There was a significant improvement in health status after chest physiotherapy (mean (SEM) LCQ total score before 12.4 (0.9) *v* after physiotherapy 15.1 (0.9); mean difference 2.7 (0.7); $p<0.001$). The improvement in QOL was significantly greater than the LCQ minimal clinically important difference (MCID) of 1.3. Health status improved by more than the MCID in 16 (70%) patients. A significant improvement was seen in all LCQ health related domains: physical ($p=0.001$), psychological ($p<0.001$) and social ($p=0.02$). The health status of patients with chronic cough improved with chest physiotherapy regardless of gender, age, and duration of cough. Our findings suggest a potential role for chest physiotherapy in the management of patients with refractory chronic cough. Further randomised controlled studies are required to confirm these findings.

P111 THE TREATMENT OF CHRONIC COUGH WITH DISOFROL

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Introduction: American guidelines suggest the use of antihistamines in the treatment of chronic cough due to post nasal drip. UK experience has been poor. We have previously reported to the society that the recommended antihistamine (unlicensed in the European Union), dexbrompheniramine (DEX) inhibits the capsaicin receptor, TRPV1, one of the primary sensory receptors for cough (Sadofsky LR, *et al. Thorax* 2005;**60**:ii108).
Aim: To determine whether Disofrol (DEX 6 mg/pseudoephedrine 120 mg combination) is beneficial in treating chronic cough irrespective of the diagnosed causality of cough.
Method: Fifty seven patients (70% female) mean age 56 years, with intractable chronic cough were dispensed with open label Disofrol, twice

Abstract P109 Mean change in LCQ scores (SD)

	Global rating of change			
Change in LCQ QOL score	Same (−1/0/1)	MID (−3/−2/2/3)	Moderate (−5/−4/4/5)	Large (−7/−6/6/7)
Total score	−1.3 (3.1)	1.3 (3.3)	1.7 (2.3)	2.7 (4.6)
Physical	−0.6 (0.9)	0.2 (0.8)	0.7 (1.0)	1.3 (1.2)
Social	−0.3 (1.2)	0.2 (1.1)	0.7 (0.9)	1.3 (2.3)
Psychological	−0.1 (1.1)	0.8 (1.1)	0.5 (0.8)	1.2 (2.1)

MID, minimal important difference.

daily, for 4 weeks. The aetiology of cough included gastro-esophageal reflux disease (47%), idiopathic (32%), cystic fibrosis (7%), asthma (5%), and other causes (9%). Patients were asked to complete a visual analogue scale for the severity of cough before and after treatment. The mean cough score before and after treatment was compared using Wilcoxon signed ranks test. Adverse events (AEs) caused by the treatment were also recorded.
Results: 63% of patients had an improvement in cough following treatment. Overall the mean (SD) visual analogue cough score following treatment was significantly lower than before treatment, 4.81 (2.68) *v* 7.75 (1.47), $p<0.001$. Response to therapy was independent of diagnosis. 44% of patients experienced AEs of varying severities. The most common AEs included dry mouth (28%), drowsiness (28%), and sleep disturbances (20%). 52% of patients who suffered an AE discontinued treatment.
Conclusion: Disofrol is an efficacious treatment of intractable chronic cough irrespective of the diagnosis. While a placebo response is possible this patient population displays minimal response in blinded studies. The side effect profile suggests that the tolerability could be increased if DEX was given without the decongestant.

P112 BACLOFEN IN COUGH SECONDARY TO GASTRO-OESOPHAGEAL REFLUX DISEASE

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Introduction: Baclofen has been shown to increase lower oesophageal sphincter tone and alter the cough sensitivity. We have examined the response to Baclofen in patients with gastro-oesophageal reflux cough selected from the Hull Cough Clinic.
Methods: A retrospective analysis of the response to baclofen prescribed for gastro-oesophageal reflux cough identified using our probability based diagnostic algorithm (Kastelik J, *et al. Eur Respir J* 2005;**25**:235–43) was done. 29 patients (23 women) aged 40–80 years who had previously been tried on high dose proton pump inhibitors received baclofen for their reflux-induced cough. The maintenance dosage varied between 10 mg/day to 40 mg/day with the majority on 15 mg/day. Fifteen patients (51%) reported substantial benefit in symptom relief. Ten (34%) reported no effect on their cough. One person found transient beneficial effects. There was worsening of cough in 2 patients.
Conclusion: Baclofen is a useful therapy in cough secondary to gastro-esophageal reflux disease. The probable mechanisms by which this benefit is obtained are (1) decrease in the transient relaxations of the lower esophageal sphincter and (2) alteration of the cough sensitivity.

This poster was presented at the American Thoracic Society meeting in San Diego, USA.

P113 TREATMENT OF CHRONIC COUGH WITH MORPHINE

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Introduction: Cough is the commonest complaint for which a medical consultation is made (Schappert SM. *Nat Am Med Care Survey* 1993;**230**:1–16). At Hull Cough Clinic patients are investigated and managed using a probability-based algorithm (Kastelik *et al. Eur Respir J* 2005;**25**:235–43) similar to that recommended by the ERS task force (Morice *et al. Eur Respir J* 2005;**24**:481–92) Using this algorithm we have been able to reach a final diagnosis in 93% of patients. However 7–10% remain undiagnosed or fail to respond to treatment. In such patients there is a case for use of non-specific drugs that provide symptomatic control especially when treatments directed at the clinical cause of the cough are ineffective. The ''gold standard'' non-specific antitussives are opiates such as codeine and pholcodeine, although evidence of efficacy has been conflicting.
Method: Hull Cough Clinic patients with intractable cough were treated with opiates in the form of slow release morphine sulphate (MST) 5 to 10 mg bd. Of 1189 patients seen, 94 (8%), (mean cough duration 8.31 (0.93) years), (73% female) were treated with MST, of these 41% had gastro oesophageal reflux disease, 43% no diagnosis and other causes included asthma, bronchiectasis, and post nasal drip (16%). After individual assessment, treatment with 5 mg MST bd was increased to 10 mg bd if symptomatic control was suboptimal. This treatment regime resulted in 50% of patients demonstrating a significant improvement in cough, 16% had no change and 34% were lost to follow up. 52% had tolerable side effects and 13.8% experienced side effects resulting in treatment withdrawal. The most prevalent adverse events were constipation (6.4%) and drowsiness (3.2%).
Discussion: Our experience shows that where a diagnosis cannot be determined or the established treatments are unsuccessful, morphine is an effective and safe treatment. However it is important that patients are assessed on an individual basis since the dosage of morphine is a patient dependant variable which must be individualised according to patient metabolism, age, and response to morphine.

P114 COMPUTERISED ANALYSIS OF COUGH SOUND CHARACTERISTICS IN DIFFERENT RESPIRATORY DISEASES

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The automated, computerised detection of cough from sound based recordings could have many clinical applications. One possibility is that the characteristics of cough sounds differ between respiratory conditions. We have analysed data from a total of 688 individual cough sounds manually selected from ambulatory recordings performed in ten patients presenting with chronic cough due to cough variant asthma (n = 4), eosinophilic bronchitis (3), and gastro-oesophageal reflux disease (3).

All selected cough sounds were listened to and segmented into three phases according to the usual description of cough sound components: an initial burst of sound or first cough sound, an intermediate phase and a second cough sound. The following parameters were calculated for each of the three phases: duration; fraction of the total energy; centre frequency; maximum frequency; and bandwidth. Statistical analysis showed significant differences in the cough sound parameters between the three disease groups studied (see table). It also showed a well defined temporal structure of cough sounds, with significant differences in the parameters between the different phases.

Linear discriminant analysis (LDA) was also applied to these parameters. Classifiers were trained with two thirds of the data and used to classify the remaining sounds as CVA, EB or GORD coughs. Groups were compared pairwise and correct classification results from 88% to 93% were obtained. The classification results were always better when using the parameters of each phase than when using parameters to describe the complete cough sound.

The results of this pilot study suggest that there are significant differences in acoustic parameters of cough sounds from patients with different respiratory conditions and that the temporal structure of cough sounds should be considered when analysing these signals. Computerised analysis of the temporal and spectral characteristics of cough sounds could provide new information about the evolution of cough in different respiratory conditions. Further work is required to determine whether this is clinically helpful.

Abstract P114

	Duration (ms)			Centre frequency (Hz)			Max frequency (Hz)		
	1	2	3	1	2	3	1	2	3
CVA	52*	225	69	359*	516	391*	1469*	1672	938
EB	57	168*	115*	234*	578	266*	1734*	1734	578*
GORD	59	217	68	516*	1172*	297*	3281*	3399*	781

Data expressed as median values.
*Statistical significance to other groups.

Respiratory health in children

P115 DUST EXPOSURE AND RESTRICTIVE LUNG DISEASE IN CHILDREN IN KARAKALPAKSTAN, UZBEKISTAN

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Objective: To investigate the association between dust exposure and restrictive lung disease in children aged 7–10 years in the autonomous region of Karakalpakstan, Uzbekistan.
Background: Since the 1960s there has been a gradual yet dramatic reduction in the volume and surface area of the Aral Sea. Vast areas of salty sea bed have been exposed and the area has experienced an increase in dust storms. Local communities believe that the dust storms are having an impact on their health.
Methods: A cross sectional survey was conducted using a questionnaire on children aged 7–10 years living in 18 communities in Karakalpakstan. The children's lung function was tested and anthropometric data recorded in both the summer (May to August) and winter (September to December). Local dust deposition rates were monitored on a monthly basis. We used linear and logistic regression in our analyses.
Results: Dust levels in Karakalpakstan, and in particular the areas close to the Aral Sea are high. Dust deposition levels were considerably higher in the summer than in the winter. In the winter, when dust levels were low, an increase in total dust exposure was associated with an increase in FVC by 191.1 ml and there was a 20% decreased risk of having restrictive lung disease for every increase in total dust exposure of one standard deviation. In the summer, when dust levels were high, an increase in total dust caused a decrease in FVC by 161.9 ml and a doubling of the risk of having restrictive lung disease for every increase in total dust exposure of one standard deviation.
Conclusion: In the winter, the children living in close proximity to the Aral Sea with the highest annual levels of dust exposure have the best lung function. The reasons for this are not clear, but may be due to their socioeconomic status and the healthier diets of these communities which used to be relatively affluent fishing villages. In the summer, the reverse is true; the children living near the Aral Sea have the worst lung function and are at an increased risk of having restrictive lung disease. These findings suggest that the high levels of dust experienced in this area during the summer have a short term adverse effect on children's respiratory health.

P116 AN INTERNATIONAL COLLABORATIVE INITIATIVE TO DEVELOP RELIABLE REFERENCE RANGES FOR PULMONARY FUNCTION IN YOUNG CHILDREN

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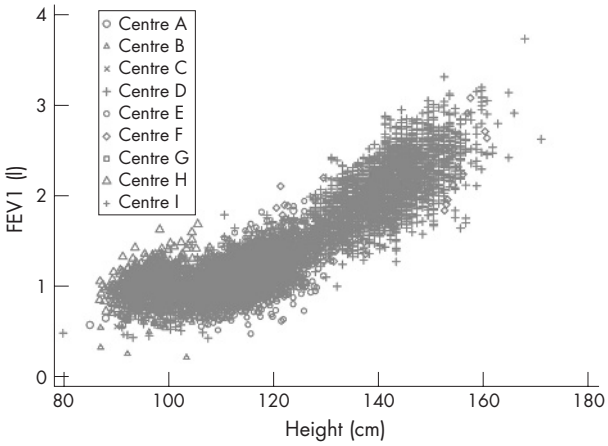
Background and Aims: Despite recent advances in preschool pulmonary function testing (PFT),[1] the lack of appropriate reference ranges limits the application and interpretation of these tests in this age group. The Asthma UK collaborative initiative aims to develop reference ranges from collated lung function measurements for spirometry, interrupter resistance and specific airway resistance in children aged 2–9 (http://www.growinglungs.org.uk).
Methods: To date, of the 64 centres identified as potential collaborators, 31 have agreed to participate. Data collection which includes centre specific information (equipment, protocols and population characteristics) and individual demographic and lung function data has been completed in 14 centres. Quality control of PFTs will be conducted in a systematic manner to assess comparability between centres. Reference ranges will be developed using the LMS method[2] and GAMLSS[3] to model the curvilinearity, heteroscedasticity and skewness in the distribution of lung function measurements.
Results: Preliminary results from 10 714 spirometry measurements in young children (6140 <7 years) indicate that collation of reference data for lung function in this age group is feasible (fig). After adjustment for height there are substantial nonlinear age trends in FVC and FEV_1, plus evidence of left skewness in the distribution. Data collection is ongoing.
Conclusions: The curvilinear relationship between height-adjusted FEV1 and age emphasises why currently available linear reference ranges for school age children should not be extrapolated to younger age groups. Application of modern statistical methods to larger datasets than hitherto available will improve the reliability of reference ranges for preschool PFTs.



Abstract P116 Preliminary results of collated spirometry (FEV1) measurements in children <10 years of age from nine centres.

1. **Stocks J**. Pulmonary function tests in infants and young children. Chapter 9, In: Chernick V, Boat TF, Wilmott RW, Bush A (eds), *Kendig's disorders of the respiratory tract in children*. Seventh edition. Philadelphia, PA, USA: Elsevier, 2006.
2. **Cole TJ**, Green PJ. *Stat Med* 1992;**11**:1305–19.
3. **Rigby RA**, Stasinopoulos DM. *Appl Statist* 2005;**54**:507–54.

P117 PAEDIATRIC PATIENT HAND HELD ASTHMA RECORDS

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Asthma affects 5.2 million people (3.7 million adults and 1.1 million children) in the UK. Despite the availability of evidence based asthma management guidelines and pharmacological advances in treatment many patients are failing to reach the desired standard of asthma control (Asthma UK, 2004).[1] Strategies that optimise prescribing, adherence to treatment and educate patients how to appropriately respond to deteriorating asthma and exacerbations by offering personal action plans can have significant impact on asthma morbidity (British Lung Foundation (BLF), 2004).[2] Despite the wide availability of personal action plans is has been reported that only 5% of asthma sufferers have a personalised, written asthma action plan, in spite of evidence that self management tools not only improve health outcomes for people with asthma but also reduce the need for emergency consultations. Over the past 2 years we have been working to develop a children's asthma hand held patient record. The record has been individualised to the child's age and disease status and provides guidance regarding treatment adjustment depending on disturbance to daily activities, symptoms and lung function. It details when to seek emergency care and provides information on diagnosis, investigation and treatment history, prevention advice, and contact details of family members and healthcare professionals. Free text is available for the child/parent and carer to record events both retrospectively and prospectively. Integral to the record is a removable credit card sized emergency card. One hundred families have taken part in the pilot phase and have complete two questionnaires; one related to the record and the other the emergency card, at 3 and 6 month post record distribution. The results so far have been extremely positive. The presentation and style of the record scored highly, 80% liking the size and 70% liking the colour. Fifty per cent have actively used the record, taking it to GP consultations, hospital visits and school. The free text section has been used by the child/parent to record days when unwell, and future appointment dates. Twenty to thirty per cent of children report they are carrying the record with them all the time, particularly when going on school trips. Over 80% reported they found the record extremely useful and easy to follow. One parent reported she had used the day-to-day section to monitor her child's progress and as a result the GP altered medication that resulted in her child achieving improved asthma control. The evaluation of the emergency asthma card is as equally positive with 100% of users reporting they liked the size of the card and the content. Over 50% of the children were carrying the card with them all the time. This project is now going to be extended to a wider population.

1. **Asthma UK**. Where we stand, 2004.
2. **British Lung Foundation**. Lung Report III – Casting a shadow over the nation's health, 2004.

P118 POLYMICROBIAL INFECTION IN CYSTIC FIBROSIS INFANTS AT FIRST PRESENTATION

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Recent molecular biological based studies have identified a diverse range of bacterial species in cystic fibrosis (CF) sputum.[1] In this abstract we report the use of Terminal Restriction Fragment Length Polymorphism Profiling (T-RFLP) to identify the bacteria in tracheal and bronchial lavage specimens from twin infants newly diagnosed with CF. Twin 1 presented at 6 months of age with acute intestinal obstruction and cough and twin 2 was noted to have cough and breathlessness at the same time of diagnosis. Fibreoptic bronchoscopy was performed prior to antibiotic therapy for acute symptoms. Tracheal suctioning, bronchial wash, and broncho-alveolar lavage (BAL) were obtained from twin 1 and bronchial wash and BAL specimens from twin 2.

DNA was extracted from each of the samples and a phylogenetically informative region of the 16S rRNA gene amplified. Amplicons were digested with a restriction endonuclease and separated according to length using an automated DNA sequencer to generate a profile of the total bacterial content of each sample. Bands within this profile were then assigned to bacterial species according to their length.

Conventional cultures on selective media for CF pathogens identified *S aureus* in Twin1 and *S aureus* plus a non-lactose fermenting Coliform in twin 2. T-RFLP profiling identified a complex bacterial community including 28 species in twin 1 and 11 in twin 2. 16S rRNA cloned fragment lengths were consistent with the presence of *Chlamydia, Burkholderia, Bordatella, Alcaligenes* Streptococci and *Moraxella*. Bands indicative of well recognised CF pathogens including Pseudomonads, *S aureus*, *H influenzae*, and *S maltophilia* were detectable at low levels. Whilst differences occurred in the range of species identified between specimens, there was common clustering of species across all of the samples. Both infants were improved after prolonged broad spectrum antibiotics. These findings suggest that complex bacterial communities are readily established during acute respiratory exacerbations in CF infants. Most species are not grown by conventional culture and species other than those traditionally recognised as CF pathogens are also present. Cluster analyses demonstrated a similar range of species to those seen in older expectorating individuals. However band intensities were more evenly distributed without the predominance of any individual CF pathogen as commonly seen in older children and adults.

1. **Rogers GB**, Carroll MP, Serisier DJ, *et al*. Characterization of bacterial community diversity in cystic fibrosis lung infections by use of 16s ribosomal DNA terminal restriction fragment length polymorphism profiling. *J Clin Microbiol* 2004;**42**:5176–83.

P119 THE PAEDIATRIC ADVANCED WARNING SCORE IN ACCIDENT AND EMERGENCY: VALIDATION OF A PHYSIOLOGY BASED ''EARLY WARNING SCORE'' FOR PAEDIATRIC ADMISSIONS

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Introduction: The use of Early Warning Scoring Systems has become commonplace over recent years. Evaluation of such systems has taken place in clinical settings such as adult acute medical admissions units, postoperative surgical wards and, more recently, Accident and Emergency (A&E). There is, however, no early warning system validated for use in children. We propose that the use of a Paediatric Advanced Warning Score (PAWS) would identify children attending A&E in need of urgent medical assessment and appropriate intervention.

Methods: We designed a PAWS chart. The chart uses physiological parameters (respiratory rate, work of breathing, oxygen saturation, temperature, capillary refill, heart rate, and conscious level), taking into account age related differences between normal values, to produce a numerical score. The more abnormal the physiological parameters recorded, the higher the PAWS score obtained. We validated the scoring system by performing a retrospective analysis of paediatric patients attending A&E. We compared patients who required admission to the Paediatric Intensive Care Unit (PICU) with a control group of children who were admitted to the general paediatric ward. The A&E cards were identified and the PAWS scores were calculated, based on data recorded at presentation. We then compared the PAWS scores between the two groups in order to see whether the PAWS chart would be able to identify those children in need of admission to a critical care area.

Results: The range of PAWS scores for patients admitted to PICU was 0–17, compared with 0–6 in the patients admitted to the general paediatric ward. Using a cut-off score of 3 or above, PAWS was able to identify patients requiring PICU admission with a sensitivity of 72% and a specificity of 90%.

Conclusions: A physiology based scoring system can help identify patients with significant illness. Assessment of paediatric patients is complicated by the range of normal parameters in different age groups. By drawing together clinical data as a single numerical score plotted on a colour-coded chart, abnormal physiology is more readily identified. This may be useful in the assessment and monitoring of sick children.

Abstract P119

	PICU (n = 50)	General ward (n = 50)
PAWS score >3	36	5
Median PAWS score	5	0

P120 SYSTEMATIC REVIEW OF THE COMMON THERAPIES IN CHRONIC NON-SPECIFIC COUGH IN CHILDHOOD

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Introduction: Chronic non-specific cough (NSC) is a common and troublesome paediatric problem. NSC is defined as non-productive cough in the absence of identifiable respiratory disease or any known aetiology. It is increasingly recognised as a separate entity albeit without any identifiable cause. The aim of this systematic review (SR) was to evaluate the common therapies used in children with chronic NSC.

Methodology: Two authors (AG and MM) searched MEDLINE (from January 1951 to December 2005), CINAHL (from January 1982 to December 2005), EMBASE (from January 1974 to December 2005), and the Cochrane databases (2005) for the subject headings cough and children. The search was limited to chronic, recurrent or persistent cough. All randomised controlled trials (RCT) or SR of RCTs were included. References were reviewed and additional relevant articles were identified. We excluded studies where there was another apparent cause for chronic cough.

Results: See table.

Abstract P120 Common therapies used for chronic NSC in children

Therapy	Evidence	Data limitations and considerations
Asthma type therapy		
Inhaled beta2-agonists	SR	Non-beneficial; only 1 small RCT
Mast cell stabilisers	SR	No RCT; single cohort study only
Methylxanthines	SR	No RCT; adverse events
Anticholinergics	SR	No RCT
Inhaled corticosteroids	SR	RCT = 2; non-beneficial; high placebo effect; adverse events
Gastro-oesophageal reflux treatment	SR	RCT = 3; data inconclusive
Anti-microbials	No RCT	SR in chronic '*wet*' cough—some benefit
Others	No RCT	No data

Discussion: There is a clear lack of adequate RCTs in the management of children with chronic NSC. This SR does not support the empirical treatment approach in children with chronic NSC (as opposed to specific cough). This clearly differentiates the management of chronic cough in children to that in adults whereby empirical treatment is widely advocated and used. In those with chronic wet cough, antibiotics have shown to be of some benefit and the use of inhaled corticosteroids in limited situations may be justified. However evaluation of response to treatment which is not necessarily attributable to the medication itself, is important in the clinical context.

P121 TISSUE PLASMINOGEN ACTIVATOR FOR EMPYEMA IN CHILDREN

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Background: BTS guidelines for the management of pleural infection in children were published in 2005 (BTS Guidelines for the Management of Pleural Infection in Children. *Thorax* 2005;60(Supplement)). Published data on experience using tissue plasminogen activator (tPA) as a fibrinolytic therapy in childhood empyema is limited.
Aim: To report outcomes using tPA for empyema in children from a tertiary referral paediatric hospital.
Methods: Observational study of all cases of parapneumonic effusion and empyema requiring chest drain insertion and tPA in our centre from January 2005–June 2006.
Results: Thirty children (15 male) were prescribed tPA following chest drain insertion. Median age at presentation was 5.8 years (interquartile range (IQR) 3.5–9.8 years). Initial median (IQR) haematological and biochemical results; CRP 241.5 mg/l (154.3–321.5), WBC 20.1×10^9/l (16.2–31.6), Hb 11.5 g/dl (9.9–12.4), Na^+ 135 mmol/l (133–135). Length of stay in our centre was 9 days (IQR 7–12), but total length of stay including days of hospital admission prior to transfer was 12 days (IQR 10.0–15.8). Each patient received a median of 5 chest radiographs (IQR 4–7) and a chest ultrasound. Antibiotics were administered for a median of 21 days (IQR 16–22) with a median of 11.5 days of intravenous antibiotics. 43.3% of initial drain insertions took place out of hours (5pm or later or at weekends). 27 pigtail and 3 large-bore drains were used (median drain size 10Fr (IQR 10–12)). tPA was administered within 4 hours of chest drain placement. The median tPA dose administered was a single 2 mg dose followed by a bolus of 20 ml 0.9% saline and clamping of the drain for one hour. Eight patients (26.7%) received a microbiological diagnosis from either blood or pleural fluid culture (*Streptococcus pneumoniae* in 7 patients, *Haemophilus influenzae* in 1 patient). The drain was removed after a median of 5.5 days (IQR 4–7.8). No tPA complications were recorded and there were no deaths. Three patients (10.0%) required a secondary thoracic procedure (debridement of empyema rind by thoracotomy), 2 required 24-hour admissions to PICU postoperatively, and 1 required HDU care.
Discussion: tPA is a useful, well tolerated adjunct to chest drainage for empyema in childhood with 90% of our patients recovering without requiring a further thoracic procedure.

P122 AN AUDIT OF ORGANISMS ISOLATED FROM TRACHEAL SECRETIONS IN CHILDREN WITH TRACHEOSTOMIES ON LONG TERM VENTILATION

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Background: Children on invasive long term ventilatory (LTV) support can have respiratory exacerbations, defined as increased oxygen or ventilatory requirements, which can result in hospital admissions and inpatient morbidity.
Aims: Identification of all micro-organisms found in tracheal secretions in all children on invasive LTV attending a single centre. Examination of the relationship between respiratory exacerbations and positive isolates and the role of antibiotic therapy in organism clearance. Also to assess whether the underlying condition—that is, neuromuscular (NM), skeletal dysplasia (SD) or chronic lung disease (CLD) affected the organisms isolated.
Methods: Sixteen children were identified from our clinical database: 10 NM, 4 SD and 2 CLD. Microbiological cultures and case records were examined retrospectively from Nov '02 to Nov '05 and the relation between positive isolates and exacerbations noted.
Results: 334 potentially pathogenic organisms were isolated from 509 tracheal specimens (66%); 318 bacterial, 3 fungal and 12 viral (majority RSV or Paraflu). The NM group had 191 (57%): 185 bacterial, 2 fungal and 4 viral. The SD group had 72 (21.5%), of which 67 were bacterial while the CLD group had 70 (21%), 66 of which were bacterial. 36% of the isolates were *Staphylococcus aureus*, 12.5% *P aeruginosa*, 8.8% *H influenzae*, 7.2% *Moraxella catarrhalis* and 6.6% MRSA. 75 exacerbations occurred; 40 in the NM, 24 in the SD and 11 in the CLD groups respectively. 60 exacerbations (80%) were associated with positive bacterial growths—usually *Staph aureus*. However, only 27% of bacterial isolates were associated with exacerbations, compared to 100% of viral isolates. Differences existed between the bacterial species in that 50% of the *H influenzae* isolates were associated with exacerbations, compared to only 20% of the *Staph aureus* isolates. 86% of exacerbations with positive bacterial cultures received antibiotics. In 70% of those children the same organism was isolated again after treatment.
Conclusions: The commonest organisms isolated were *Staph aureus* and *P aeruginosa*. Bacterial cultures are often positive at the time of exacerbations but this may reflect continuing bacterial airway colonisation rather than infection. In this small sample, the underlying disorder did not appear to affect the organisms isolated. The place of routine antibiotics in the management of exacerbations needs re-evaluation.

P123 OUTCOME OF WHEEZY INFANTS WITH ATOPIC BACKGROUND AT EARLY SCHOOL AGE: 5 YEAR FOLLOW UP TRIAL

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Wheezing in infancy is common, and although the majority of wheezy infants do not develop persisting asthma, it is important to identify subgroups who are likely to do so to allow targeted intervention.

We followed up, at primary school age, a group of infants with wheezing and atopic tendency who had taken part in an intervention study (Chavasse *et al. Arch Dis Child* 2001;**85**:143–8). We assessed their current wheezing and atopic status using items from the ISAAC questionnaire. We measured lung function—spirometry and interrupter resistance (R_{int}), exhaled nitric oxide, and bronchial reactivity using histamine challenge. We also compared lung function at follow up with lung function parameters measured in infancy.

Questionnaires were returned on 26 children, mean age 8 years. 19 children had been given a diagnosis of asthma at some stage, and 12 had wheezed in the last 12 months: 14 currently had a bronchodilator inhaler and 9 were on inhaled steroid treatment. 11 had suffered from eczema at some stage, and this was still active in 10. Six children were reported as having hayfever.

13 children attended for testing. Mean (SD) per cent predicted for FEV1 was 98.4% (12.4) and R_{int} 106.5% (32.7). Mean exhaled nitric oxide was 13.6 (13.9) ppb. Mean (SD) PC_{20}Histamine was 1.63 mg/ml (2.15). One child, who was not currently on asthma treatment, had marked airway obstruction (FEV1 66% predicted) and PC_{20} 0.25 mg/ml: lung function was normal after 6 weeks of low dose inhaled steroid.

Interrupter resistance at follow up correlated strongly with total respiratory system resistance in infancy ($r=0.71$).

Wheezy infants with atopic tendency (personal history or first degree family history) are very likely to continue to have reactive airways and respiratory symptoms at school age.

P124 TWIN PEAKS: THE CHANGING EPIDEMIOLOGY OF COMPLICATED PNEUMONIA AND EMPYEMA IN CHILDREN

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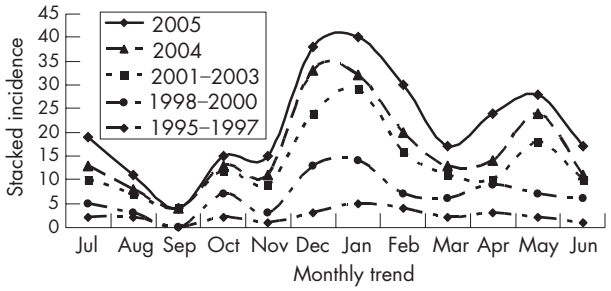
The increase in paediatric empyema in the UK and elsewhere over the last 12 years has been well documented, but the rate of increase has now accelerated.[1] This process is increasingly associated with a more severe pneumonic process involving lung necrosis and subsequent cavitatory lung disease.[2] Over the last 11 years 281 children (median age 5.2 years M:F 1.6:1, 47.5% of patients <5 years) have been referred to this centre with a presumptive diagnosis of empyema. 49 (17%) patients had either solitary pneumonia or a small additional fluid collection managed conservatively. The remaining 232 (83%) were managed surgically. The number of patients requiring surgical management has nearly doubled to 50/year over the last 12 months, increasing the rate from 5.6 to 9.7/100 000 children per year. In addition, the length of the usual winter season is lengthening with the emergence of a



Abstract P124.

second semi-distinct spring peak over the last three years (fig). The increase in empyema cases has been associated with emergence of *S pneumoniae* serotype 1 as the dominant serotpye, but this does not fully explain the increased incidence of cavitatory disease. It is not yet clear whether these problems represent an increase in the effective virulence of the organism, increased susceptibility of the host or changes in the environment.

The Health Protection Agency has agreed to introduce enhanced national paediatric empyema surveillance for England and Wales from the autumn of 2006 and a similar programme will be introduced in Scotland and Northern Ireland. All pleural fluid specimens will be subject to a pneumococcal PCR, with positive specimens being serotyped using the bioplex system. Clinical data will be submitted online using an anonymised audit tool, with data being collected from every paediatric centre within the UK. This programme will allow for more much effective monitoring of this rapidly changing problem.

1. **Spencer DA**, Iqbal SM, Hasan A, *et al. BMJ* 2006;**332**:1333.
2. **Ramphul N**, *et al. Pediatr Pulmonol* 2006;**41**:750–3.

P125 RESPIRATORY MUSCLE PRESSURE MEASUREMENT IN CHILDREN WITH CYSTIC FIBROSIS

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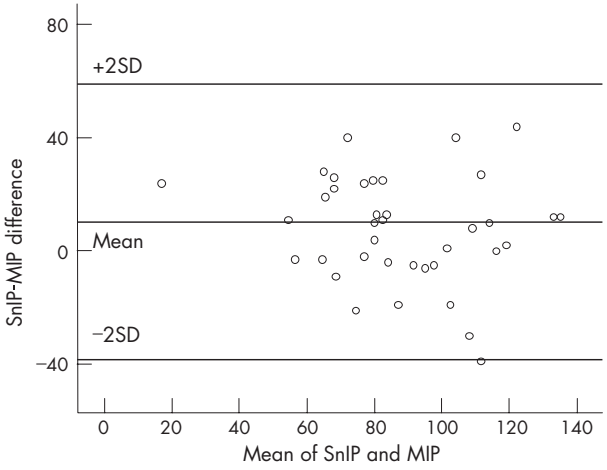
Background: Skeletal muscle wasting is reported in cystic fibrosis (CF). However, data relating to respiratory muscle strength in CF adults are conflicting, with reports of decreased, normal or supranormal respiratory muscle strength, while data relating to respiratory muscle performance in CF children are sparse.
Aims: To assess and compare non-invasive measures of respiratory muscle pressure in children with CF.
Methods: Measures of respiratory muscle pressure were made using a hand-held respiratory pressure meter (RPM01 MicroMedical, UK). Sniff inspiratory pressure (SnIP), as well as mouth inspiratory (MIP) and expiratory (MEP) pressures were measured in seated subjects. SnIP and MIP were measured from FRC, and MEP from TLC. Nose-clips were worn for MIP/MEP. Respiratory muscle pressures were converted to standard deviation scores (SDS) using reference data.[1] Spirometry was also performed in all subjects and measures converted to SDS using reference data.[2]
Results: Forty subjects were studied (20 male) with a mean (SD) age of 12.6 (2.4) years. FEV1 SDS ranged from −5 to +2, with a mean (SD) of −2.1 (1.7) SDS. Mean (+/−2 SD) for respiratory muscle pressure SDS were as shown in the table.

Limits of agreement for SnIP and MIP in CF were assessed by Bland-Altman plot. (fig) Mean (10.1) and SD (24.5) of differences are similar to those reported in healthy children.[1, 3] No correlation between FEV1 SDS and SnIP SDS ($r^2 = -0.001$), MIP SDS ($r^2 = 0.01$), or MEP SDS ($r^2 = -0.01$) was noted.

Abstract P125 SDS for SnIP, MIP and MEP in CF

	SnIP	MIP	MEP
Mean SDS	−0.3 SDS	0.1 SDS	−0.3 SDS
+/−2SD SDS	−2.7, 2.1 SDS	−2.4, 2.6 SDS	−2.8, 2.2 SDS



Abstract P125 Bland and Altman plot of SnIP versus MIP in CF

Discussion: Respiratory muscle pressures in children with CF are similar to those in healthy children, as are limits of agreement for SnIP and MIP, despite a mean FEV1 of −2.1 SDS. Preserved respiratory muscle function in CF is suggested. This may reflect a specific training effect due to increased work of breathing in CF.

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2. **Rosenthal M**, *et al. Thorax* 1993.
3. **Rafferty G**, *et al. Pediatr Pulmonol* 2000.

Mechanisms of respiratory infection

P126 ETHICAL PLANNING FOR AN INFLUENZA PANDEMIC

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Introduction: Pandemic influenza guidelines have recently been developed. However, there is little research into how ethically acceptable these plans will be to society.
Methods: Two hypothetical ethical scenarios that could arise in a pandemic were developed. The first scenario considers the attitude of NHS staff towards professional and ethical responsibilities of health care workers when faced with high personal risk at work. The second scenario considers the problem of resource allocation—which patient (A, B, or C) should get the last Intensive Care Unit (ICU) bed? (''A''—25 year old student with severe primary viral pneumonia and multi-organ failure, with an estimated mortality of 80%; ''B''—67 year old patient with an influenza exacerbation of COPD with an estimated mortality of 30% and a long term survival of 3 years; ''C''—51 year old non-European Union private patient who developed postoperative pneumonia following a coronary artery bypass operation with an estimated mortality of 40%). The postal survey was distributed to 1018 staff at City Hospital Campus, including doctors, nurses, students, and other ward staff.
Results: 403 (40%) of surveys were returned: 183 doctors, 133 nurses, 53 medical students and 34 other staff responded. Scenario 1: 84% of staff felt is was unprofessional for a doctor or nurse to leave work in a pandemic. 76% felt it was unethical for them to leave. 79% of responders would stay and work during a pandemic and 17% felt there should be a legal framework to force NHS employees to work during a pandemic. Having children at home did not significantly alter response rates. Scenario 2, see table. When given the choice of patient A or B only, doctors were more likely than nurses to chose patient A (89% *v* 67%, $p<0.001$).
Discussion: The General Medical Council states: ''you must not refuse to treat a patient because you may be putting your self at risk … you should take reasonable steps to protect yourself.'' In accordance with this, most staff surveyed felt they should (professionally) and would (voluntarily) work during a pandemic despite high personal risk. A quarter felt it was ethical to leave work while 17% felt there should be legal powers to enforce working. An even wider difference of opinion regarding resource allocation was noted. These ethical issues will arise multiple

Abstract P126 Number of responses: ''who should get the last ICU bed: A, B, or C?''

Answer	n (%)
A	218 (54)
B	48 (12)
C	135 (33)
Unsure	2 (1)

times during a pandemic. They therefore deserve attention as an integral part of pandemic planning.

P127 MANAGEMENT OF COMMUNITY ACQUIRED PNEUMONIA: ARE WE FOLLOWING THE BTS 2004 CAP GUIDELINES UPDATE?

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Introduction: Community acquired pneumonia (CAP) is associated with significant morbidity, mortality, and use of health service resources. BTS 2004 update CAP guidelines CURB-65 score (6-point score, one point for each of confusion, urea >7 mmol/l, respiratory rate ⩾30/min, low systolic (<90 mmHg) or diastolic (⩽60 mmHg) blood pressure, age ⩾65 years) is valuable in defining severity and identifying patients that may be suitable for home or outpatient management. Certain features on discharge are associated with adverse clinical outcomes. The 2004 guidelines[1] state that patients should be reviewed within 24 hours of planned discharge home and those suitable for discharge should not have more than one of the following characteristics present. These clinical ''instabilities'' include temperature >37.8˚C, heart rate >100/min, respiratory rate >24/min, systolic blood pressure <90 mmHg, oxygen saturation <90%, inability to maintain oral intake and abnormal mental status. The aim of this audit was to assess whether the BTS guidelines are followed with regards severity assessment and discharge planning.
Method: All patients admitted between 11/10/2004 to 22/12/2004 under the emergency adult medical take to Frenchay Hospital Bristol which serves a population of about 200 000. Data were prospectively collected and included demographic variables, clinical features, and clinical and laboratory parameters. All patients who fulfilled BTS definition of CAP were included
Results: Thirty one admissions were diagnosed with CAP with 64% were above the age of 65. Average length of hospital stay was 11.67 days. 58% were admitted to a respiratory ward. 32% had no form of respiratory specialist input, 1 patient was admitted to intensive care. The CURB 65 score was not recorded on all admissions; it was not computable on the admission clerking in 35.4%. 35.4% were suitable to be considered for home treatment. 16% were suitable to be considered for short inpatient stay (SIPS) treatment or hospital supervised outpatient treatment. The mortality rate was 19%. Microbiological test requested did not correlate with severity of CAP. Discharge planning: no patients had more than 1 instability within 24 hours of discharge, though these were identified from the observation charts, medical, and nursing notes.
Conclusion: Improvements are required in severity assessments for CAP and the documentation of the CURB 65 score in the admission notes—this requires educating the junior doctors. 35.4% were suitable for home treatment and 16% for SIPS or hospital supervised outpatient treatment which would have saved unnecessary hospital bed days occupancy. Admitting the patients to respiratory wards or involving the respiratory teams in their care will improve management.

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P128 POSITIVE MICROBIOLOGY IS MORE FREQUENT IN PATIENTS WITH SEVERE COMMUNITY ACQUIRED PNEUMONIA

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Introduction: British Thoracic Society guidelines recommend initial microbiology investigations such as sputum and blood cultures in all patients with severe community acquired pneumonia (CAP) and in patients with non-severe CAP who have not received prior antibiotic therapy. The aim of the study was to investigate if the likelihood of either a positive sputum or blood culture was linked to the severity of CAP.
Methods: We studied 84 adult patients admitted to the Royal Infirmary of Edinburgh with CAP between December 2005 and June 2006 that had sputum and/or blood cultures within 48 hours of admission and had not received prior antibiotic therapy (within 7 days). The severity of pneumonia was assessed using both the CURB score (new mental confusion, urea >7 mmol/l, respiratory rate ⩾30/minute, systolic blood pressure <90 mmHg, and/or diastolic blood pressure ⩽60 mmHg) and C reactive protein (CRP, recently identified as an independent marker of severity of CAP). The Mann-Whitney U test was used to analyse data and a p value less than 0.05 (two- tailed) was considered as statistically significant.
Results: There were 74 and 52 patients that had sputum and blood cultures sent respectively. Positive microbiology is more frequent in patients with severe CAP (table).
Conclusion: Positive microbiology is more likely in patients with severe CAP.

P129 AN AUDIT OF THE USE OF NEBULISED 7% HYPERTONIC SALINE TO TREAT PATIENTS WITH BRONCHIECTASIS OR MUCUS HYPERSECRETION

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Introduction: The short term benefit of mucus clearance with nebulised 7% hypertonic saline (HS) in bronchiectasis (BTS) has been recently demonstrated.[1] We aimed to determine whether initial improvements were sustained with prolonged treatment and whether this was limited to patients with CT confirmed BTS or extended to include patients with mucus hypersecretion (MH) only.
Methods: A retrospective audit of case notes of patients treated with hypertonic saline over a period of eight years was performed. Patients were classified as having either BTS (from CT findings) or MH (defined from clinical presentation and absence of CT evidence of BTS). Lung function data were collected at baseline, prior to initiating therapy, at 3 months after starting therapy and at the most recent point whilst still receiving treatment. Subjects who did not tolerate HS therapy and received it for less than four months were excluded.
Results: 169 suitable patients were identified of whom case note records were available for 125. Eight patients did not tolerate HS therapy and were excluded from subsequent analysis. 70 of the remaining 117 patients (59.8%) had BTS on CT. 24/117 (20.5%) subjects had non-BTS MH. There were inadequate or absent records to classify 23/117 (19.7%). The mean duration of treatment and follow up was 20.7 months. In the BTS group the mean (95% CI) FEV1 rose by 7.8% from 1.91 l (1.73–2.09) to 2.06 l (1.85–2.27) at 3 months and by 14% from baseline to 2.18 l (1.95–2.42) at the most recent assessment. In the MH group the mean FEV1 rose by 37% from 1.62 l (1.30–1.99) to

Abstract P128 Median (IQR) CURB and CRP levels in patients with positive and negative sputum and blood cultures (comparisons are made between patients with positive and negative cultures. *p<0.05 and **p<0.01)

	Number		CURB median (IQR)		CRP (mg/l) median (IQR)	
Cultures	+ve	−ve	+ve	−ve	+ve	−ve
Sputum culture	23	51	1.5 * (1–2)	1 (0–1)	148* (62–261)	68 (36–144)
Blood culture	10	42	3** (2–3)	2 (1–2)	344** (256–447)	98 (36–216)
Total cultures	33	93	2* (1–2)	1 (1–2)	196** (100–323)	88 (36–197)

2.22 l (1.88–2.63) at 3 months and by 39.5% from baseline to 2.26 l (1.88–2.63) at the most recent assessment.
Discussion: Patients in the BTS group showed a gradual and progressive improvement in lung function. Patients in the MH showed a rapid and significant improvement in lung function after 3 months of treatment, which did not significantly improve after this but was sustained. The previously reported benefit of nebulised HS therapy has been shown to be maintained with prolonged treatment and there may continue to be additional improvement. Treatment with HS in patients with non-BTS MH shows a rapid and large increase in FEV1 that is sustained with prolonged treatment.

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P130 ANAEROBIC BACTERIA IN ADULT NON-CYSTIC FIBROSIS BRONCHIECTASIS

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Introduction: Pathogenic bacteria are believed to be important in the disease mechanism in bronchiectasis, contributing to inflammation and impairing the patient's quality of life. A number of patients in our bronchiectasis clinic have anaerobic bacterial infection, but there is very little information about the implications of these pathogens, whether they should be specifically targeted with antimicrobials and what the best protocol for treatment might be.
Methods: In our bronchiectasis clinic we performed quantitative bacterial culture routinely on all spontaneous sputum specimens over a 6 month period for aerobic and anaerobic bacteria to assess the incidence and potential patterns of colonisation. We performed a smaller cross sectional study in which sputum results were analysed with clinical information concerning the nature and severity of the disease, current antibiotic usage and measures of inflammation in sputum and blood.
Results: In total, 94 patients provided 161 sputum specimens. 71 specimens from 53 patients grew anaerobic organisms. Sputum purulence did not predict the presence of anaerobes. *B melaninogenicus* and Gram negative rods comprised the majority of anaerobic isolates. 43 patients provided more than one sample. Of these, 18 patients were always negative, 8 always positive, and 17 had variable results. The mean anaerobic bacterial load (although high) was lower than the mean aerobic bacterial load (1.3E+07 and 1.8E+09 cfu/ml respectively, $p<0.001$). There was a negative association with the presence of pseudomonas species ($p<0.05$). 52 patients were recruited into the cross sectional study. Patients with anaerobes had fewer lobes affected on CT scan ($p<0.01$), higher TLCO % predicted ($p<0.01$) and lower sputum neutrophil count ($p<0.05$). Patients colonised with pseudomonas species had worse TLCO % predicted, dyspnoea score and higher systemic and sputum inflammation than those without. Examination of sputum quality by squamous cell contamination suggested that oral contamination did not influence the results.
Conclusions: (1) Anaerobic bacteria are present in many patients with bronchiectasis but they are not associated with worse disease. (2) The presence of pseudomonas appears to reduce the likelihood of isolation of anaerobic bacteria. (3) The importance of anaerobic infection in bronchiectasis may relate mostly to β-lactamase production which may reduce the efficacy of β-lactam antibiotics against aerobic co-pathogens in vivo. Several patients regularly cultured anaerobes at high bacterial load and without coexisting aerobic infection, suggesting they require treatment in their own right. Better information is required to guide management in these cases. Spontaneous sputum would be satisfactory for use in a clinical trial to investigate this issue, provided appropriate care was taken in sample collection, selection, and handling.

P131 IS SPUTUM LOAD A USEFUL OUTCOME MEASURE FOR CLINICAL TRIALS IN BRONCHIECTASIS?

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Introduction: Controversy surrounds the use of sputum load as an outcome measure in clinical trials examining the efficacy of airways clearance methods. Contamination with saliva, swallowing of secretions and reluctance to expectorate have been cited as limitations. Dry weight of sputum overcomes some of these issues and may more accurately reflect treatment related changes in tracheobronchial secretions. Dry weight is however more difficult to determine as it requires an oven and can take up to 24 hours to complete. The aim of this study was to determine the relationship between wet and dry weight sputum and its sensitivity to change.
Methods: Twenty patients (11 M) with moderate to severe bronchiectasis (admission FEV1% predicted 37.75 (10.93)) requiring hospitalisation and intravenous antibiotics for an acute exacerbation were recruited. Sputum was collected during physiotherapy airways clearance sessions on the first and final day of admission. Expectorated sputum was collected in preweighed cups which were reweighed immediately after collection on Sartorius scales with 0.01% accuracy. The samples were then incubated in an oven at 65˚C and routinely weighed until weight loss had stabilised.
Analysis: SPSS version 11.5. Pearson's *r* and paired *t* test.
Results: There was a strong correlation in wet to dry weight (g) sputum first day ($r=0.951$; $p=0.01$) and final day ($r=0.973$; $p=0.01$); dry weight to water content (g) first day ($r=0.945$; $p=0.01$); final day ($r=0.96$; $p=0.01$). There was no significant difference in the percentage dry/wet weight between first day and final day (mean (95%CI)) 1.95 (−2.79 to 6.69) ($p=0.399$). There was no significant change from first day to final day in FEV1% predicted −2.45 (−5.95 to 1.05) ($p=0.160$). There was a significant change from first day to final day in inflammatory markers: WCC($\times 10^9$/l) 1.65 (0.46 to 2.84) ($p=0.009$) and CRP(mmol/l) 26.14(1.40 to 50.87) ($p=0.039$). Two patients were unproductive on the final day. There was no significant change between first and final day: wet weight sputum (g) 1.35 (−3.95 to 6.65) ($p=0.599$); dry weight (g) 0.07 (−0.23 to 0.38) ($p=0.625$); or water content (g) 0.63 (−4.88 to 6.14) ($p=0.812$) ($n=18$) in the airways clearance session. However, there was a significant decrease in 24 hour wet weight sputum (g) between first and final day 8.73 (0.41 to 17.05) ($p=0.004$).
Conclusion: During an acute exacerbation there was a strong correlation between wet and dry weight sputum. There is no significant difference in sputum weight expectorated between first and final day airways clearance sessions. In contract there was a significant change in 24 hour sputum weight. Sputum weight maybe a useful outcome measure for clinical trials in bronchiectasis. Dry weight has no advantage over wet weight.

P132 LYMPHOPENIA AND ITS RELATION TO FUNGAL INFECTION, LENGHT OF STAY, AND MORTALITY IN THE CRITICALLY ILL PATIENTS

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Introduction: Lymphopenia is a well known complication of critical illnesses especially severe sepsis and multi-organ failure. It is attributed to increased lymphocyte loss both through caspase mediated and mitochondrial dependent apoptosis. Similar loss of lymphocytes may occur in critically ill patients with other disorders. There is a well known correlation between the severity of illness and incidence of lymphopenia. We conducted a retrospective observational study to determine whether there was any association between lymphopenia and length of stay, mortality and incidence of fungal infection in the critically ill patient.
Method: Clinical records of 342 critically ill patients admitted to a 16 bedded adult ICU from 1 November 2005 to 30 April 2006 were studied (fig 1). Information regarding lymphopenia duration and severity, diagnosis of fungal infection and colonization, ICU length of stay and 28 days mortality were recorded for each patient. Chi-square and Mann-Whitney U tests were used to analyse the data.
Results: 210 (63%) patients had lymphopenia ($<1.0\times10^9$) during their stay on ICU; 24 (12%) suffered from severe lymphopenia ($<0.5\times10^9$). 101 (48%) from prolonged lymphopenia (3–14 days), and 15 (7%) had prolonged severe lymphopenia. 55 (26.2%) lymphopenic patients had either fungal colonisation or infection whilst on ICU, this was statistically different compared with the control group (8.1%). P value <0.0001. 102 (49%) of the lymphopenic patients had a long stay in ICU ($\geq$10 days). The median length of stay was 9 days for patients with lymphopenia, 2 days for the control group, p value<0.0001. Of the 210 lymphopenic patients, 55 (26%) patients died within 28 days of ICU admission. This was not statistically different compared with the control group (25.8%) (fig 2).
Conclusion: This study demonstrates that lymphopenia in critically ill patients is associated with increased incidence of fungal colonisation and infection and increased length of stay in ICU. Whether this was a cause effect relationship or simply was a surrogate marker of severity of illness is not clear. There was no significant association between lymphopenia and mortality, although, a tendency for increased mortality was observed in the subgroup with severe lymphopenia.

		Patients with lymphopenia	Patients without lymphopenia
	Number	210	124
Age	Mean	52.6	47.7
	Standard deviation	18.56	17.9
Sex – Male	Number	134	65
	Percentage	63.8%	52.4%
Sex – Female	Number	76	59
	Percentage	36.2%	47.6%
Lymphocyte count	Mean	1.13	1.98
	Standard deviation	0.9	0.9

Abstract P132 Figure 1 Demographics.

		Patients with lymphopenia n = 210,62.9%	Patients without lymphopenia n = 124, 37.1%	P value	Confidence interval
28 days mortality n = 87, 26.0%	Number	55	32	0.9341	0.586556 to 1.624561
	Percentage	26.2%	25.8%		
Length of stay	Median	9	2	<0.0001	4 to 7
	Inter quartile range	4–16	2–4		
Fungal infection or colonisation n = 65, 19.46%	Number	55	10	<0.0001	2.020243 to 8.653781
	Percentage	26.2%	8.1%		
Fungal infection only n = 32, 9.58%	Number	29	3	0.0003	2.114609 to 27.139126
	Percentage	13.8%	2.4%		

Abstract P132 Figure 2 Results.

1. **Hotchkiss RS**, *et al*. Accelerated lymphocyte death in sepsis occurs by both the death receptor and mitochondrial pathways. *J Immunol* 2005;**174**:5110–18.
2. **Felmet KA**, *et al*. Prolonged lymphopenia, lymphoid depletion and hypoprolactinaemia in children with nosocomial sepsis and multiple organ failure. *J Immunol* 2005;**174**:3765–72.
3. **Charles PE**, *et al*. Candida spp. colonization significance in critically ill medical patients: a prospective study, *Intensive Care Med* 2005;**31**:393–400.

P133 NECROTISING PNEUMONIA DUE TO PANTON-VALENTINE LEUKOCIDIN PRODUCING *STAPHYLOCOCCUS AUREUS* TREATED WITH INTRAVENOUS IMMUNOGLOBULIN

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A 30 year old female was admitted following five days of influenza-like illness with breathlessness, productive cough, haemoptysis, and pleuritic chest pain despite 24 hours of oral amoxicillin. She had a 10-pack year smoking history but no history of lung disease, risk factors for infection or immune compromise. She was normotensive, temperature 38.2°C, with tachycardia, tachypnoea, and coarse crepitations on the right side of the chest. paO_2 was 9.6 on 60% O_2. Chest *x* ray (CXR) showed bilateral alveolar shadowing. Renal function, electrolytes and liver function were normal. CURB score was 1. On clinical microbiology review, these features in a previously healthy young patient together with leucopenia (WBC 1.9, neutrophils 1.3) and a C reactive protein of 520 and suggested Panton-Valentine Leukocidin (PVL) associated staphylococcal pneumonia. PVL is an extracellular toxin produced by some *Staphylococcus aureus* isolates and is associated with soft tissue infections and severe necrotising pneumonia. Initial therapy with intravenous flucloxacillin and levofloxacin was changed to linezolid, rifampicin, clindamycin, and imipenem. Rapid deterioration with increased respiratory rate and hypotension led to intensive care unit (ICU) admission, intubation, and inotropes. Microscopy of bloody sputum and endotracheal secretions showed sheets of staphylococci and a paucity of leucocytes—typical for PVL infection. The deterioration continued, despite all measures, for the next 4 hours, until 2 g/kg intravenous immunoglobulin (IVIG) was administered with what seemed to be a dramatic effect: within 24 hours of admission to the ICU, oxygenation began to improve and inotrope requirements fell; by day 4 she was no longer inotrope dependent. Cultures revealed *S aureus*, later proven PVL positive, and treatment switched to flucloxacillin and clindamycin. However, on day 5 a rapid deterioration in ventilation, urine output, and blood pressure occurred, CXR consistent with abscess formation at the right hilum. Bronchoscopy showed generalised inflammation only. Linezolid was restarted with fusidic acid. The patient continued to deteriorate and died on day 6. Postmortem showed completely necrotic, haemorrhagic lungs, due to the inexorable necrosis caused by PVL toxin already excreted by the sheets of staphylococci present in the lung tissue before antimicrobial treatment, and not neutralised by IVIG.

Conclusion: We believe that this was the first clinical use of IVIG in PVL disease. The UK's Chief Medical Officer recently highlighted a guidance document on PVL disease issued by the Health Protection Agency. This case underlines the importance of recognising the classical presentation of PVL-*Staphylococcus aureus* pneumonia in healthy young people with an influenza-like prodrome, tachycardia, hypotension, haemoptysis, and leucopenia, and is a reminder that CURB scoring may underestimate the severity of disease in young people.

P134 A 12 MONTH REVIEW OF RESPIRATORY COMPLICATIONS OF HAEMATOLOGY INPATIENTS

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Patients with haematological problems frequently develop lung complications, the management of which is often challenging. At our teaching hospital, we have established a consultant led service to advise on haematology patients with respiratory complications and set protocols for advising bronchoscopy. We present the clinical characteristics of 12 months of referrals to this service. A total of 53 referrals were received, comprising 37 patients. The median age was 54 years of age (range 15–77), and 54% of patients were male. The underlying disease was leukaemia in 48%, lymphoma in 30%, and myeloma in 14%. 43% of patients had had a bone marrow transplant, and 40% of referrals were associated with recent significant neutropenia. The common clinical presentations were fever (57%), dyspnoea (60%), and cough (36%). The common radiological presentations were consolidation (30%), ground glass shadowing (19%), pulmonary nodules (15%), pleural effusions (13%), and ''tree and bud'' changes (6%). 28% of patients underwent a fibre optic bronchoscopy. Positive microbiological data were obtained in 54% of episodes and from the respiratory tract in 26% (sputum 11%, BAL 11% and nasopharyngeal aspirate in 4%). Gram negative bacteria were the dominant pathogens isolated, identified in 32% of episodes (*Pseudomonas aeruginosa* and *Klebsiella* species 9% each, *Escherichia coli* in 8%). Gram positive bacteria were identified in 9% of episodes, viruses in 8% and fungi in 4%. The commonest diagnosis was bacterial pneumonia (28%). Other common conditions were fluid overload (9%), invasive filamentous fungal infections, non-specific pneumonitis, viral bronchiolitis, bronchiolitis obliterans (6% of referrals each), bacterial lung abscess, candidiasis, and metastatic bacterial nodules (4% each). Mortality was high, with 34% of patients dying within the study period including all three patients admitted due to exacerbations of bronchiolitis obliterans. These data show that although haematology patients are affected by a wide range of respiratory complications by far the commonest problem encountered is bacterial pneumonia. Fluid overload is also common. In addition, by targeting bronchoscopy to specific presentations a microbiological diagnosis can be obtained in 40% of patients.

P135 DOES VISUALISATION OF THE BRONCHIAL TREE ADD VALUE WHEN INVESTIGATING POSSIBLE LUNG INFECTION?

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Background: Fibre optic bronchoscopy (FOB) is commonly used to investigate possible lung infection. However it is expensive, requires

considerable staff training and equipment maintenance; and because of its invasive nature, is often tolerated only after sedation. Sputum induction with nebulised saline is a non-invasive and cheaper alternative to FOB. Its diagnostic yield in possible infection is similar to FOB. However it does not allow visualisation of the bronchial tree or ''site specific'' sampling at areas of radiographic abnormality. We hypothesised that observed abnormalities at FOB performed for diagnosis of possible infection are in fact rare in clinical practice.
Method: Consecutive FOBs performed between 01/2005 and 06/2006 were analysed. Cases where the indication was possible lung infection were identified. Bronchoscopic findings were obtained from a standard report form. Laboratory results and demographic data were obtained from the hospitals' computer systems.
Results: Four hundred and twenty six FOBs were performed of which 113 (27%) were for possible infection. These 113 individuals had a median age of 47 years (range 16–86). 23/113 (20%) were HIV-infected, 20 (18%) HIV-uninfected and 70 (62%) had unknown HIV serostatus. Specific infectious agents were demonstrated in 42/113 (37%). In these, the final diagnoses were: 28/42 (67%) tuberculosis (TB); 6/42 (14%) pneumocystis pneumonia; 4/42 (10%) non-tuberculous mycobacteria; 4/42 (10%) aspergillus. Sputum was produced by 15/28 (54%) of TB cases before FOB. All had a negative smear for acid fast bacilli (AFB) but in 13/15 (87%) TB was subsequently cultured. AFB smear of bronchoscopic samples were positive in 6/15 (40%). Bronchoscopic abnormalities were visualised in 12/42 (29%) of cases diagnosed with infection. In all cases the abnormality noted was either excessive secretions or inflamed mucosa and these findings did not add to the diagnosis. In 15/71 (21%) of cases not diagnosed with infection, bronchoscopic abnormalities were visualised. In 4 subjects this aided diagnosis: 1/4 foreign body observed; 2/4 abnormal mucosa diagnosed as sarcoidosis on biopsy; 1/4 squamous metaplasia on biopsy. Therefore in total 4/113 (4%) had a visualised abnormality that enhanced diagnosis.
Conclusions: From our data we conclude that in cases of suspected lung infection visualisation of the bronchial tree by FOB rarely assisted with final diagnosis. We suggest therefore that non-invasive sputum induction may provide the same diagnostic information as FOB, but at a lesser cost and with greater patient acceptability.

P136 DEVELOPMENT OF AN IN VITRO MODEL TO INVESTIGATE THE EFFECT OF GLUCOSE ON THE INTERACTION BETWEEN RESPIRATORY EPITHELIA AND BACTERIAL PATHOGENS

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Background: Glucose concentrations are 12.5 times lower in normal human lung liquid than in plasma (Brennan *et al. Thorax* 2005;**60**:ii93) but are elevated in patients with hyperglycaemia or lung inflammation. Ventilated patients on intensive care with elevated lung liquid glucose concentrations were more likely to acquire respiratory *Staphylococcus aureus* infection than those with normal lung liquid glucose (Philips *et al. Thorax* 2005;**60**:761–4). The aim of the study was to develop an *in vitro* model to investigate the effect of different glucose concentrations on the interaction between respiratory epithelium and *S aureus*.
Methods: Immortalised respiratory epithelial cells (H441 cells) grown in RPMI (10 mM glucose) were incubated for 2 hours in RPMI with 1, 2.5, 5, or 10 mM glucose, then infected with 10^6 CFU wild type *S aureus* (strain 8325–4). Infected and uninfected monolayers were compared after a further 24 hours for confluence using phase contrast microscopy and cell numbers following trypsinisation and trypan blue staining. In supernatant cytokines were measured using a luminex system (Biorad) and *S aureus* numbers were determined by Miles & Misra.
Results: We report preliminary results obtained during model development (uninfected controls n = 1, infected monolayers n = 2). After culture in 1 and 2.5 mM, but not 5 and 10 mM glucose, infected monolayers were less confluent than controls. Total epithelial cell count/well appeared lower in infected monolayers (IM) than in controls (CM) at 1 mM (IM 4, CM 53) and 2.5 mM (IM 59, CM 116), but not at 5 mM (IM 113, CM 128) or 10 mM (IM 93, CM 88). However at 10 mM glucose 25% cells in infected monolayers were dead, compared to 1% of cells in control monolayers. Prior to infection, cell supernatant contained IL-8 (19 116 (4299) pg/ml) and IL-6 (71 (8) pg/ml) (n = 12). In controls IL-8 decreased (−11 212 (2721) pg/ml) and IL-6 was unchanged after 24 hr culture, irrespective of glucose concentration. In infected monolayers IL-8 increased at 5 and 10 mM glucose (+14 661 (4090) pg/ml (n = 4), but decreased at 1 and 2.5 mM glucose (−16 727 (5349) pg/ml, n = 4) (p = 0.029). By contrast infection increased IL-6 in supernatant more at 1 and 2.5 mM glucose (+477 (124) pg/ml) than at higher glucose concentrations (+58 (69) pg/ml) (p = 0.029). Supernatant bacterial counts were 5.6×10^5 prior to incubation and: 1 mM 1.5×10^6; 2.5 mM 4.5×10^4; 5 mM 6.2×10^3; 10 mM 5.7×10^2 mM after 24 hours. At 10 mM glucose large numbers of *S aureus* were seen attached to the monolayer.
Conclusions: We have demonstrated co-culture of respiratory epithelial cells and *S aureus* at different glucose concentrations. Preliminary studies indicate that the epithelial-bacterial interaction is altered at different glucose concentrations. Further experiments are now warranted to extend this study.

P137 ACQUISITION OF PENICILLIN RESISTANCE BY CELL WALL DEFECTIVE BACTERIA

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Introduction: We have previously shown that transient cell wall defective (CWD) variants of *Staphylococcus aureus*, induced by passaging on a medium with high osmolality (CWD medium) in the presence of sub-lethal concentrations of penicillin, remain resistant to penicillin after reverting to a cell wall competent (CWC) form. The CWC progeny are meticillin-resistant, *mecA*- and beta-lactamase-negative, and have no mutations in penicillin-binding proteins (Fuller *et al. Antimcrob Agents Chemother* 2005;**49**:5075–80). Here we aim to determine the kinetics of the penicillin resistance and whether it is constitutive or inducible.
Methods: *S aureus* ATCC 9144 cells (wild type) were grown in high osmolality (modified brain-heart infusion) or control (Lauria-Bertani) broth, with and without benzyl penicillin at subminimum inhibitory concentrations (MIC). CWD bacteria were indicated by the presence of Gram negative cells on a conventional Gram stain and sensitivity to penicillin G was determined using E-test strips. *S aureus* cells (wild type) were passaged 10 times in progressively higher penicillin concentrations, causing the proportion of Gram negative (CWD) cells to increase to 100%. The nature of resistance was tested by following growth of CWC cells after the addition of sub-MIC levels of penicillin.
Results: In both media *S aureus* remained Gram-positive without penicillin, but became Gram-negative (CWD) in benzyl penicillin at sub-MIC concentrations. The yield of CWD cells was much greater in the high osmolality medium. On serial passaging with increasing concentrations of benzyl penicillin, recovery of CWD cells was consistently maximal in the 4th and 10th transfers but fell in the 5th and 6th transfers. The fall in yield of CWD cells coincided with a steep increase in MIC from 0·25 mg/l to 32 mg/l. Maximum MIC obtained was (96 mg/l). CWD cells yielded by addition of sub-MIC levels of penicillin to CWC that had been growing without antibiotic caused a lag period and reductions in growth rate and saturation density, suggesting that the penicillin resistance requires gene induction and cell adaptation.
Conclusions: The presence of penicillin G in the medium was found to be important for the formation of CWD cells which increased dramatically in the CWD medium, which has an elevated osmolality. Penicillin resistance is acquired in a stepwise rather than a linear fashion and correlates with a change in the Gram staining reaction of a large proportion of the cells in the population. In penicillin-free media CWD cells are unstable; reverting rapidly to a CWC form that still has penicillin resistance. In this way, we propose that low dose and intermittent administration of penicillins may result in a stable form of meticillin-resistant *S aureus* that is *mecA*- and beta-lactamase-negative and has no mutations in penicillin-binding proteins.

Lung cancer: diagnostic procedures

P138 INTEROBSERVER VARIATION AND THE EFFECT OF EXPERIENCE IN THE DIAGNOSIS OF LUNG CANCER WITH A VIDEOBRONCHOSCOPE/ AUTOFLUORESCENCE SYSTEM

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Introduction: Autofluorescence (AF) bronchoscopes have been developed to improve bronchoscopy as a tool for the diagnosis of lung cancer and pre-invasive lesions. The benefit of an AF system separate to the new videobronchoscopes has not been tested previously. Previous studies

have examined the use of the white light (WL) mode followed by the AF mode and not each mode separately (Chiyo *et al Lung Cancer* 2005;**48**:307–13). Also, the interobserver variation for the two modes has not previously been examined. We assessed the separate use of each mode of a new AF system (Olympus Tokyo) by multiple bronchoscopists.
Methods: Forty two patients having a diagnostic bronchoscopy for possible lung cancer were studied. At each procedure the endobronchial tree was examined under both WL and AF with, prior to biopsy, the on-screen images systematically saved to disc. Any abnormal areas seen under either mode were then biopsied as well as 2 normal (control) areas. The 129 saved images (WL and AF) of the biopsied areas were placed in a random order and then shown to 10 bronchoscopists, 5 experienced and 5 inexperienced (<500 procedures). They graded the mucosa shown in each image for abnormality. Their diagnostic performance was assessed against the histological ''gold standard'' with sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy all calculated. Interobserver variation was assessed with weighted kappa values (κ).
Results: Both bronchoscopy modes performed well with mean sensitivity/specificity being 83%/75% for WL and 87%/79% for AF. The level of operator experience did not have a significant effect on these measures. The experienced bronchoscopists were, however, significantly better at the WL mode than the AF mode: specificity 79% *v* 66% (p = 0.043), PPV 60% *v* 46% (p = 0.049), accuracy 80% *v* 71% (p = 0.043) (two-sample *t* test). This was different for the inexperienced operators: they were better with the AF mode: NPV 95% *v* 91% (p = 0.042). Overall there was substantial interobserver agreement but this was significantly better for the WL mode than the AF mode: κ 0.70 *v* 0.57 (p = 0.0086) for the experienced bronchoscopists and κ 0.72 *v* 0.64 (p = 0.015) for the inexperienced.
Conclusion: The impressive performance of the WL mode and lack of added benefit from AF for experienced operators probably reflects the clarity of the images provided by the new videoscopes. The AF mode did however improve the ability of less experienced operators to correctly identify normal mucosa, potentially a useful role. It is reassuring that interobserver variation was low and compares favourably with many routinely used diagnostic tests. This model for assessing a new bronchoscopic diagnostic technique worked well and could be used again.

P139 UTILITY OF ENDOBRONCHIAL ULTRASOUND (EBUS): A COMPARATIVE STUDY BETWEEN CONVENTIONAL TRANSBRONCHIAL NODAL ASPIRATION (TBNA) AND EBUS GUIDED TBNA

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Introduction: Treatment options for lung cancer critically depend on tissue diagnosis and staging. Methods of sampling mediastinal lymph nodes and masses include transbronchial nodal aspiration (TBNA), a well established bronchoscopic technique. TBNA is relatively safe but underused with only one third of chest physicians performing the procedure (Munavvar M *et al*. Survey of the Practice of Interventional Bronchoscopy in the UK. *Thorax* 2004;**59**(Suppl II):76). It is a ''blind'' procedure and therefore diagnostic yield varies between 15% and 83%, a problem addressed by using real time imaging with endobronchial ultrasound (EBUS) guided TBNA. The Olympus Optical Corporation, Tokyo, developed a specially designed curved linear array bronchoscope with a transducer at the tip and a prototype version has been used with excellent results (Yasufuku K, *et al*. *Chest* 2004;**126**:122–8; Rintoul RC, *et al*. *Eur Res J* 2005;**25**:416–21). The aim of this prospective study was to evaluate the initial impact of EBUS on diagnosing and staging mediastinal tumours at Lancashire Teaching Hospitals.
Methods: The equipment was purchased in April 2006, with the service up and running in May 2006. In this study, we compared the diagnostic yield of all EBUS guided TBNA procedures performed by a single operator (MM) between May 2006 and July 2006 with data from conventional TBNA of corresponding nodes. A total of 8 patients and 9 nodes were sampled using EBUS and 12 patients and nodes using blind TBNA. Cases were selected based on CT appearances. Subcarinal nodes were excluded from the study.
Results: Diagnostic yield improved from 46.2% with blind TBNA to 88.9% with EBUS. Six males and 6 females were sampled with blind TBNA, age range 56–83 (mean 70.5). EBUS was used to sample 5 male and 3 female patients, age range 45–81 (mean 66.4). No significant complications were recorded.
Conclusions: EBUS guided TBNA is a novel way to diagnose and stage lung cancers allowing a more rapid and accurate diagnosis as it is carried out at the initial bronchoscopy. Difficult lesions <1 cm in size can be targeted, not usually accessible by conventional TBNA. Less passes are required for cytological analysis, saving time and resources. Mediastinoscopy can be avoided, which is more invasive, expensive, and carries associated risks. Furthermore, some groups of nodes not within the range of mediastinoscopy can also be sampled.

P140 EARLY EXPERIENCES OF TRANSBRONCHIAL NODE ASPIRATION IN THE DIAGNOSIS AND STAGING OF SUSPECTED LUNG CANCER AT WATFORD DISTRICT GENERAL HOSPITAL

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Introduction: Transbronchial fine-needle aspiration (TBNA) sensitivities reported in the literature range between 0.50–0.76, with specificities ranging between 0.92–1.00. The complication rate was reported as 2–5%, including haemorrhage and pneumothorax.
Methods: 15.4% (2/13) of hospitals in our cancer network presently offer this technique as part of their routine cancer work-up. TBNA has been offered in our unit since October 2005. We present the results of the first 35 patients who underwent TBNA as part of their routine investigation for suspected lung cancer. Enlarged nodes were identified by computerised tomography (CT) before bronchoscopy. TBNA was attempted if the following node groups were involved on CT: right paratracheal, anterior carinal, sub-carinal, posterior carinal, right bronchial, and right and left hilar. Aspiration sites were defined according to Wang's previously published endobronchial maps.
Results: TBNA provided a diagnosis in 89% of cases (31/35); identifying cancer in 30 cases and excluding disease in 1 case. TBNA samples were non-diagnostic in 11% of cases (4/35). In 7 of 18 cases when both TBNA and standard samples (mucosal biopsies, bronchial brushings or bronchial washings) where obtained bronchoscopically, TBNA provided diagnostic samples when standard samples failed to. This avoided the need for repeat invasive investigations. In 12 cases there were no endobronchial abnormalities and no standard samples were obtained. TBNA provided the diagnosis in all 12 cases. In total TBNA provided a diagnosis unobtainable by conventional bronchoscopy in 54% of cases (19/35). The diagnostic yield was higher for N2 station nodes (25/29–86%) compared to N1 station nodes (3/5–60%). The mean short-axis diameter of ''positive'' N2 and N1 nodes were 1.7 cm and 0.9 cm respectively. We report 2 cases of haemorrhage (1 minor, 1 major), and 1 pneumothorax (small and treated conservatively). Total complication rate for TBNA was 8.5% (3/35).
Conclusion: In summary in our series of patients, CT targeted TBNA from enlarged nodes is a safe technique with a high diagnostic yield. TBNA compliments standard biopsy techniques, in many cases is the sole diagnostic source and offers the key benefit of confirming nodal involvement. TBNA can be adopted safely by standard endoscopy units without endobronchial ultrasound. Other benefits include reduced reliance on expensive imaging and surgical procedures otherwise required to assess nodal involvement. We recommend introduction of selected TBNA into the routine process of investigating probable lung cancer.

Abstract P139

	R paratra	L hilar	R hilar	Pretrach	L paratra	Diag yield
EBUS	4/4 POS	1/2POS	0/1POS*	1/1POS	1/1 POS	8/9 = 88.9%
Blind	3/7 POS	1/1POS	0/2POS	1/2POS	1/1 POS	6/13 = 46.2%

*Indicates a true negative result based on pathology reports and MDT discussions.

P141 IS THERE A POTENTIAL FOR THE INCREASED USE OF TRANSBRONCHIAL NEEDLE ASPIRATION FOR CYTOLOGICAL DIAGNOSIS OF LUNG CANCER TO AVOID MORE INVASIVE TESTS? A UK DISTRICT GENERAL HOSPITAL EXPERIENCE

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Background: Transbronchial needle aspiration (TBNA) using flexible bronchoscopy is a minimally invasive procedure used to obtain histological diagnosis in patients with mediastinal lymphadenopathy. Its diagnostic accuracy ranges from 63 to 85% (Frey, *et al. Chest* 2004;**126**:819S). Despite being a much simpler and better-tolerated technique than mediastinoscopy, it is underutilised in the UK.
Aims: We aimed to see if TBNA would reduce the number of patients requiring other more invasive, surgical procedures to obtain a histological diagnosis of lung cancer and increase the number of patients having a histological diagnosis overall.
Methods: Retrospective case note and radiological imaging review of all patients with suspected lung cancers who were discussed at a multidisciplinary team meeting between April to June 2006. Out of a total number of 195 patients discussed, 40 were eligible for the study after excluding those with positive histology from flexible bronchoscopy and those with no mediastinal adenopathy on computed tomography (CT) of the thorax.
Results: See table.
Conclusion: Increasing availability of TBNA in UK hospitals should help us increase the number of patients obtaining histological diagnosis of lung cancer and also potentially avoid more invasive and hazardous techniques.

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Total patients (n)	40
Mean age (range)	70 (51–89)
Patients with obvious parenchymal mass on CT thorax, n (%)	31 (77.5)
Patients with mediastinal lymph nodes suitable for TBNA, n (%)	32 (80)
Patients suitable for TBNA, but not having histological diagnosis by any other method, n (%)	9 (28.2)
Patients suitable for TBNA, who had histological diagnosis by more invasive methods, n (%)	8 (25)
Patients who had histological diagnosis made by CT guided needle biopsy	10 (31.3)
Total no of patients who could have potentially had a TNBA, avoiding other higher risk techniques and increasing histological yield, n (%)	27 (84.5)

P142 CANCER YIELD OF PERSISTENT HAEMOPTYSIS AND ABNORMAL CHEST *X* RAYS NOT INDICATIVE OF MALIGNANCY

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Introduction: Although patients presenting with persistent haemoptysis (defined as that occurring for three weeks or more) and a normal chest *x* ray are known to have a low incidence of lung cancer (only 5–6%), those with an abnormal chest *x* ray suggesting malignancy have a much higher incidence (up to 71%) (*Eur Resp J* 2003;**22**(Suppl 45):8). However, the incidence of lung cancer in those with persistent haemoptysis and an abnormal chest *x* ray which is not indicative of malignancy is unknown, but this is a group of patients who may commonly be referred to the rapid access outpatient service of any lung cancer unit. To investigate this further, we looked at the incidence of lung cancer in such patients attending our large lung cancer unit.
Method: We have operated a rapid access lung cancer clinic (attracting up to 300 patients per year) since 2000 and have kept a comprehensive database of all referrals to date. From this, we identified those patients who had been referred with persistent haemoptysis and an abnormal chest *x* ray which did not suggest malignancy.
Results: Of 4839 patients processed, 121 (2.5%) fulfilled the above criteria. Of these, an ultimate diagnosis of cancer was made in 53 patients (44%), of which 28 (53%) had squamous or otherwise unspecified non-small cell carcinoma, 14 (26%) were adenocarcinoma, 6 (11%) were small cell carcinoma, 4 (8%) had a clinical diagnosis of lung cancer, and 1 (2%) had a vocal cord squamous cell carcinoma. Those with cancer were not more likely to be current smokers (81% *v* 73%, $\chi^2 = 0.96$, p = NS), be older (median age 74 *v* 69; $t = 0.099$, p = NS), or have worse spirometry (FEV1% predicted: mean 68 *v* 75, $t = 0.13$, p = NS), but were more likely to be male (70% *v* 50%, $\chi^2 = 4.82$, $p < 0.05$), and were less likely to have bilateral changes on chest *x* ray (9% *v* 27%, $\chi^2 = 5.61$, $p < 0.025$). Only one third of the patients with lung cancer had a normal bronchoscopy, compared with 98% of the remainder ($\chi^2 = 55.2$, $p < 0.001$).
Conclusion: Although patients with persistent haemoptysis and a normal chest *x* ray have a low risk of lung cancer, those with an abnormal chest *x* ray, even if it is not suspicious of malignancy, have a high incidence of the disease and therefore merit urgent referral to and investigation by the lung cancer unit.

P143 HAEMOPTYSIS WITH A NORMAL CHEST RADIOGRAPH: A 5 YEAR FOLLOW UP AFTER A NORMAL BRONCHOSCOPY

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Introduction: Haemoptysis may be a presenting symptom of lung cancer, even in patients with a normal/non-suspicious chest *x* ray. Case series have suggested a prevalence of lung cancer between <1% and 21% of all patients presenting with these features. This audit set out to ascertain the prevalence of lung cancer in our patients who presented with haemoptysis and a normal chest *x* ray, and to determine whether any who had normal investigations subsequently developed lung cancer during a 5 year follow up, at a time when routine pre-bronchoscopy CT scanning was not performed in our unit.
Setting: Respiratory Service in a UK District General Hospital serving a population of 300 000.
Method: Patients presenting with haemoptysis and a normal/non-suspicious chest radiograph from April 1998 to March 2001 were identified using the hospital Lung Cancer Management System Database (Unisoft). Radiographic findings were cross-checked with the hospital radiology reporting system. Five year outcome data for lung cancer were obtained from the hospital lung cancer multidisciplinary meeting database. Further corroboration was obtained from our hospital general records.
Results: Seventy three patients (median age 57 years) with haemoptysis and a normal chest *x* ray underwent bronchoscopy in the 3-year period. Fifteen were <44 years old, 44 were aged between 45 and 69, and 14 were 70 years or more. One patient (1.4% of cohort) was diagnosed with lung cancer (squamous cell carcinoma of the proximal right main bronchus) as a result of the initial bronchoscopy. Over the next 5 years, 2 other patients (2.7% of cohort), whose initial investigations were negative for lung cancer and who had been discharged from follow up, were subsequently diagnosed with lung cancer. Case 1: 65 at first bronchoscopy, had squamous carcinoma diagnosed 2 years later. Case 2: 70 at first bronchoscopy, had adenocarcinoma diagnosed just prior to 5 years later.
Conclusions: Our audit findings support the practice of performing bronchoscopy in patients with haemoptysis even should the chest *x* ray not suggest lung cancer. In those whose initial bronchoscopy did not reveal lung cancer, the incidence of subsequent lung cancer diagnoses over the 5-year follow up period was small, and was of approximately the same order as that expected from North Trent lung cancer incidence data.

P144 IDENTIFYING CLINICAL AND RADIOLOGICAL FACTORS ASSOCIATED WITH THE DEVELOPMENT OF PNEUMOTHORAX COMPLICATING PERCUTANEOUS CT-GUIDED LUNG BIOPSY

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Background: Pneumothorax (PTX) is a recognised complication of percutaneous CT guided lung biopsy (CTLB) occurring in about 20% of cases. This study aims to identify variables associated with the occurrence of PTX and to estimate accuracy of predicting PTX risk during CTLB.

Method: Patients undergoing co-axial cutting needle CTLB at University Hospital Aintree between January 2000–03 were identified from the radiology database. The case notes and complete imaging of 134 patients (mean age 69 years; 55% M) were available for the study. The path taken by the cutting needle (20 G in all cases) during CTLB was marked on each staging CT scan by an independent observer & these scans were then reviewed independently by 2 thoracic radiologists (rad1 & 2) blinded to the clinical details and procedure related complications. Each radiologist documented lesion and biopsy path characteristics, CT emphysema severity score (nil-mild-mod-severe) as well as predicting PTX risk during CTLB using a percentage Visual Analogue Scale.
Results: PTX occurred in 32 (24%; mean age 70 years) cases; 5 (16% of this group; 3.7% total) requiring intercostal drainage. Biopsies complicated by PTX were associated with smaller lesion size (3.29 *v* 4.92 cm; *t* test; $p<0.005$), greater lesion depth (mean 1.89 *v* 0.87 cm rad1; 1.80 *v* 0.92 cm rad2; *t* test; $p<0.005$), non-adherence of lesion to the pleural margin (χ^2 test; $p<0.005$; rad 1 & 2) and increased FEV1 (mean 2.06 *v* 1.73 l; *t* test; $p<0.05$). Patient age (mean 70 *v* 68 years; *t* test; $p>0.05$), gender (χ^2 test; $p>0.05$), lesion location (χ^2 test; $p>0.05$), currently smoking (χ^2 test; $p>0.05$), total pack years smoked (mean 45 *v* 42 years; *t* test; $p>0.05$), emphysema score (χ^2 test; $p>0.05$) and biopsy path crossing a major lung fissure (χ^2 test; $p>0.05$) were not associated with increased likelihood of PTX during CTLB. In those PTX requiring drainage, a trend to reduced FEV1 (mean 1.68 *v* 2.13 l; *t* test; $p=0.1$), smaller lesion size (mean 2.3 *v* 3.48 cm; χ^2 test; $p=0.1$) and increased lesion depth (rad1: mean 3 *v* 1.69 cm, $p=0.09$; rad2: 2.9 *v* 1.59 cm, $p=0.06$) was noted compared to those PTX managed conservatively. Median risk of PTX was estimated at 22.5% by rad 1 and 25% in rad2 in those biopsies complicated by PTX; furthermore, in the 5 PTX requiring intervention, PTX risk was estimated at $\leqslant 25\%$ in 3 and 4 of these by rad 1 and 2.
Conclusions: During CTLB, smaller and deeper lesions with no pleural adherence are associated with increased likelihood of PTX. Age, emphysema score, lesion location, needle crossing a major fissure were not associated with development of PTX. These factors may help to inform future risk assessment though predicting PTX occurrence during CTLB appears to be difficult.

P145 PREDICTING THE OCCURRENCE OF PULMONARY HAEMORRHAGE COMPLICATING PERCUTANEOUS CT-GUIDED LUNG BIOPSY: A STUDY OF CLINICAL AND RADIOLOGICAL VARIABLES

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Background: Pulmonary haemorrhage (PH) is an infrequent though recognized complication of percutaneous CT guided lung biopsy (CTLB) occurring in about 5% of cases. This study aims to identify factors associated with PH and to estimate the accuracy in predicting risk of PH during CTLB.
Method: Patients undergoing co-axial cutting needle CTLB at University Hospital Aintree between January 2000–03 were identified from the radiology database. The case notes and complete imaging of 134 patients (mean age 69 years; 55% M) were available for the study. The path taken by the cutting needle (20 G in all cases) during CTLB was marked on each staging CT scan by an independent observer & these scans were then reviewed independently by 2 thoracic radiologists (rad1 & 2) blinded to clinical details and procedure related complications. Each radiologist documented various lesion and biopsy path characteristics, presence of pulmonary artery dilatation (PAD) and predicted PH risk during CTLB using a percentage Visual Analogue Score. Blood pressure (BP) recordings taken 10 minutes pre and post procedure were available in 125 cases. PH was defined as haziness along the needle track; new air space shadowing and/or haemoptysis post biopsy.
Results: PH occurred in 5 patients (3.7%) but none required transfusion and no deaths occurred. Comparing this group with those CTLBs not complicated by PH, a non-significant trend was noted between increasing age (76 *v* 68 years; *t* test; $p=0.09$) and cumulative pack years smoked (70 *v* 43 pack years; *t* test; $p=0.08$). No relationship was found between PH complicating CTLB and gender, an established diagnosis of systemic hypertension, having a presenting symptom of haemoptysis (χ^2 test; $p>0.05$), whether currently smoking (χ^2 test; $p>0.05$), pre-biopsy BP (mean 146 *v* 142 mmHg; $p>0.05$), location of lesion (χ^2 test; $p>0.05$), histology subtype (χ^2 test; $p>0.05$), proximity of a blood vessel to biopsy path (χ^2 test; $p>0.05$) and lesion depth (rad 1: mean 1.9 *v* 1.08 cm; rad 2: 1.2 *v* 1.12 cm; *t* test; $p>0.05$). Rad 1 and 2 noted the presence of PAD in 6 and 7 cases respectively yet none of these resulted in PH. Rad 1 noted a trend towards presence of a blood vessel abutting the lesion itself and the development of PH in CTLB (χ^2 test; $p=0.06$) yet this was not observed by rad 2 (χ^2 test; $p=0.4$). In the 5 biopsies complicated by PH, both rad 1 and 2 estimated PH risk at $\leqslant 15\%$.
Conclusions: Pulmonary haemorrhage complicating CTLB was not found to be associated with, among other factors, pulmonary artery dilatation radiologically, lesion size and depth, a presenting symptom of haemoptysis and diagnosis of systemic hypertension. Predicting the occurrence of PH during CTLB appears to be difficult.

P146 PRELIMINARY EXPERIENCE USING LARGER CORE AUTOMATED NEEDLES FOR PERCUTANEOUS CT-GUIDED LUNG MASS BIOPSY: IS THERE ANY IMPROVEMENT IN DIAGNOSTIC ACCURACY AND COMPLICATION RATES?

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Objective: To assess whether using larger core (16 Gauge), automated needles improves the diagnostic accuracy in percutaneous CT-guided biopsies performed for suspected lung cancer. The safety profile of the procedure using this modification was also carried out.
Materials and Methods: Data were collected retrospectively on 45 consecutive percutaneous CT-guided lung mass biopsy procedures over a period of 18 months. There were 24 male and 21 female patients (median age 62 years, range 58–79 years). All cases were referred for biopsy of lesions suspected of being primary lung malignancy or metastases. The aim of the biopsy was (1) to confirm the presence of malignancy and (2) to identify the type of malignancy. The procedure was performed in a standardised way, using local anaesthetic and16G automated cutting needles without co-axial access. A single core (16G×2 cm) was obtained in 40/45 cases and 2 cores (two needle passes) were obtained in 5/45cases.
Results: Samples considered adequate for a full histological diagnosis were obtained in 45/45 cases. In one case inflammatory changes were identified on two separate biopsy procedures and a histological diagnosis of cancer was only made after the resected lobe was examined. No deaths directly linked to the modified procedure occurred. Major complications included clinically significant pneumothorax requiring further hospitalisation and treatment in 2/45 cases (4%) and significant haemoptysis in 1/45 case (2%). Minor complications such as asymptomatic CT-detected parenchymal haemorrhages and pneumothoraces occurred in 8/45cases (17%).
Conclusions: The use of 16 Gauge automated core needles for CT-guided percutaneous biopsy has got a high diagnostic accuracy with no increase in any of the clinically significant complications that are associated with the procedure.

P147 OUTCOME OF PATIENTS ATTENDING RAPID ACCESS LUNG CLINIC WHO UNDERGO CT THORAX BUT NO BRONCHOSCOPY

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Introduction: The benefits of having CT thorax before bronchoscopy have been well established (NICE guidelines 2005), and following the initiation of our rapid access lung clinic (RALC) our Trust adopted this policy. Consequently, patients that would have had bronchoscopy in the past now don't have it if the CT Scan is not suggestive of malignancy.
Aim: To identify these patients and follow them up for a 2-year period to see if any of these patients re-presented with lung cancer.
Method: We retrospectively audited the first 50 patients who underwent CT Thorax but no bronchoscopy during the study period of March 2003 to June 2004. In the above patients the reasons for not undergoing bronchoscopy were as follows: (1) metastatic disease: 5 (10%); (2) patients' wishes: 8 (16%); (3) pleural effusion: 6 (12%); (4) CT Scan not suggestive of malignancy: 31 (62%). These 31 patients that did not undergo bronchoscopy because CT did not suggest malignancy were then analysed for further symptoms and investigations during two years follow up.

Mean age (SD): 71 (11). Current smokers: 7 (22%), ex smokers: 14 (44%), never smoked 10 (32%). Mean pack years of smokers (SD): 24 (13)

CXR on first appointment: normal 4 (12%), abnormal but not suggestive of malignancy 23 (74%), and suggestive of malignancy 4 (12%).

CT scan reported as follows: normal 7 (22%), consolidation 2 (6%), chronic changes 8 (26%), pleural disease 6 (20%), others 8 (26%).

20/31 (64%) patients were followed up for an average of 12 months. 15/20 (75%) of these did not develop any further symptoms. 10/15 patients underwent further investigations in the form of CXR and 1 patient had a follow up CT scan. All of these patients were well at the end of the study and the final diagnoses were: bronchiectasis 2, COPD 5, benign pleural disease 3, pneumonia 2, others 3.

5/20 (25%) did develop further symptoms. All of them underwent further investigations in the form of CT and CXR. Final diagnoses in those patients were as follows: benign nodules 2, mesothelioma 2, CCF 1.

11/31 (36%) were not followed up in our clinic. 2/11 (20%) patients re-presented with further symptoms and were diagnosed as having other malignancies thought to be unrelated to the primary presentation. 9/11 (80%) remain well.

Final outcome of 2 year follow up: deceased 8/31 (26%); causes of death were other primary cancers and infection. None of the 31 patients died of lung cancer.

Conclusion: In this study not performing bronchoscopies in patients with non-malignant looking CTs did not have any adverse affect on outcome. No lung cancers were missed.

P148 TIMING OF COMPUTED TOMOGRAPHY AND BRONCHOSCOPY IN THE INVESTIGATION OF LUNG CANCER IN THE PENINSULA CANCER NETWORK

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NICE guidance for management of lung cancer recommends that all patients with suspected lung cancer should undergo a CT scan of the thorax prior to fibreoptic bronchoscopy (FOB) and/or CT-guided biopsy to obtain tissue diagnosis.

We undertook an audit of all patients with a tissue-proven diagnosis of lung cancer made within the five acute Trusts serving our Cancer Network. We surveyed the number of patients undergoing CT prior to FOB, the diagnostic yield when FOB was used as a first line investigation and how histology was obtained.

Four out of five Trusts provided data for patients diagnosed with tissue-proven lung cancer between January and December 2004. A total of 450 patients were diagnosed, with diagnosis confirmed by bronchial biopsy in 240 (53%), CT-guided biopsy in 79 (18%), surgical biopsy in 73 (16%) and by other means (for example, Lymph node FNA, liver biopsy) in 58 (13%).

In 285 (63.3%) cases NICE guidance was adhered to with a CT undertaken prior to definitive tests for tissue diagnosis. Of these, 123 (43%, 27.3% of total cases) had an investigation other than bronchoscopy as first line to successfully obtain tissue. Diagnostic pick up rate on patients having a bronchoscopy was 72.3% in those patients having the procedure before a CT scan and 78.3% in those bronchoscoped post scan.

Abstract P148

	CT First	+ve FOB if FOB first (%)	+ve FOB if CT first (%)
Trust A (n = 49)	25 (51%)	15 (65%)	17 (94.4%)
Trust B (n = 127)	106 (83%)	13 (68.5%)	63 (81.8%)
Trust C (n = 145)	90 (62%)	30 (60%)	26 (72%)
Trust D (n = 129)	64 (53%)	52 (86.7%)	26 (86.7%)
TOTAL (n = 450)	285 (63%)	110 (72.3%)	105 (78.3%)

Abstract P149 Table 1

Intended Rx	Before PET	After PET	Remainder
O	25	21	1 D,1 PAL,1 SUR,1 S
S	64	40	1 D,13 O,10 SUR
SUR	13	6	2 D,1 S, 3 O, 1 Referred

There was considerable inter-Trust variability in use of CT pre FOB. In the main, use of CT first increased bronchoscopic yield. Results have been disseminated to Trusts via the Network Site Specific Group.

P149 USE OF PHRASES CONTAINED IN PET SCAN REPORTS TO HELP DIRECT PATIENT MANAGEMENT

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Introduction: PET scans are being increasingly used to help stage lung cancer. Although this is mainly as a tool before surgery or radical oncological treatment, they can also be employed in the assessment of lung nodules or help define the nature of small lymph nodes where CT scans are equivocal. However, the degree of uptake of the radio-isotope by the region of interest can be variable and may be reported as such. This may influence the clinician in developing their subsequent management plan. We therefore looked at the phraseology of the PET scan report in our unit on the outcome for the patient.

Method: We audited all PET scans performed in our large lung cancer unit between March 2005 and June 2006. We looked at the intended management before PET (Surgery (S), Oncology (O), or Surveillance (SUR)) and the ultimate outcome (which also included Palliative care (PAL) and Discharge (D)), and whether PET changed lung cancer staging. We noted the description of PET positivity, which was coded by the reporting radiologist as intense increased uptake (IIU), highly increased uptake (HIU), increased uptake (IU), moderate increased uptake (MOIU), mild increased uptake (MIU), hot spot (HS), and normal (N). We looked for any correlation between the outcome and the term used to describe PET isotope uptake.

Results: 102 patients (mean age 69 years (range 41–95), mean FEV1 %predicted 72 (21–132), mean FVC %predicted 88 (46–145), median PS 1 (0–3), 50 male) were investigated. The outcome is shown in table 1. In 25 cases PET downstaged disease, upstaged it in 22, and 55 were unchanged. Overall in 7 cases PET was unhelpful (2 missed lymph nodes, 2 PET +ve but not cancer, 2 overestimated, and 1 underestimated the disease). Observation of the wording of the PET report is shown in table 2.

Conclusion: PET changed the management plan in a quarter of the patients in this series. The phraseology of the PET report also gave the clinician clues to help direct the management plan.

P150 DOES THE USE OF PET IN THE STAGING PROCESS FOR NON-SMALL CELL LUNG CANCER SIGNIFICANTLY DELAY SURGICAL TREATMENT?

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Introduction: Positron Emission Tomography is a beneficial and cost-effective adjunct in the staging of non-small cell lung cancer, particularly in reducing the number of futile thoracotomies. It is unclear how much delay the use of this limited resource adds to the diagnostic and staging process, and how this impacts on eventual tumour growth and mortality.

Abstract P149 Table 2

Outcome	IIU	HIU	IU	MOIU	MIU	HS	N
D	0	0	0	2	0	0	2
O	27	2	7	0	0	1	0
S	22	4	12	0	2	2	0
SUR	4	0	2	1	1	0	9
PAL	1	0	0	0	0	0	0

Aim: To estimate how much delay combined computed tomography and positron emission tomography (CTPET) imaging adds when included in the staging workup of non-small cell lung cancer and the effect this may have on tumour size at the time of operation and mortality of surgically operable non-small cell lung cancer patients.
Methods: Forty consecutive patients were retrospectively selected who had a primary non-small cell lung cancer resected by one thoracic surgeon and were referred from one health board between 2001 and 2004. CTPET has been routine in preoperative assessment at our institution since 2002. Twenty patients did not receive a CTPET in their staging process and 20 did receive a CTPET scan in addition to a diagnostic CT scan. The duration between diagnosis (date of CT scan) and treatment (surgical resection) was calculated and the two group means compared. The growth of the tumour during the surgical workup period was estimated by subtracting the maximum size of the tumour reported by the pathologist after resection and the maximum size on the CT scan. Although the methodology for these two measurements differs, this confounder is equal for both groups. Mortality was also determined for both groups.
Results: Mean age for both groups was 70 years old (range 45–78) and 68% of the patients were male. There was no significant difference in age ($p=0.21$) or sex ($p=0.74$) between the two groups. Mean (standard deviation) durations from diagnosis to surgery were compared (no CTPET 83 (29) days *v* 112 (32) days CTPET; $p=0.005$). The mean (standard deviation) increase in tumour size was not significantly different (no CTPET 0.30 (1.69) cm *v* 0.92 (0.98) cm CTPET; $p=0.2$). Overall one-year survival was 84%. One-year survival was not significantly different between the two groups (no CTPET 79% *v* 82% CTPET).
Conclusion: The mean delay added by CTPET scanning is 29 days. There was a non-significant increase in tumour growth before resection in the CTPET group. The addition of CTPET does not appear to impact on early mortality.

P151 AN EXPERIENCE OF PET SCANNING IN NON-SMALL CELL LUNG CANCER IN A TERTIARY CENTRE

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Introduction: Although the NICE guidelines on the management of lung cancer (NICE, 2005) state the need for rapid access to ^{18}F-deoxyglucose positron emission tomography (FDG-PET) in all patients with non-small cell lung cancer (NSCLC) being considered for radical therapy, experience in the UK has been limited by the lack of routine availability of PET scans in most areas of the country. Having used PET scans in the diagnosis and staging of our patients for around 4 years we believed it important to assess the extent to which individual management plans had been changed as a result of the PET scan findings compared to the conventional work up pre-2002.
Aim: To evaluate the impact of FDG-PET scanning in the routine diagnosis, staging, and management of patients with NSCLC in a tertiary hospital set up in the UK.
Methods: Retrospective analysis of all patients who underwent PET scanning for primary NSCLC in our department. Referral of patients for PET was made by the lung cancer multidisciplinary team (MDT).The findings were directly compared with the contrast-enhanced CT scan of the thorax and abdomen. The data were extracted from the lung cancer database, case notes, minutes of the MDT meeting, and CT and PET scan reports.
Results: A total of 309 PET scans were performed during the period from March 2002 to September 2005. Over the same period a total of around 1575 new cases of lung cancer and mesothelioma were diagnosed by the unit—therefore PET scans were used in 20% of our new patients. The final diagnosis was primary NSCLC in 257 (83%) and metastatic disease to the lung in 38 (12%). Seven scans were repeated in four patients who had adjuvant chemotherapy and data were not available for 7 patients. We specifically looked into the change in nodal (N) and metastasis (M) status post PET compared to CT alone. Data on N status were not available for 31 scans. In the remaining 226 patients PET scan resulted in nodal down staging in 59 (26%) (N2/3 to N0/1 in 58 patients and N3 to N2 in 1 patient), upstaging in 19 (8.4%) (N0/1 to N2/3 in 10 patients, N2 to N3 in 9 patients) and stayed the same in 148 (65.6%) patients. Data on M staging is available on all patients. 21 (8%) of patients were upstaged (M0-M1), 72 (28%) were downstaged (M1-M0) and 164 (64%) were unchanged. The downstaged group included 10 patients in whom the diagnosis was uncertain on CT, which turned out to be benign lesions on PET. In patients with primary lung cancer, 178 scans were performed specifically to assess suitability for surgery. In this group PET scan resulted in a change in the TNM staging in 117 (65.7%) of (downstaged n=94, upstaged n=23) and no change in 61 patients.
Conclusion: PET scanning has had a major impact on management decisions in our busy MDT and many patients would have been inappropriately treated if information based largely on CT was all that had been available. It is essential that all hospitals who manage patients with lung cancer have rapid access to PET scanning facilities.

P152 DO PET SCANS HELP REDUCE UNNECESSARY SURGERY FOR LUNG CANCER?

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Introduction: PET scanning is being increasingly in the diagnosis and staging of lung cancer. Recent NICE guidelines indicate that when radical treatment (including curative surgery) is contemplated for patients with lung cancer, PET scanning should be undertaken to look for mediastinal and distant spread, thereby preventing unnecessary treatment. To investigate this further, we looked at the outcome of PET scanning on our patients with suspected or proven lung cancer where surgery would have been the treatment of choice in the absence of PET.
Method: We looked at all patients who had PET scan for investigation of lung cancer in our large lung cancer unit. We selected all patients where the MDT decision was to perform a PET scan prior to referral for surgical resection, and audited the effect of the PET scan on the ultimate treatment plan.
Results: Sixty three patients (mean age 69.7 years (range 45–91), mean FEV1% predicted 76 (34–132), mean FVC% predicted 90 (51–135), median PS 1 (0–2), 31 male), fulfilled the criteria. The PET scans were performed at a mean of 26 days (range 3–36) following the MDT decision, and were reported a mean of 4 days later (0–8). In 21 patients (33%) the PET scan had an impact on subsequent management. Of these, in 2 cases (10%) they were discharged (PET scan normal), in 10 cases (48%) they were kept under surveillance (6 normal PET, 1 downstaged, 1 increased uptake but CT biopsy negative, 2 no change of staging), in 9 cases (43%) they were referred for oncological treatment (7 were upstaged, 2 had a poor PS). Of the remaining 42 (67%), 40 had surgery and 2 declined. In the operated group, the PET scan upstaged the disease in 2 cases, downstaged it in 7 cases but there was no change in the remaining 31 cases. However, in 3 cases where the PET scan downstaged the disease or suggested a benign lesion, surgery confirmed malignancy (false negative), and in two cases PET suggested malignancy but the surgical specimen was benign (false positive).
Conclusion: In this series PET scanning changed the management in one third of cases and in some of these surgery was avoided, preventing unnecessary risk to the patient. It was also useful in downstaging the disease in other cases. However, it gave false results in 12.5% of the cases who went to surgery. Larger studies are needed to assess its exact sensitivity or specificity for patients with lung cancer.

Pathomechanisms of COPD

P153 GENDER DIFFERENCES IN THE RELATION BETWEEN LUNG FUNCTION AND C-REACTIVE PROTEIN IN THE ENGLISH LONGITUDINAL STUDY OF AGEING (ELSA)

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Background: It has recently been reported that the inflammatory mediator C-reactive protein (CRP) is inversely related with lung function in a middle aged non-smoking population. However, important confounders such as social class were not considered in this analysis.
Method: We examine the relationship of CRP with forced expiratory volume (FEV1) in a large national population (English Longitudinal Study of Ageing, ELSA) aged 50 years and over who were resident in England, 2004. We explored the relationships in males and females separately.
Results: Data were available in 2272 males, 2572 females. The median FEV1 was 2.77 litres males and 2.01 litres females. In analysis of normalised data, significant Pearson correlations were observed in both men and women ($r=-0.26$ males and $r=-0.21$ females, both $p<0.01$). When analyses were restricted to never smokers (29% of male, 44% of female population), unadjusted correlations remained

significant (males $r=-0.18$, females $r=-0.22$, both $p<0.01$). However, in males the association between CRP and FEV1 became non significant following adjustment for age and wealth, as an index of social position (adjusted beta −0.13, p=0.23). In women the relationship remained significant (adjusted beta, −0.22, $p<0.01$). The association in females was unaffected by removal of those with overt lung disease (n=282 females) from the analysis or adjustment for body mass index.
Conclusions: We conclude in a non-smoking population, that the association of CRP with lung function is largely mediated by social position in males but not in females. Other, as yet undefined, measures are likely in to contribute in females but may include metabolic and hormonal factors, physical activity as well as the gender differences in the cytokine response to exercise, but these require further evaluation.

P154 GENE EXPRESSION PROFILING OF THE EFFECTS OF CIGARETTE SMOKE ON MACROPHAGES

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Aims: Cigarette smoke (CS) causes oxidative stress, and is the major cause of chronic obstructive pulmonary disease (COPD). We have investigated the effects of CS on macrophage gene expression.
Methods: Monocyte derived macrophages from 6 COPD patients were incubated with CS extract (CSE) (control, 1, 10, and 25%) for 6 hours. Cells were harvested in TRIzol, and RNA extracted for gene array analysis (Affymetrix U133 +2.0 Human Genome Chips) and quantitative TaqMan PCR. Array analysis was by mixed-model analysis of variance and Dunnetts test to determine significant results when compared to control. A twofold change with $p<0.01$ was considered biologically significant compared to control. All probe sets that were found to be significant in at least one concentration underwent functional analysis using DAVID (see http://apps1.niaid.nih.gov/david/).
Results: *Affymetrix analysis*: 24 probe sets at 1%, 401 probe sets at 10% and 778 probe sets at 25% CSE exhibited a biologically significant change.
Functional analysis: Functional analysis identified groups of genes (⩾2-fold change and $p<0.01$ at one CSE concentration or more) involved in cell growth (147 probe sets), cellular metabolism (137), signal transduction (133), nucleobase metabolism (129), organogenesis (74), cell death (43), and cell adhesion (25). Cluster analysis of these groups is on-going.
Quantitative PCR: Quantitative PCR of 36 genes confirmed array changes. These included a decrease in the anti-inflammatory cytokines IL-10 and an increase in pro-inflammatory IL-8 (for example, 86% decrease and 121% increase respectively at 10% CSE). There was also evidence of decreased IL-1β and IL-6 expression.
Conclusions: Acute CSE exposure affects pro- and anti-inflammatory gene expression in macrophages, as well as cell survival and metabolism genes. Our Affymetrix data are confirmed by quantitative PCR. Ongoing cluster analysis will identify groups of regulated genes.

P155 HISTOLOGY OF THE DIFFUSE EPITHELIAL RESPONSE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PERIPHERAL LUNG SHOWS THAT MATURE TYPE II PNEUMOCYTES ARE NOT THE MAJOR COLONISING CELL

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Introduction: Widespread colonisation of epithelial-like cells is a common finding in COPD lung resections and in the lungs of long term healthy smokers. These cells line alveolar surfaces and the external laminae of airways and blood vessels. Many researchers have speculated that these cells are proliferating type II pneumocytes but they have not been systematically studied. We have employed a panel of antibodies to examine the possible phenotype of these cells: surfactant A (mature type II pneumocytes), pan-cytokeratin {5, 6, 8, 17, and 19} (epithelial cells), cytokeratin 7 (non-differentiated adult epithelial cells), cytokeratin 5/6 (basal epithelial cells) and p63 (basal epithelial cells).
Methods: COPD peripheral tissue from individuals undergoing lung volume reduction surgery for emphysema was ethically acquired from Glenfield Hospital, Leicester. Sections were evaluated using H&E staining. Immunohistochemistry was carried out with the above panel on formalin fixed paraffin embedded sections, using DAB chromagenic detection.
Results: LVRS histology demonstrated a range of reactions from active inflammation and pneumonitis to post-inflammatory remodelling. Epithelial-like cell proliferation was noticeably associated with the latter group. The pan-cytokeratin antibody stained all epithelial cells including the colonising cells in the parenchyma. These cells are arranged linearly across the alveolar surfaces with occasional aggregations in the alveolar nodes. Surfactant A staining was seen on many of the alveolar surfaces and within macrophages and type II cells, but not on the colonising epithelial cells. Cytokeratin 5/6 was only seen in basal airway epithelium, similar to the expression of p63, although p63 staining was more widespread. There was sporadic staining of cytokeratin 7 within the airways and a subpopulation of colonising epithelial cells.
Conclusion: H&E evaluation suggests that colonising cells may have a reparative function because of their association with the post inflammatory phenotype. The negative surfactant staining of these cells strongly suggests that they are not mature type II pneumocytes. In addition these cells show a positive pan cytokeratin staining, not a characteristic of type II cells. The lack of cytokeratin 5/6 staining and the inconsistent p63 staining suggest that these cells are not proliferating basal epithelial cells. Cytokeratin 7 staining was variable suggesting considerable heterogeneity within this population. Further work is in progress to further characterise phenotype of these cells.

P156 INFLAMMATORY CELL INFILTRATION INTO PROXIMAL AIRWAY SMOOTH MUSCLE BUNDLES IN SUBJECTS WITH AND WITHOUT CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: Increased mast cell microlocalisation to the airway smooth muscle (ASM) bundle is a feature of asthma. Several studies have consistently reported that the mast cell is the only inflammatory cell to infiltrate the ASM-bundle. In contrast in COPD and smokers without COPD, infiltration of the ASM-bundle in the small airway by several inflammatory cell types has been reported with an increase in neutrophilic infiltration compared to controls. To date, the inflammatory cell infiltrate within the ASM-bundle in the large airway in COPD has not been elucidated.
Methods: Large airway samples were collected from surgical resection specimens from 9 COPD subjects (GOLD stages 1–2), and age matched controls with no evidence of obstructive airways disease including 9 smokers and 8 non-smokers. All samples were embedded in glycol-methacrylate resin and using immunohistochemistry, samples were stained for the presence of mast cells (tryptase+), lymphocytes (CD3+), macrophages (CD68+), neutrophils (NE+) and eosinophils (MBP+) within the submucosa and ASM.
Results: We identified numerous mast cells, CD68+ and CD3+ cells in the ASM irrespective of subject group in the resection material (see table). However, there was a paucity of neutrophils and eosinophils in the ASM-bundle in all groups.
Conclusion: Infiltration of the large airway ASM by a several inflammatory cell types was observed in resection samples from subjects

Abstract P156

	COPD	Smokers no COPD	Never Smokers
Mast cells/mm^2	4.98 (12.5)	8.51 (15.2)	7.89 (5.93)
CD68+ cells/mm^2	3.91 (13.1)	7.69 (9.67)	10.6 (11.7)
CD3+ cells/mm^2	3.22 (4.59)	1.19 (7.31)	1.26 (4.82)

Median (IQR) cells/mm^2 ASM .

with and without COPD. In contrast to a previous report in small airways neutrophilic infiltration into the large airway ASM was unusual.

P157 MOLECULAR ANALYSIS OF BACTERIA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE SPUTUM SAMPLES

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Introduction: Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality in many countries. The lungs of COPD patients are prone to colonisation by bacteria. Although the precise role of the bacteria in the progression of the disease is not fully understood, there is a clear need to better characterise these microbes. Previous analyses of bacteria in COPD sputum has relied on methodologies that require in vitro cultivation prior to analysis. For many reasons this limits the species that can be detected. This study tests the hypothesis that there is a diverse bacterial community of present in sputum sampled from COPD patients. To test this hypothesis, this study used culture independent and hence non-selective methodologies.
Methods: Sputum samples were collected from 20 COPD patients. Phylogenetically-informative sequences were amplified from DNA extracted directly from bacteria in these sputa. These sequences were analysed by Terminal Restriction Fragment Length Polymorphism (T-RFLP) analysis[1] to generate a profile of the total bacterial community present and, in four instances, by sequencing clones from prepared libraries.
Results: A total of 66 clones were sequenced. Species from 10 different bacterial genera—*Acinetobacter*, *Bacillus*, *Haemophilus*, *Moraxella*, *Ochrobactrum*, *Pseudomonas*, *Rhodococcus*, *Sphingomonas*, *Stenotrophomonas*, and *Neisseria*—were identified. The number of individual species detected in the T-RFLP profiles generated from the 20 sputum samples ranged from 2 to 19, with a mean value of 7.9 (SD 5.8). A total of 106 separate species were detected in the sample set. The species with the most intense band typically represented 62.7% (17.1) of the total lane signal, with the second and third ranked species typically representing 18.0% (12.0) and 10.5% (6.1) respectively. The species with the dominant band was derived from a recognised COPD pathogen in only two samples, where *P aeruginosa* was identified. The other species dominant in samples represented a range of organisms, both Gram-negative and Gram-positive, opportunistic pathogens and species common to natural environments.
Conclusions: The lower respiratory tract in COPD patients is therefore colonised by a relatively complex bacterial community. This community includes both species traditionally associated with COPD respiratory infections and previously unreported species. The impact of this community on respiratory health is as yet undetermined.

1. **Rogers GB**, Carroll MP, Serisier DJ, *et al*. Characterization of bacterial community diversity in cystic fibrosis lung infections by use of 16s ribosomal DNA terminal restriction fragment length polymorphism profiling. *J Clin Microbiol* 2004;**42**:5176–83.

P158 RELATIONSHIP BETWEEN EXHALED NITRIC OXIDE AND EOSINOPHILIC AIRWAY INFLAMMATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Identification of eosinophilic airway inflammation is important in chronic obstructive pulmonary disease (COPD) as it is associated with a response to short term corticosteroid therapy, and with a reduction of exacerbations with long term therapy. A raised forced expiratory nitric oxide (FeNO), is an attractive biomarker of eosinophilic airway inflammation, since it is easy to measure and delivers immediate results where available. We set out to determine whether there is a relationship between eosinophilic airway inflammation and FeNO in COPD.
Method: We analysed data from 79 subjects (54 male: 25 female) with COPD as diagnosed under BTS guidelines: mean (SD) age 68 (7.6), post bronchodilator % predicted FEV1 38.2 (15.3). 59 subjects were ex-smokers and 20 subjects were currents smokers, mean (SD) pack years for all subjects 49 (28.8). Measurement of exhaled nitric oxide and sputum induction were carried out according to standard protocols.
Results: Overall there was no correlation between levels of exhaled nitric oxide and sputum eosinophil counts ($r=0.174$, $p=0.125$). The relationship was closer in current smokers than in ex-smokers.
Conclusions: Exhaled nitric oxide is not a marker of eosinophilic airway inflammation in COPD.

P159 BRONCHOALVEOLAR LAVAGE OF SMOKERS HAVE INCREASED LYMPHOCYTE CHEMOKINE RECEPTOR EXPRESSION

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Background: Progression of chronic obstructive pulmonary disease (COPD) in cigarette smokers is associated with increased lymphocyte numbers in the lungs. Lymphocyte chemotaxis to the lung in COPD is poorly understood. Aims: to identify lymphocyte chemokine receptors with increased expression in lungs of COPD patients by (a) comparing BAL *v* blood; (b) COPD BAL *v* healthy smokers (HS) BAL.
Methods: BAL and blood CD4 and CD8 lymphocytes from COPD patients and HS were characterised by FACS analysis of chemokine receptors: CCR5, CXCR3 (Th1 cells) CCR3, CCR4, and CCR8 (Th2 cells)
Results: See table. COPD patients and HS had numerically greater CCR3, CCR8 and CCR5 expression in BAL CD8 cells compared to blood. These differences were all statistically significant ($p<0.05$) in the COPD group, but only for CCR5 in HS. This suggests that CCR3 and CCR8 expressing CD8 cells are selectively recruited in COPD. BAL and blood CD8 CXCR3 and CCR4 expression were similar in both groups. BAL CD8 CCR3 and CCR5 expression were significantly increased in COPD patients and HS compared to healthy ex smokers (HEX).
Conclusions: (1) CCR3, CCR8, and CCR5 can be termed ''lung homing''. (2) CCR3 and CCR8: evidence COPD specific. (3) Smoking increases CCR3 and CCR5. We provide evidence that lung CXR expression may change due to oxidative stress or inflammatory mechanisms in smokers.

Abstract P159 Median chemokine receptor expression (%) on CD8 cells

		CCR3	CCR8	CCR5	CXCR3
HS	BAL	18	18	40	49
	Blood	1	1	3	36
COPD	BAL	21	18	46	42
	Blood	8	8	10	27

BAL CD8 numbers were raised in COPD compared to HS (medians/ml $\times 10^2$: 25.8 *v* 6.6 $p=0.05$); CD4 numbers were similar in both groups.

P160 GRANULOCYTE TRAFFICKING IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Chronic obstructive pulmonary disease (COPD) is an inflammatory condition of the airways characterised by intense neutrophilia. We have used sub-imaging doses of 111 indium (111In) labelled granulocytes and high sensitivity whole body counting to assess neutrophil (PMN) trafficking and loss in patients with COPD.
Methods: Participants were transfused with autologous 111In-labelled PMNs (0.2 mSv) isolated using discontinuous plasma Percoll gradients and subsequently underwent whole body counting over a 10 day period. A single slit collimator was placed on the lower detector in order to obtain a longitudinal profile of PMN distribution. 111In profile and whole body retention data were obtained at 45 minutes, day 1, 2, 4, 7, and 10 in 7 ex smoking (XS)-COPD patients (mean FEV1 0.9 l) and 9 currently smoking (CS)-COPD patients (mean FEV1 1.0 l), 10 bronchiectasis patients, 12 healthy non-smokers, and 5 healthy smokers. Daily sputum samples were counted for 111In.
Results: Mean 111In PMN retention (SD) at day 7 were: non-smokers 94.5% (1.9), healthy smokers 93.5% (4.4), XS-COPD 94.2% (1.5), bronchiectasis 89.4% (8) but with a significant loss in the current smoker subgroup of COPD patients of 92.1% +/− 3 ($p<0.05$ compared to healthy non-smokers). The peak 111In signal in the sputum occurred at day 2 in both patient groups. At the initial scan (45 minutes) PMNs predominantly localised to the liver/spleen region in all patients. Thereafter cells additionally distributed to pelvic and thoracic areas. Thoracic SPECT using imaging doses of 99mTc-labelled PMNs (3 mSv) in 2 controls and 2 COPD subjects demonstrated 18.4% and 18.7% (values expressed as % of total thoracic activity) respectively of the 99mTc-PMN

uptake over the lung at 4 hours post injection with the remaining signal in the rib and vertebral body bone marrow (BM) compartment. Patlak analysis demonstrated quantifiable uptake within the lung and bone marrow over 4 hours.

Conclusion: Low dose autologous 111In neutrophil retention affords a measure of neutrophil loss through the airways, which appears to be more intense in CS-COPD and may be a useful method for monitoring granulocyte flux in CS COPD. This technique also permits accurate monitoring of PMN trafficking to the liver/spleen and BM compartments. Lung uptake is quantifiable using thoracic SPECT and Patlak analysis with less than 20% of the signal being within the lungs at 4 hours.

Funded by a non-commercial grant from AstraZeneca UK.

Data from this study have previously been submitted to ATS 2006 and COPD 5.

P161 CIRCULATING MATRIX METALLOPROTEINASES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND BONE DISEASE

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Background: The role of circulating matrix metalloproteinases (MMP) in COPD is not fully defined. Within the airway compartment, MMP-1 and −9 have been implicated in COPD. Meanwhile, circulating MMP-9 are elevated in patients with osteoporosis. We have previously reported that patients with COPD have a high prevalence of bone thinning (osteoporosis and osteopenia) across a spectrum of severity of COPD and hence explored MMP-9 in patients with COPD with respect to presence of osteoporosis.

Method: Patients with confirmed COPD (n=70) and healthy subjects (HS) (n=39) underwent dual *x* ray absorptiometry to determine bone mineral density (BMD) and hence presence of osteoporosis. Circulating MMP-9 (ng/ml) was measured together with inflammatory mediators.

Results: Patients had a median (range) age of 66 (39–82) years; 32 patients had a FEV1>50% pred, 38 with FEV1<50% pred. There were more patients (n=19, 27%) with osteoporosis compared to HS (n=5, 13%), χ^2, p=0.002. Patients had greater geometric mean (SD) MMP-9: 38.48 (2.24) compared to HS 20.12 (1.99)ng/ml, p<0.001. Among the patients, MMP-9 was greater in those with osteoporosis: 51.29 (2.33) compared to those with no osteoporosis: 32.3 (2.12), p<0.01. There was no difference in MMP-9 between those with FEV1< or >50% predicted, although $\log_{10}$ MMP-9 was related to FEV1 (r=0.424, p<0.001). HS had a lower MMP-9 compared to patients – in either group: with or without osteoporosis, p<0.01. $\log_{10}$ MMP-9 was related to BMD lumbar (r=−0.361, p<0.001), BMD hip (r=−0.287, p<0.01), in the whole population and also in patients: BMD lumbar (r=−0.364, p<0.01), BMD hip (r=−0.234, p=0.05). There was no such relation in HS. IL-6, TNF-α sr I and II were greater in patients (all p<0.01). In the whole population, $\log_{10}$ MMP-9 was related to $\log_{10}$ IL-6 (r=0.305, p=0.001) and similarly with TNF-α sr I and II.

Conclusions: Circulating MMP-9 is elevated in patients with COPD. Osteoporosis is prevalent in COPD patients and such patients have greater MMP-9 levels. BMD is related to MMP-9. The link of matrix metalloproteinase with both COPD and osteoporosis suggests similar pathophysiology.

Support received from GSK.

P162 COMPARISON OF METHODS FOR MULTIPLE FLOW RATE MODELLING OF EXHALED NITRIC OXIDE IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Modelling exhaled nitric oxide (FeNO) at multiple flow rates estimates NO airway wall concentration (Caw_{NO}), airway wall diffusing capacity (Daw_{NO}), alveolar concentration ($Calv_{NO}$) and maximal flux ($J'aw_{NO}$). Different mathematical modelling methods are described; there is no gold standard method or standardisation of the number of flow rates. For three different published methods, we (1) investigated the effect of the number of flow rates on model parameters and (2) compared the degree of error between modelled and actual data. FeNO was measured using Niox analyser (Aerocrine) at 10, 30, 50, 100, and 200 ml/s in 50 chronic obstructive pulmonary disease (COPD) patients and data applied to three different methods based on (i) complete non linear fitting of data or (ii) linear fitting to calculate $Calv_{NO}$ followed by non linear fitting (mixed methods). Parameters estimated from 5 and 4 flows were compared by repeated measures ANOVA. FeNO was significantly reduced (p<0.05) at all flow rates in COPD smokers compared to ex-smokers. Using 5 flows, all three methods showed reduced Caw_{NO} in smokers, while two methods also showed reduced Jaw_{NO} (p<0.05). There was no difference for $Calv_{NO}$ or Daw_{NO}. Table shows comparison of 5 and 4 flow rate data as ratio (95% confidence interval) except for Daw_{NO} (median difference). Only mixed method 2 was relatively independent of the number of flows. The median error between modelled and actual data derived using the least squares fitting technique was significantly lower for the non-linear method (1.96) compared to mixed methods (3.31 and 3.62). Caw_{NO} is reduced in COPD smokers, but these results can be dependent on the number of flow rates used. Complete non-linear modelling gives the most accurate fit to the actual data.

P163 BRONCHOALVEOLAR LAVAGE OF SMOKERS HAVE INCREASED CD4 REGULATORY LYMPHOCYTES

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Background: The progression of chronic obstructive pulmonary disease (COPD) is associated with increased lymphocyte numbers in the lungs. CD8 cells are well documented but fewer data exist about CD4 cells. CD4 cells are capable of effector and immunoregulatory functions. We have assessed the phenotype of bronchalveolar lavage (BAL) lymphocytes compared to those of peripheral lymphocytes in COPD patients and a control group of healthy smokers (HS).

Methods: BAL and blood samples were obtained from HS (n=19 mean age: 59.7, mean FEV1 2.67 l, mean pack year history: 34.4 years) and COPD patients (n=26 mean age: 65.9, mean FEV1 1.71 l, mean pack year history: 51.1 years). Cell surface markers for regulation (CD25, CTLA4, neuropilin and C27), activation (CD69), memory (CD45RO), and T cell integrin (CD103) were triple immunoflorescence labeled and assessed by flow cytometry.

Results: There was no difference in BAL CD4 numbers in COPD and HS (medians/ml $\times 10^2$: 15.2 *v* 12.9). BAL CD4 cells displayed increased activation and memory status compared to PBMC in both COPD and HS. BAL CD4/CD25^{bright} expression was increased compared to PBMCs in

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		5 *v* 4 highest flows	5 *v* 4 lowest flows
Non-linear	Caw_{NO}	2.02 (1.45 to 2.83)*	0.70 (0.61 to 0.81)*
	$Calv_{NO}$	1.99 (1.43 to 2.75)*	0.86 (0.79 to 0.92)*
	Daw_{NO}	19.55*	−1.24*
	$J'aw_{NO}$	0.72 (0.58 to 0.90)*	1.10 (1.06 to 1.14)*
Mixed 1	Caw_{NO}	1.68 (1.34 to 2.11)*	0.56 (0.38 to 0.83)*
	$Calv_{NO}$	†	0.76 (0.61 to 0.94)*
	Daw_{NO}	−4.24*	−1.01*
	$J'aw_{NO}$	0.91 (0.76 to 1.08) NS	1.12 (1.03 to 1.23)*
Mixed 2	Caw_{NO}	0.92 (0.72 to 1.18) NS	1.12 (0.89 to 1.41) NS
	$Calv_{NO}$	†	0.68 (0.53 to 0.88)*
	Daw_{NO}	0.650 NS	0.38 NS
	J'_{awNO}	1.27 (0.96 to 1.68) NS	0.97 (0.86 to 1.09) NS

*p<0.001; NS, not significant.
†$Calv_{NO}$ is calculated using 200 and 100 ml/s, hence is the same whether using the 5 or the 4 highest flow rates.

Abstract P163 Mean CD4 surface marker expression (%)

		CD25^{bright}	CTLA4	CD27	CD103	CD45 RO	CD69
CD4 BAL	HS	28.8	0.95	3	26.9	96	40.4
	COPD	23.1	4.4	5.0	39.7	95	50.0
CD4 blood	HS	2.3	0	10	0.3	48	0
	COPD	5.0	0	21.5	5.6	54	0

both groups, indicative of increased regulatory cell numbers. BAL CD4 cells also expressed increased regulatory markers CTLA4 and neuropilin (BAL 13.5%, blood 0%). BAL CD4CD25^{bright} cells expressed less CD27 compared to PBMCs, suggestive of reduced regulatory ability. There were no significant differences for BAL markers between COPD and HS.
Conclusions: We have demonstrated that a subpopulation of BAL CD4 cells from COPD patients and HS display a regulatory phenotype. There was no difference between COPD and HS, indicating that smokers with and without airflow obstruction have lung T regulatory cells. The reduced BAL CD4 coexpression of CD27 suggests reduced regulatory function. This is a potential mechanism of disease progession; reduced T regulatory function in smokers may allow the progression of inflammation.

P164 CONCEPTUAL AND PROPORTIONAL CLASSIFICATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PHENOTYPES

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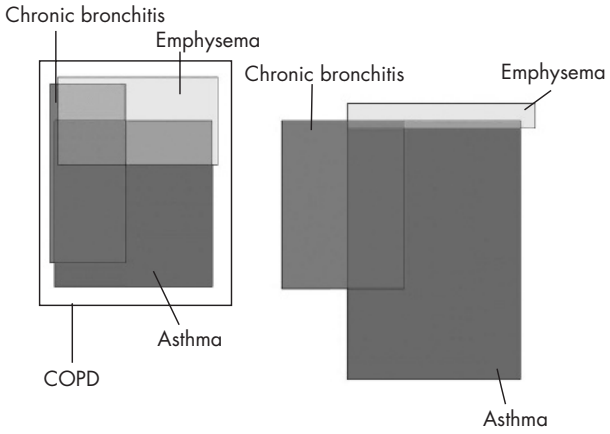
Background: Chronic obstructive pulmonary disease (COPD) encompasses a group of disorders characterised by incompletely reversible airflow obstruction, with overlapping subsets of different phenotypes including chronic bronchitis, emphysema and asthma. Attempts to quantify the proportion of COPD subjects with these phenotypes have been limited.
Methods: A cohort derived from a population-based survey of adults aged 25–75 years undertook questionnaires, lung function tests and CT scans. The proportion of subjects in each of 15 distinct phenotypes was determined, based on combinations of chronic bronchitis, emphysema, and asthma, with and without airflow obstruction.
Results: A total of 713 subjects completed the investigative modules of whom 112 (15.7%) had COPD (defined as a post bronchodilator FEV1/FVC of <0.7). The relative proportions of the phenotypic subgroups of subjects with and without COPD are shown in the proportional figure. Asthma with incompletely reversible airflow obstruction was the predominant COPD phenotype with only a small proportion of subjects with COPD having the classical phenotype of chronic bronchitis with emphysema but no asthma. One quarter of subjects with an FEV1/FVC<0.7 did not meet criteria for chronic bronchitis, emphysema or asthma and may represent a group with predominant small airways disease.



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Conclusion: This study has provided novel ways of conceptualising the COPD phenotypes and can be used as a basis for further research into the pathogenesis and treatment of this heterogeneous disorder.

P165 COMPARISON OF REGIONAL VENTILATORY AND PERFUSION DEFECTS IN SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: Patchy defects of ventilation (V) and perfusion (Q) are well recognised on lung scintigraphy in chronic obstructive pulmonary disease (COPD). However, we have not found any systematic analysis. We aimed to compare V and Q defects in a pilot study in patients with severe COPD. We have slightly modified Barter's classification (Barter SJ *et al. Am Rev Respir Dis* 1985;**132**:148–51) for grading defects in ^{81m}krypton scans of smokers.
Methods: We studied 8 patients with severe smoking related COPD, 4 during hospitalisation for an exacerbation. Anterior and posterior scans were performed seated, to improve image acquisition. ^{81m}Krypton was used for V and ^{99m}Technetium macroaggregated albumin for Q scans. All scans were analysed blind by 2 observers, graded normal (0) or abnormal: minor changes (1) moderate-diffuse (2) or severe (3) and largely matched or unmatched. Discrepancies (none of >1 grade) were resolved by a third opinion, also blinded (WES, Consultant in Nuclear Medicine).
Results: Six of the 8 COPD patients were male, mean age was 61.4 (SD 9) years, mean height was 168 (SD 11) cm, and mean weight was 64 (SD 7) kg. Mean FEV1 was 1.0 (SD 0.5) l (mean 34% pred), mean PEF was 177 (SD 77) l/min, (mean 36% pred), mean kCO was 0.76 (SD 0.3) mmol/min/kPa/l (mean 49% pred). Mean V scan grade was 1.8 (range 0–3) and mean Q grade was 2.0 (range 1–3). V defects were more marked than Q defects in 5 patients and most were regionally matched. There was a trend towards a correlation between grades of V and Q (r=0.7, p=0.05) and V grade tended to be higher in patients with lower FEV1 (r=0.57, p>0.1).

Despite problems of differential attenuation, body habitus and Technetium injection upright this technique provides semiquantitative information on regional ventilation and perfusion in COPD, with low radiation dose, relatively cheaply. A larger group of patients with a greater range of severity, including more with a non-emphysema phenotype, should be investigated.

A similar version of this abstract will be presented at ERS in September 2006.

P166 ETHNIC DIFFERENCES IN SPIROMETRY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Aim: This retrospective study aimed to discover whether lung function in patients with chronic obstructive pulmonary disease (COPD) differed according to ethnicity. It was based in Leicester where the largest minority group comprises people whose ethnic origins are in south Asia.
Methods: The database from the Respiratory Physiology Unit contained all measurements of lung function between 1990 and 2005. Data were filtered to exclude all patients of non-white or non-Asian origin. Diagnosis was not routinely entered into the database so we excluded patients under 40 years, those in whom the post-bronchodilator FEV1/FVC exceeded 70%, and those with significant response to bronchodilator (increase in FEV1>200 ml). Since there are recognised differences in FEV1 and FVC between different ethnic groups, subsequent analysis

Abstract P166 Mean FEV1/FVC (%) according to subgroup

		Asian	White
Male	Smokers	52.3	51.0
	Non-smokers	57.6	56.9
Female	Smokers	56.7	53.5
	Non-smokers	61.5	58.4

was restricted to FEV1/FVC. Where patients had made repeated visits, only data from the first visit were included. Mean values of FEV1/FVC were compared by regression analysis, taking account of age, gender, ethnicity, and smoking history (non-smokers compared with ever-smokers).
Results: The filtering strategy yielded 8747 patients including 407 (5%) Asians. Each subgroup included at least 90 patients apart from Asian female ever-smokers (n=6). Respiratory function was better in nonsmokers ($p<0.001$) and in females ($p<0.001$) (table). FEV1/FVC was 1.31% higher in Asians than whites ($p=0.033$).
Discussion: This retrospective study has shown a difference in FEV1/FVC between patients of Asian and white ethnicity, which is approximately half the size of the gender effect. Although this was a retrospective study that employed a filtering strategy rather than having a contemporaneous recorded diagnosis, the observation is important because the burden of COPD justifies the need to identify patient groups with different respiratory function, as the first step in identifying factors related to outcome of disease which may be open to modification.

P166A HIGH SENSITIVITY C REACTIVE PROTEIN LEVELS CORRELATE WITH PULMONARY INFLAMMATION AND FEV1 IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: C reactive protein (CRP) levels are frequently raised in chronic obstructive pulmonary disease (COPD) and correlate with impaired functional capacity and psychological distress (Broekhuizen *et al. Thorax* 2006;**61**:17). In severe COPD, CRP has been shown to relate with pulmonary inflammation, however, the relation between high sensitivity C reactive protein (HSCRP) and markers of pulmonary inflammation has not been clarified in patients with a broad range of disease severity.
Methods: Sixty nine patients with well characterised COPD (GOLD stages 1–4) and chronic sputum production were studied. Interleukin-1 beta (IL-1β), tumour necrosis factor alpha (TNFα), interleukin 8 (CXCL8), leukotriene B4 (LTB4), and myeloperoxidase (MPO) were measured in sputum supernatant. High sensitivity CRP (CRP) was measured in plasma.
Results: The median CRP was 94nM (IQR 50–128) with 52 patients (75%) having HSCRP levels which would be considered to be raised (>40 nM). CRP correlated negatively with FEV1 ($p=0.02$) and positively with sputum concentrations of CXCL8 ($p=0.007$), LTB4 ($p=0.01$), TNFα ($p=0.03$) and IL1β ($p=0.03$). Patients with raised CRP had a lower FEV1 ($p=0.01$) and higher concentrations of CXCL8 ($p=0.04$) and MPO ($p=0.02$) compared with those in the normal range.
Conclusion: A raised CRP concentration in plasma is associated with worsening lung function and a higher pulmonary burden of inflammation in COPD. This suggests an overspill of inflammation from lung to plasma rather than higher systemic inflammation drives the lung disease.

Oxygen assessment and provision

P167 THE OUTCOME OF A REVIEW OF OXYGEN ORDERS FOLLOWING PATIENTS' ATTENDANCE AT AN OXYGEN CLINIC

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Background: The provision of domiciliary oxygen therapy underwent radical changes in England and Wales in February 2006. The Royal College of Physicians[1] and The British Thoracic Society[2] provided recommendations and guidance that patients with domiciliary oxygen should be followed up to ensure optimised management.
Aim: To review the outcome of assessment of patients attending the newly established oxygen clinic in a 652 – bedded District General Hospital.
Method: Copies of the home oxygen order forms (HOOF) recording the orders of oxygen therapy for patients discharged from the hospital were sent to the oxygen service clinical lead. The clinical lead provided the discharged patients with a follow up appointment in the oxygen clinic at 6 weeks after discharge. Other patients seen in the respiratory outpatient department were referred to the oxygen clinic as necessary. The outcome of the patients who had attended the weekly oxygen clinic between 13 March to 12 June 2006 was recorded and reviewed.
Results: Thirty patients (19 female) were reviewed during this period. The mean age of the patients was 71 years (range 56–85). The primary diagnosis was chronic obstructive pulmonary disease (24), chronic asthma (1), bronchiectasis (1), pulmonary embolism (1), heart failure (2), lung cancer (1). Seven patients had more than one diagnostic category. The patients had a mean FEV1 of 0.97 l (range 0.35–1.88), mean FVC 1.89 l, (range 1.11–3.17); SpO_2 92% (range 82–97%); mean PaO_2 9.26 kPa (range 6.46–11.26), $PaCO_2$ 5.25 kPa (range 4.21–6.76) with patients breathing room air. 20 patients (66%) had alterations made to their oxygen therapy. Of these six patients had oxygen therapy withdrawn (concentrator=3), ambulatory oxygen (3). One patient refused withdrawal of her portable oxygen supply.
Conclusions: A significant number of patients discharged from hospital with some form of oxygen therapy had different oxygen therapy requirements by 6 weeks following their hospital discharge. The results of this review provide evidence in support of the BTS guidelines' recommendation that follow up arrangements are required for patients discharged home on oxygen therapy.

1. **Domiciliary Oxygen Therapy Services**. Clinical Guidelines and Advice for Prescribers. A report of the Royal College of Physicians, 1999.
2. The Clinical Components for the Oxygen Service in England and Wales. BTS, January 2006.

P168 EARLY EXPERIENCE OF A PHYSIOTHERAPY LED AMBULATORY OXYGEN CLINIC

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Background: In March 2006 we developed the first Scottish physiotherapy led Ambulatory Oxygen Service, running in parallel with our Interstitial Lung Disease (ILD) clinic, in Aberdeen Royal Infimary. A protocol was developed based on the BTS 2004 guidelines.[1] Patients underwent a structured assessment including baseline oximetry, 6-minute walk test (6MWT), with oximetry monitoring and measurement of Borg score (perception of breathlessness/fatigue). Patients (and their carers) views on ambulatory oxygen therapy and their anticipated use of this, were sought.
Results: Twenty six patients (16 male) were referred in the first 4 months, median age 68 (range 19–83) of whom 1 still smoked, 16 were ex-smokers, and 9 were life long non-smokers. Of these patients, 20 had ILD (of whom 13 had idiopathic pulmonary fibrosis), 4 had chronic obstructive pulmonary disease, and 2 had cystic fibrosis. 19/26 patients had no oxygen at home prior to assessment, but were reporting effort related dyspnoea with the potential for exercise desaturation (<90%) during their 6MWT. 18/26 patients were prescribed ambulatory oxygen following their assessment, but only 6/18 of had full correction of their hypoxia on exercise, principally because of limited availability of portable high flow oxygen (CD) cylinders in Scotland. Of the remaining 8 patients who were not prescribed oxygen, 4 patients declined ambulatory oxygen, despite their assessment suggesting potential benefit, and 4 were found not to require it. Since starting our clinic, 4/18 patients have subsequently been reviewed, and found to be using their ambulatory oxygen appropriately. 5/18 patients completed their baseline tests outwith the clinic, but of the remaining 13 patients, 6/13 demonstrated varying degrees of improvement in all 3 outcome measures (walking distance, oximetry, and Borg scores) with ambulatory oxygen and 7/13 showed improvement in 2 out of 3 outcome measures.
Conclusions: Our preliminary data suggest that patients with chronic lung disease, the majority of whom had ILD do derive subjective and objective benefit from ambulatory oxygen, although it is unfortunate that high flow ambulatory oxygen cylinders are currently difficult to source. Furthermore, we have found that physiotherapists are ideally placed to coordinate such a service. A more rigorous evaluation of the benefits of ambulatory oxygen, including impact on health related quality of life, is needed.

1. **BTS**. Clinical Component for the home oxygen service in England and Wales 2004.

P169 HIGH FLOW OXYGEN AS A RISK FACTOR FOR DEATH IN PATIENTS ADMITTED TO HOSPITAL WITH ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Background: There is concern about an association between the administration of high flow oxygen (HFO) and death, in hospitalised patients with acute exacerbations of COPD (AECOPD). So far the epidemiological evidence is relatively weak.(Durrington, *et al. Q J Med* 2005, Denniston, *et al. Clin Med* 2002, Murphy, *et al. Emerg Med J* 2001) There have been no attempts to evaluate whether any putative association is confounded by poor lung function. We evaluated the relation between HFO and in-hospital death, in a cohort of more than 1000 admissions with AECOPD.
Methods: Consecutive patients with AECOPD, admitted to Kings College Hospital between September 2003 and July 2006, were identified by specialist COPD nurses. The first blood gas taken in hospital was recorded and the inspired O_2 recorded. HFO was defined as $FiO_2>28\%$ or >2 l/min O_2 via nasal speculae. Lung function was measured in stable state in our lung function laboratory and categorised according to GOLD criteria. Death was recorded in our COPD database and cross checked with the hospital computerised administrative system. Each patient's last admission to hospital with AECOPD was used for analysis.
Results: Six hundred and eight patients contributed at least one admission to the dataset. Eighty nine (14.6%) of these ended in death. 339 (56%) were men, median age 72 years (5th–95th centile, 50, 87), 321 of 464 (69.2%) had an FEV1% predicted of less than 50%, 97 of 503 (19.3%) received HFO. In univariate analyses, risk factors for death in hospital included; HFO (odds ratio OR 2.40, 95% CI 1.38, 4.15), Gold Class (FEV1<30% compared with FEV1 50–80% OR 12.09, CI 2.82, 51.71) and age (years) (OR 1.05, CI 1.03, 1.08). The effects of HFO and Gold Class were independent of age. However, HFO was not significantly associated with death when Gold Class was included in the regression model. This may be because the risk of death associated with HFO was smaller in those whose lung function had been done (n = 391, OR 1.88, CI 0.88, 3.69) than in those in whom the lung function had not been done (n = 112, OR 3.24, CI 1.28, 8.21).
Conclusions: These data support the contention that high flow oxygen is associated with a doubling of the risk of death in AECOPD. Whether the effect is independent of other risk factors for death remains in doubt. Large numbers of patients recruited prospectively, or a randomised trial, may be required to properly adjust for potential confounding variables.

P170 ASSESSMENT FOR LONG TERM OXYGEN THERAPY AT A DISTRICT GENERAL HOSPITAL: DOES OVERNIGHT $PACO_2$ PROVIDE ADDITIONAL INFORMATION?

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Introduction: Long term oxygen therapy (LTOT) is of proven survival benefit in chronically hypoxic patients with chronic obstructive pulmonary disease (COPD). Current guidelines for assessing patients for LTOT do not make recommendations on whether overnight studies are required based on findings that daytime hypoxia is closely correlated to overnight hypoxia (Stradling *et al* 1983). Due to concerns over the development of hypercapnia the current practice for LTOT assessment at our hospital is to perform arterial blood gas analysis after 1 hour of LTOT (1 hour ABG), and again after overnight LTOT (overnight ABG) as an inpatient.
Aims: We wished to assess whether overnight ABG identified patients that had significant rises in $PaCO_2$ that were not identified at the 1 hour ABG.
Method: We retrospectively analysed 150 LTOT studies conducted at our DGH between 1998 and 2005. Of these, 64 met all the criteria for LTOT and had complete data for baseline, 1 hour, and overnight ABGs.
Results: Patient characteristics n = 64 (male = 41), mean age 71 (range 53–88) current smokers n = 6, mean FEV1 0.62 l (range 0.15–1.89 l), BMI 25.5 (range 14.8–44.8). Results showed good correlation between resting $PaCO_2$ and one hour $PaCO_2$ ($r=0.90$); between resting $PaCO_2$ and overnight $PaCO_2$ ($r=0.79$); and between 1 hour $PaCO_2$ and overnight $PaCO_2$ ($r=0.89$). Although mean $PaCO_2$ rose by 0.43 kPa, mean pH was well maintained. Five patients who had a normal pH at 1 hour developed acidosis overnight, mean pH 7.33 (7.31–7.33).
Discussion: These results show a strong correlation between $PaCO_2$ at baseline, 1 hour and overnight. However there was a small group of patients who only developed acidosis after overnight oxygen. Further research may identify the subgroups that are more at risk of nocturnal hypercapnia (possibly the obese patients or those with daytime hypercapnia). We believe that questions about the role of overnight studies remain unanswered.

P171 TOO MUCH OF A GOOD THING? OXYGEN ALERT CARDS ARE HELPFUL FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS AT RISK OF OXYGEN TOXICITY

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Introduction: It is well established that optimal oxygen therapy needs to be provided for patients with COPD while they are being transferred to hospital, or assessed in A&E. (Murphy *et al* 2001, Durrington *et al* 2005). The objective is to give appropriate oxygen to support their needs while avoiding the risk of CO_2 retention and respiratory acidosis.
Method: Working with ith the ambulance service we have designed a set of criteria to identify patients at risk of oxygen toxicity. These patients are issued with an oxygen alert card. This information is recorded on the ambulance service database. From January to June 2006, 16 patients were issued with a card. Patient notes were audited for: hospital admissions, method of transport, journey time, written verification that the card was used and oxygen concentration administered during the journey.
Results: Of the 16 patients issued an oxygen alert card 10 (62.5%) were readmitted during this period. 5 patients (31%) had one admission, 3 patients (18%) had two admissions, 2 patients (13%) had three admissions. Six patients (38%) were not readmitted during this period. Therefore we audited 17 admissions. Sixteen patients (94%) arrived at hospital using the ambulance service, either as a 999 call or following assessment by the GP who requested admission. Journey time included time spent by the paramedic at the patients home. The mean journey time was 42 minutes (range 31–63 minutes). Eight patients (47%) had a record of use of the oxygen alert card in the ambulance report form. One patient (6%) presented himself to A&E where 28% oxygen was administered. Eight patients (47%) had no formal verification of use of the oxygen alert card in their notes. In 15 of the 17 admissions the patient was given controlled oxygen. In only two cases was an inappropriately high concentration of oxygen used.
Discussion: The audit of flow rates administered was encouraging. We feel this demonstrates success of this system. It may be a reflection of the liaison with the ambulance service and the education delivered by the respiratory nurse specialist when launching the oxygen alert card. We believe these results demonstrate the importance of registering the issuing of the card on the ambulance service data base. The ambulance

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ABGs	Baseline mean (range)	1 hour	Overnight
pH	7.42 (7.30–7.49)	7.40 (7.29–7.47)	7.40 (7.26–7.53)
pCO_2	5.85 (2.95–8.81)	6.14 (3.35–9.11)	6.28 (3.55–8.79)
pO_2	6.99 (5.14–7.98)	9.76 (6.90–15.61)	9.22 (6.45–13.89)

journey time appears long, but we felt it important to include the time spent in the home when the patient was already receiving oxygen. The results suggest that there has been an increased awareness of the importance of delivering controlled oxygen to patients at risk of oxygen toxicity and that use of an oxygen alert card is an effective method of identifying these patients.

P172 COMPARISON OF NON-INVASIVE MEASUREMENT OF PCO_2 AND O_2 SATURATION WITH ARTERIAL BLOOD GAS MEASUREMENT DURING ASSESSMENT FOR LONG TERM OXYGEN THERAPY

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Background: Arterial blood gas (ABG) sampling is an essential part of patient assessment for long term oxygen therapy (LTOT). It is an invasive & potentially painful procedure. The TOSCA device (Transcutaneous Oxygen Saturation & Carbon Dioxide Analysis Monitor, Linde AG) allows non-invasive monitoring of pCO_2 and SpO_2 through a single sensor applied to the ear lobe.
Aim: To determine the accuracy of pCO_2 and SpO_2 measurements using transcutaneous monitoring compared with ABG (Rapidlab 348) and to assess whether LTOT could be safely prescribed using TOSCA measurements alone following an initial baseline arterial blood gas measurement.
Method: Consecutive patients presenting to our oxygen assessment clinic had concurrent ABG & TOSCA monitoring. Comparison was made of pCO2 and SpO2 on room air and after administration of 2 litres O2 via nasal prongs for 60 minutes. Values obtained using the two methods were compared by the method of Bland & Altman using STATA 9 (StataCorp, Texas).
Results: 159 measurements were made in 102 subjects (52% male, mean age 73 years) with the following mean ABG values at baseline: pO_2: 8.05KpA (95% CI 7.80–8.31), CO_2 5.81KpA (95% CI 5.6–6.02) and SpO_2 90.5% (95% CI 89.6–91.4). TOSCA values for SpO_2 were on average 0.97% (95% CI −1.3% to −0.64%) below those measured by ABG. The reference range for the difference in the reading was (mean +/−2SD) −5.2% to +3.2%. The variance of the difference in measurements made using the 2 devices increased significantly for patients with lower oxygen saturations (Pitman test $p<0.0001$). TOSCA values for CO_2 were on average 0.26 KpA (95% CI −0.35 to −0.18) below those measured by ABG (Reference range: −1.3KpA to +0.8KpA) with stable variance across the range of measurement. Finally the ability of TOSCA to accurately reflect changes in CO_2 was measured ($n=35$). The change in CO_2 obtained using the TOSCA device was 0.14KpA (95% CI −0.34 to 0.05) below that measured directly by ABG (reference range: −1.272 to +0.98KpA).
Conclusion: The TOSCA device underestimates pCO_2 and SpO_2 compared to ABG but mean differences are not big enough to be of clinical significance. In addition precision of the SpO_2 measurement decreased with increasing patient hypoxia as is usual with pulse oximetry. Variability of TOSCA measurements is high but all patients undergoing LTOT assessment who had a rise in pCO_2 of up to 1KpA were correctly identified using this non-invasive measurement.

TOSCA Equipment was loaned by Linde AG.

P173 REVIEW OF A FLIGHT ASSESSMENT SERVICE

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Background: Air travel is increasingly common, with a single UK airline carrying over 33 million passengers annually and over 1 billion people traveling by air worldwide each year. Longer flights are associated with increased risks of oxygen desaturation, especially in patients with chronic lung disease.
Aims and Objectives: To review the flight assessment service provided by the Lung Investigation Unit (LIU) at our Trust against BTS guidelines (Managing passengers with respiratory disease planning air travel 2002, revised 2004).
Patients and Methods: 124 patients (66 males; mean age 63 (SD 10) years) underwent flight assessment (current cost £209 per test at our unit) over a period of approximately 5 years (January 2001–February 2006). Data were collected from the LIU's electronic database.
Results: The single largest recorded disease category for which flight assessments were performed was COPD (38%). 104 of the 124 patients had baseline pulse oximetry; 25 had resting saturations >95%, 9 had saturations <92% and 70 had values of 92–95%. Sixty five of the 70 patients with intermediate saturations (92–95%) had hypoxic challenge testing (HCT) with 15% inspired oxygen. Fifty five of these had a positive test, indicating significant desaturation and the need for supplemental in-flight oxygen. All 25 of the patients with baseline saturations >95% had HCTs (contrary to the guidelines), as did 3 of those with saturations <92% (all patients with baseline saturations <92% will require in-flight oxygen). Surprisingly, 11/25 (44%) of HCTs in those with baseline saturations >95% were positive. Overall 66 of 124 patients fulfilled the criteria for in-flight oxygen.
Conclusion: Flight assessments are expensive tests and screening oximetry is not being used according to BTS guidelines; all patients with saturations >95% at baseline had hypoxic challenge tests performed. However, a significant proportion of these patients (44%) would appear likely to desaturate while flying.

P174 IS THE HOME OXYGEN ORDER FORM FIT FOR PURPOSE?

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Introduction: Since February 2006 hospital doctors or suitably trained nurses have been able to prescribe home oxygen for patients using the home oxygen order form (HOOF). The HOOF specifies the daily usage of oxygen and the requirement for ambulatory oxygen. It was designed to be simple to complete and assumes appropriate assessment has taken place. In a pilot study in December 2005 we found evidence of inadequate assessment resulting in inappropriate and incomplete recommendations for home oxygen. The HOOF demands no information on blood oxygen levels or respiratory function. We decided to assess whether the introduction of the HOOF had improved the quality of prescribing of oxygen.
Method: The notes of all patients for whom a HOOF was submitted from the Trust in May 2006 were audited. For each patient, the recommendations on the HOOF were compared with the diagnosis, spirometry, blood gas results and mobility in the hospital notes to assess the appropriateness of the request for home oxygen. We looked for measurement of hypoxia (PaO_2 £7.3kPa) and its correction with oxygen (at the HOOF flow rate) to a PaO_2 8kPa as defined in the guidelines. The hours of oxygen were compared with the guidelines for each diagnosis.
Results: See table. Only 7 (50%) of the 14 patients for LTOT had a measurement of the PaO2 achieved on the oxygen prescribed on the HOOF. In only 6 (42%) of 14 requests for LTOT did both the flow rate reflect the measured blood gases and the hours requested match the guidelines for the diagnosis.
Discussion: Despite an average of 45 minutes of respiratory nurse specialist's advice before each HOOF was submitted there was still failure to assess patients appropriately or prescribe the correct oxygen. (see C Eames *et al* submitted BTS winter meeting, 2006)
Conclusion: Inclusion of assessment data on the HOOF is crucial to ensure accurate prescribing of oxygen. Introduction of the HOOF in its

Abstract P174 Twenty five HOOFs were completed for 22 patients.

Category	n	PaO_2 £7.3kPa on air	PaO_2 8kPa on O2 as HOOF	Hours of O_2 appropriate
Palliative	6	N/A	N/A	N/A
LTOT	13	8 (1)	7 (1)	8 (1)
LTOT + ambulatory	1	1	0	1
Ambulatory only	2	1 (1)	0 (1)	(1)

( ) data unavailable.

current state has not improved this. In the absence of formal reassessment (which is not funded in our district) the HOOF is not fit for purpose.

P175 REGIONAL DIFFERENCES IN AMBULATORY OXYGEN PROVISION IN THE UK

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In January 2004 the Scottish Executive produced new guidelines for the provision of domiciliary and portable oxygen therapy (Scottish Executive NHS HDL (2004) 01). Similar guidelines for England and Wales have since been produced by the Department of Health (DOH). Both include the provision of ambulatory oxygen for patients on long term oxygen therapy (LTOT) who are able to leave the house. Patients who are not on LTOT but are seen to benefit clinically may also be prescribed ambulatory oxygen following an appropriate physiological assessment. However, the assessment criteria recommended by the Scottish Executive differ from the subsequent recommendations for England and Wales of the British Thoracic Society (BTS) (Clinical Component for the Home Oxygen Service in England and Wales, January 2006, BTS website).

We followed a simple protocol for the assessment of patients' response to ambulatory oxygen using a treadmill exercise test. This is a single blind, controlled trial, with the patient receiving either oxygen or air (2 litres/minute) via a nasal cannulae. After the patient has been breathing the test gas for 5 minutes the oxygen saturation (SaO_2) and breathlessness score (BS) using the Borg scale are recorded. Patients are then asked to stand on the treadmill before the treadmill is started and the patient exercised for a maximum of 15 minutes. The pace of the treadmill is set at 1.0 or 1.5 mph depending on fitness. SaO_2 and BS are recorded every minute until the patient stops or SaO_2 falls below 80%. The patient is then rested for 30 minutes before the assessment is repeated with the second test gas. According to the Scottish guidelines a 10% increase in walking distance and/or a 10% reduction in BS are considered to be positive indicators for the provision of ambulatory oxygen. In contrast, the BTS guidelines define desaturation and specify that ambulatory oxygen should only be prescribed if exercise desaturation is corrected and there is an improvement in exercise capacity and/or breathlessness.

To date, 37 patients (24 males) have been assessed and 21 have demonstrated an improvement in exercise capacity whilst receiving ambulatory oxygen. Under the Scottish guidelines a further 7 patients would have qualified for ambulatory oxygen on BS alone. In contrast, using the BTS guidelines only 17 patients would have qualified for ambulatory oxygen. There is little correlation between BS, SaO_2 and exercise capacity—for example, one patient walked further on air and perceived less breathlessness despite having better SaO_2 on oxygen. Hence, the reliance of the Scottish guidelines on small improvements in walking distance and BS can result in inappropriate provision of ambulatory oxygen in patients without reversible hypoxia.

P176 DO WE NEED TO ADMIT PATIENTS OVERNIGHT FOR LONG TERM OXYGEN THERAPY ASSESSMENT?

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Background: There are no clear guidelines on how patients should be assessed for long term oxygen therapy (LTOT), particularly for the risk of CO_2 retention. Dewsbury & District General Hospital is one of the few hospitals in UK where all patients for LTOT assessment are admitted overnight to assess the risk of hypercapnia. Assessment is done as per an algorithm.
Method: We performed a retrospective study of 35 patients who had LTOT assessment at Dewsbury and District General Hospital between May 2003 and June 2005. We reviewed the blood gases, which were performed three weeks apart at the clinic (on air) and during admission (on air, on 2 l of Oxygen, on 4 l of Oxygen and early morning).
Results: 17/35 was prescribed LTOT according to the national criteria. The blood gases of 12 patients had improved when re-assessed after three weeks and therefore no further evaluation for LTOT was carried out. 6/23 patients assessed developed a significant increase in PCo2 (>1 Kpa) on oxygen therapy. Out of these 4 patients developed a significant increase in PCo2 (>1 Kpa) on 2 l of oxygen after two hours, 1 patient developed a significant increase in PCo2 (>1 Kpa) on 4 l of oxygen after two hours and 1 patient developed a significant increase in PCo2 (>1 Kpa) on 2 l of oxygen on the morning arterial blood gases.
Conclusion: 6/23 (26.1%) developed significant CO2 retention and was not prescribed LTOT. It is of interest to note that one patient developed significant hypercapnia after overnight oxygen therapy, which is not usually routinely tested in most hospitals prescribing LTOT. We recommend an overnight inpatient LTOT evaluation. A study with larger patient groups/regional data is needed.

P177 OXYGEN ASSESSMENT IN BLAENAU GWENT

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Introduction: With the implementation of the new oxygen contract formal assessment of the oxygen needs of patients is required. Many patients who use home oxygen have never been formally assessed.
Aim: To review all patients receiving oxygen in Blaenau Gwent (BG), a Local Health Board serving population of 71 000 and rationalise oxygen prescribing.
Method: Patients using oxygen in the community were identified. A list of 340 patients was supplied by Contractor Pharmacy Wales/Business services Mamhilad. The original list was refined by contacting all GP practices in BG and also all pharmacies supplying oxygen. Most of the oxygen being supplied was in the form of cylinders for short burst. 205 patients on the list were registered at Nevill Hall Hospital and the notes of these patients were reviewed to identify patients who were know to the Chest Clinic and under regular review. These patients were simply asked to fill in a consent form and a Home Oxygen Order Form (HOOF) was completed. From the remaining patients high users i.e. patients using at least 8 oxygen cylinders per week, were identified. GP's were asked to refer these patients to clinic urgently for a full medical review and oxygen assessment. All other patients were initially assessed by a nurse; some complex cases were referred on for medical review.
Results: See table.
Conclusion: Following assessment, a large amount of inappropriate oxygen prescription could be discontinued. For patients requiring oxygen, an appropriate mode of administration was arranged. This resulted in very significant financial saving. Investment is needed to ensure all patients are assessed fully.

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Number of patients established on oxygen and under regular follow up	65
Number of patients assessed	239
Patients who discontinued oxygen	
Number of patients who discontinued oxygen after assessment	92
Number of patients who had discontinued oxygen themselves	25
Total number of patients who discontinued oxygen	117
Breakdown of patients remaining on oxygen	
Number of patients changed to concentrators only	46
Number of patients changed to concentrators and ambulatory	42
Number of patients changed to portable oxygen	1
Number of patients remaining on short burst oxygen	33
Total number of patients remaining on oxygen	122

Non-invasive ventilation

P178 ''DOOR TO MASK TIME'' IN NON-INVASIVE VENTILATION FOR EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Introduction: An optimum ''target time'' for starting non-invasive ventilation (NIV) after hospital admission for exacerbation of chronic obstructive pulmonary disease (COPD) (COPDE) has not been identified though it is known that delay in starting it lead to poorer outcomes. We felt that there were some delays in our service. We carried out a retrospective audit to identify the causes and to describe an ideal ''door to mask time''. Following the audit, educational needs would be identified and acted upon before reauditing the service.
Methods: All patients commenced on NIV outside the intensive care unit are logged by the respiratory nurse specialists (RNS). 41 consecutive patients were identified from this list, covering a period of 11 months (01/03/05 to 31/01/06). Of these, 31 case notes were available and were included in the audit.
Outcome Measures: An indication to start NIV was considered if: (a) the patient had known or suspected COPD (b) the patient had acute hypercapnic respiratory failure with pH below 7.35 and (c) medical treatment had been optimised (defined by the examining doctor). If medical treatment had not been optimised, a further 2 hours was allowed to do so before repeating arterial blood gases (ABGs). An arbitrary time limit was set at two hours from ABGs to starting NIV. We could identify no time limits in the literature, but this seemed reasonable, based upon the practicalities of setting up the equipment once the RNS had been informed of the need for it.
Results: 18/24 (75%) commenced NIV within 2 hours of ABGs. Delays occurred in 6/24 (25%) of patients. In 7/31 cases, the time of starting NIV was not clear from the documentation. In 22/31 (71%) of cases, NIV was initiated in the Medical Admissions Unit (MAU) or Accident and Emergency (A&E). Only 6/31 (19%) commenced NIV on the Respiratory Ward.
Conclusion: Unacceptable delays in starting NIV were found in 25% of cases. Identifying A&E and MAU as the key areas where NIV is commenced has enabled us to concentrate further educational efforts in these areas in addition to our rolling programme on the Respiratory Wards. Simple visual reminders about NIV in respiratory failure have been created and displayed above the 2 main blood gas machines. These posters capture the junior doctors' attention and give vital information. It is accepted that starting NIV early for acidotic COPDE reduces mortality, the need for intubation and length of hospital stay. We feel a ''target time'' for NIV needs to be established nationally as a major audit indicator, much like door-to-needle time is in acute MI and thrombolysis.

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P179 PREDICTORS OF OUTCOME FOR PATIENTS ADMITTED TO A RESPIRATORY HIGH CARE WARD

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Introduction: Respiratory high care wards are increasingly prevalent. Unlike intensive care units little has been published on the predictors of outcome for patients admitted into this environment. We looked at the admissions to the respiratory high care ward at the Bristol Royal Infirmary over one year and retrospectively analysed factors affecting the outcome.
Results: One hundred and eight patient episodes were analysed. The mean age was 69 years (95% CI 66 to 72), and the mean APACHE II score was 15.87 (95% CI 14.03 to 17.71). The inpatient mortality rate was 24% (25 patients), and the six-month survival after the day of admission was 55%. In survivors the mean length of hospital stay was 13.8 days (0–88). Of the 83 patients surviving to discharge 22% (18 patients) were readmitted within a month.

We collected data on a number of factors and related them to inpatient mortality. These included; diagnosis; comorbidities; usual exercise tolerance, performance state, and abode; and physiological markers. Whole data sets were not available in all patients. The continuous variables with a statistically significant correlation to inpatient mortality are shown in table 1.

We also calculated odds ratios for inpatient death for a number of absolute variables, as shown in table 2. Other results, such as usual abode and exercise tolerance, did not significantly correlate with inpatient death.
Conclusion: Although the APACHE II score and other physiological markers correlated with inpatient death, the correlations were weak. Patients with pneumonia or those who were normally dependent on others for self care appeared to be at an increased risk of death during admission.

Abstract P179 Table 2 Factors with significant odds ratio for inpatient death

Variable	OR	95% CI
Primary diagnosis acute exacerbation of COPD	0.22	0.08–0.61
Primary diagnosis pneumonia	5.67	1.85–17.37
Dependent on others for self care	3.71	1.17–11.80

P180 OUTCOMES OF ACUTE NON-INVASIVE VENTILATION THERAPY IN CHRONIC OBSTRUCTIVE PULMONARY DISORDER PATIENTS WITH A PH LESS THAN 7.25

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Introduction: It has been suggested that chronic obstructive pulmonary disease (COPD) patients presenting acutely with a pH<7.25 and CO_2>6.0 should be considered for intubation and ventilation. However, limited critical care facilities may not allow all patients to undergo this form of therapy. At the Birmingham Heartlands hospital 11-bedded NIV multidisciplinary unit, we offer NIV to all patients with a pH<7.35 and CO_2>6.0, with close links to ITU if intubation becomes a necessity. We conducted a 2-year prospective analysis of outcomes of all patients with COPD presenting to the unit with a pH<7.25 and CO_2>6.0.
Methods: Analysis of blood gases (when NIV considered and one hour post NIV), intubation and in-hospital mortality rates in patients presenting with an exacerbation of COPD in respiratory failure (pH<7.25 and CO_2>6.0), between 1 August 2004 and 31 July 2006.
Results: In the 2-year period, 354 patients were admitted to the NIV unit with hypercapnic respiratory acidosis. These data do not include those patients in pre-arrest situation and intubated immediately. 255 (72%) were COPD, obesity 24 (7%), thoracic cage wall deformity 7 (2%), neuromuscular 4 (1%) and others 64 (18%). Of the 255 COPD subjects, 82 admissions (72 subjects: 43 females) had a pH<7.25 and CO_2>6.0. There were 4 (4.8%) intubations (1 subsequent death) due to worsening acidosis, and 16 (22%) in-hospital deaths. In 15 patients, NIV was

Abstract P179 Table 1 Factors that correlated significantly with inpatient mortality

Variable	Correlation coefficient	95% CI	p Value
Blood urea	0.42	0.22 to 0.58	0.0001
APACHE II score	0.40	0.15 to 0.60	0.025
WHO performance state	0.27	0.01 to 0.50	0.04
Age	0.23	0.04 to 0.40	0.02
Albumin	−0.35	−0.53 to −0.15	0.001
pH on admission ABG	−0.35	−0.58 to −0.06	0.018

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	Pre NIV	One hour post NIV
pH	7.16 (0.07)	7.26 (0.07)
CO_2 (kpa)	11.8 (2.9)	9.2 (2.9)
O_2 (kpa)	11.1 (5.4)	10.9 (5.5)

considered as ''ceiling of care'', 12 had ''end-stage'' COPD with multiple comorbidities, and 3 multiorgan failure. The table shows blood gas data before and 1 hour after NIV: (mean (SD)).
Conclusions: This study demonstrates that NIV therapy in subjects with a pH<7.25 has acceptable intubation rates with blood gas improvements, and may avoid unnecessary intubation/ventilation. This high risk group,-however, do have a high mortality rate due to multiple comorbidities.

P181 NON-INVASIVE VENTILATION: EVIDENCE OF EFFICACY AS MAXIMAL THERAPY IN ACUTE RESPIRATORY FAILURE OUTSIDE HDU/ICU

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Aim: To evaluate the effectiveness of ward-based non-invasive ventilation (NIV) as maximal (ceiling) treatment for acute respiratory failure and to identify factors that might influence clinical outcome.
Background: NIV has emerged as a valuable adjunct to standard medical treatment for respiratory failure, primarily in decompensated chronic obstructive pulmonary disease (COPD). Its use in such patients has been proven to decrease the need for intubation and mechanical ventilation. However, the potential of NIV as ceiling therapy in acute respiratory failure remains unclear.
Method: Data were extracted from notes of patients commenced on NIV outside HDU and ICU between June 2003 and June 2006 (n = 141; 76M, 65F, totalling 153 episodes). Indications for NIV use were: non-infective COPD (n = 27); infective COPD (n = 61); left ventricular failure (n = 8); pneumonia (n = 18); neuromuscular disorders (n = 5); OSA/hypoventilation (n = 7) and others (n = 15). Differences in smoking history, age, comorbidity, and duration on NIV were evaluated. NIV success was defined as improved arterial blood gas (ABG) indices and clinical state, or failure, if neither was achieved or patients were stepped up to ICU or died. Clinical outcome was defined as survival to discharge or death during hospitalisation. ABGs were obtained prior to and at set intervals after NIV commencement.
Results: Median time to NIV set-up was 3 hours. Across the different clinical categories, mean pH improved from 7.27 (0.12) to 7.46 (0.51), with a corresponding decrease in $PaCO_2$ (9.48 (3.23) kPa to 7.63 (2.96) kPa). Overall, 87/153 episodes (56.9%) of NIV application were successful. Specifically, survival to discharge was evident in 96/153 NIV treatment episodes (62.7%). Comparison of COPD against non-COPD groups showed that NIV was successful in 87/121 instances (72%) in the former but only 41% in the latter. Among the non-ceiling group, 54/65 (83%) episodes of NIV were associated with survival to discharge without requiring step-up care. When capped as ceiling therapy, NIV outside of the ICU setting was associated with a 41.3% survival rate (33/80 treatment episodes).
Conclusions: In the current analysis, ward based ceiling NIV was successful in two fifths of cases of hypercapnic respiratory failure. Proportionately more patients with COPD benefited from NIV than individuals with non-COPD respiratory failure. COPD patients were also twice (51%) more likely to survive to discharge than the latter (25.8%) when NIV was the pre-determined treatment limit. These findings were not due to differences in baseline pH or $PaCO_2$.

Summary: Ward based NIV is associated with survival in significant numbers of patients with acute hypercapnic respiratory failure unsuitable for ICU.

P182 CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS' EXPERIENCE OF USING NON-INVASIVE VENTILATION AT HOME: A CASE STUDY APPROACH

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Chronic obstructive pulmonary disease (COPD) is known to affect patients' quality of life and anxiety and depression (Eakin *et al. Qual of Life Res* 1993;**2**:181–91; Lacasse *et al. J Cardiopulm Rehab* 2001;**21**:80–6). Non-invasive ventilation (NIV) is a recognised treatment for patients with COPD (COPD Guideline, *Thorax* 2004;**59**(S1):1–232) but little research has been conducted into the patients' experience of using home NIV. The aims of the study were to explore COPD patients' experience of using NIV at home, their compliance with the use of the machine, their recommendations for improving its use and their rating of their quality of life and anxiety and depression. A mixed methods multiple embedded case study design was used. Quantitative data were collected from 26 participants with COPD using NIV at home, using the St George's Respiratory Questionnaire (SGRQ) and the Hospital Anxiety and Depression Scale (HADS), to inform the study and identify 8 participants for further study. The 8 cases were selected by splitting the results of the SGRQ into quartiles and then identifying two cases from each quartile using the highest and lowest scores for the combined HADS score in each quartile. Data sources for the 8 cases were: an interview at home, demographic data and their questionnaire results. These three sets of data were used to triangulate the findings from each data source. The domains of activity (mean 90.42, SD 9.12) and anxiety (mean 8.73, SD 5.14) were rated as the highest in the SGRQ and HADS respectively. Thematic analysis of the interviews identified five themes (compliance, support, quality of life, anxiety and depression and recommendations). The 8 cases demonstrated high levels of compliance with the use of NIV but some described difficulties in the initial stages. Participants attributed their success in using home NIV to their perseverance with using the machine. Whilst participants commented on the role other patients had played in helping in their use of the machine, they did not comment on any interventions by healthcare staff. Participants viewed the use of NIV as ''life-enhancing'' and did not report any interference with daily activities because of its use. Participants were concerned about the apparent lack of knowledge about NIV of hospital staff and of their GPs, which was a source of anxiety. Recommendations fell into three categories: advice and education, improvements to equipment and support for its use at home. Triangulation of the data sources demonstrated the variability between participants in terms of presentation of the disease, scores for quality of life and anxiety and depression and in self-reported experience, suggesting that patients using home NIV would benefit from identifying and self-selecting care and services appropriate to their own individual needs.

P183 THE EFFECTS OF 1 WEEK'S WITHDRAWAL OF LONG TERM NON-INVASIVE VENTILATION IN HYPERCAPNIC CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Introduction: Long term non-invasive positive pressure ventilation (NIPPV) in chronic obstructive pulmonary disease (COPD) is not of proven benefit (Wijkstra *et al.* Chest 2003; 124: 337) but increasing numbers of patients receive this treatment (Janssens *et al. Chest*

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	HCO_3-mmol/l	PaO_2 kPa	$PaCO_2$ kPa	Nocturnal O_2 Saturation%	Nocturnal $PtcCO_2$ kPa
1st	31.3 (4.3)	7.9 (1.4)	6.9 (0.8)	94 (4)	6.3 (1.1)
7th	33.2 (3.1)	7.9 (0.9)	7.2 (0.6)	93 (3)	7.8 (1)
p Value	0.06	1.0	0.164	0.7	0.027

2003;**123**:67) as recommended in current NICE guidelines (*Thorax* 2004;**59**(Suppl 1):1–232). We are examining the effects of withdrawing NIPPV in well characterised COPD patients with chronic ventilatory failure and report the first week's results.
Methods: Patients were recruited prospectively. All had severe COPD and ventilatory failure prior to commencing NIPPV (daytime PaCO2>7.5 kPa with normal pH (7.35–7.45) or nocturnal transcutaneous carbon dioxide ($PtcCO_2$) over 9kPa). All had used nocturnal NIPPV for over 1 year and were compliant with treatment, mean hours daily use 7.4 (SD 1.8). Patients were screened 4 weeks prior to withdrawal. Clinical stability was defined as a PCO_2 within 1kPa and forced expiratory volume in 1 second (FEV1) within 15% of screening value and the absence of new symptoms of cough, sputum or breathlessness. Data were recorded on the first night and the 7th night without NIPPV. There were preset criteria for restarting NIPPV. The primary outcome measure was the effect on daytime arterial blood gases (ABG). Secondary outcomes were FEV1, nocturnal oximetry and $PtcCO_2$.
Results: Values presented mean (standard deviation). Eight subjects (3 female), age 63.9 (8) years, BMI 29.2 (6.3), FEV1 0.77 (0.34) were recruited. Five were on long term oxygen therapy. None restarted NIPPV during the week. No significant changes in FEV1, PO_2 or PCO_2 occurred. There was a significant increase in nocturnal mean $PtcCO_2$ and a rise in ABG bicarbonate. Six out of eight showed a rise in daytime PCO_2 values.
Discussion: There was no significant impact on daytime ABG if NIPPV was withdrawn for 1 week in this well defined group of COPD patients. However there was evidence of deterioration in nocturnal ventilation with a rise in $PtcCO_2$. Longer follow-up will determine if this nocturnal hypoventilation is progressive and affects daytime respiratory status.

P184 MRSA: CROSS CONTAMINATION THROUGH USE OF NON-INVASIVE VENTILATION?

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Introduction: Methicillin Resistant Staphylococcus Aureus (MRSA) is a significant infection control issue in hospital clinical medical and nursing practice. With increasing use of, and indications for, non-invasive ventilation (NIV) this intervention offers further potential for cross contamination with this organism.
Methods: As a consequence of the finding of MRSA on a routine screen of an air filter from a non-invasive ventilator in a Medical High Dependency Unit a prospective infection control audit was conducted. The issue was highlighted to all relevant staff, followed by screening of all machines after each use, together with patient filter changes every 24 hours, and air filter changes between patients.
Results: All four NIV machines used in the acute service were screened over a 6 month period, according to an agreed infection control protocol, resulting in 179 samples, out of which 20 swabs produced growth on bacteriological culture. Six cultures of staphylococcus aureus were obtained during the screening period but identification of all positive samples clarified these as probable skin or environmental contamination with no evidence of MRSA within filters or airflow tubing on the machines. There appeared no issue of concern with regards to patient management or cross contamination as a consequence of any of the positive cultures.
Conclusions: We conclude that although non-invasive ventilation offers potential for cross infection this does not appear to be a clinical problem provided adequate implementation of a comprehensive infection control policy. Appropriate machine decontamination and hand cleansing is essential in combating the issues surrounding cross contamination, and there remains scope for improvement and development within this area of practice.

These data have been accepted for presentation at the European Society Scientific Meeting in Munich 2006.

Investigation and management of pleural disease

P185 A ONE YEAR RETROSPECTIVE REVIEW OF THE RADIOLOGICAL INVESTIGATIONS OF CONFIRMED MESOTHELIOMA PATIENTS IN A TERTIERY REFERAL CENTRE

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Malignant pleural mesothelioma (MPM) accounts for 17 000 deaths per year in the United Kingdom. This rate is increasing with and is estimated to peak within the next decade with 1950–2450 deaths per annum expected.[1] Modern diagnostic techniques allow prompt diagnosis with subsequent CT guided biopsy, thoracoscopy and management under the relevant multidisciplinary meeting (MDT). Prompt early diagnosis allows the patient to be considered for more radical treatment and entry into clinical trials. Early treatment with chemotherapy in a single randomized trial was thought to be advantageous to survival.[2] The NICE guidelines for the management of patients with lung cancer suggest referral for unilateral pleural effusions (with no other cause) to a chest physician/MDT.[3] and there should be a coding mechanism for this process.

The initial diagnosis is often prompted by the chest *x* ray (CXR) findings of a unilateral pleural effusion or thickening. We reviewed a cohort of patients diagnosed pathologically or clinicoradiologically with MPM from 1 May 2004 to 30 April 2005. All patients within Leicestershire who had been reviewed by the single MDT for the area and had been given a diagnosis of MPM were included. A review of the patients' investigations and radiology was performed using the MDT minutes and radiology information system (RIS) respectively.

There were 30 patients, 26 male and 4 female with an average age of 70.9 years (median 75 years). 20 casers were diagnosed histologically with the other 10 diagnosed on clinicoradiological grounds. 27 patients (90%) were found to have a unilateral pleural effusion on CXR prior to diagnosis (17 right, 10 left). 5 patients (17%) had pleural thickening on CXR. Only 3 patients (10%) had cancer referral codes on the radiological report. 2 suggested referral to a chest physician.

30 patients had an initial CXR. 29 patients had a CT with only 3 having a TMN staging in the report. 12 patients had a CT guided pleural biopsy (7 positive and 5 inconclusive). 10 patients had a follow up CT.

Time taken from initial CXR showing an ''unexplained pleural effusion'' to discussion at first MDT ranged from 0.2–27 months, with average of 4.3 months and median of 0.8 months.

This study shows that a proportion of patients had a delay in diagnosis which could have limited their treatment options. The ''unexplained'' unilateral pleural effusion on CXR needs to be highlighted as a potential radiological sign of MPM and other malignant pleural disease, both to radiologists and clinicians. A finding of unexplained unilateral effusion should prompt specialist referral to limit time delays between initial suspicion and diagnosis and treatment, appropriate coding of these CXRs aids this process.

1. **Benamore RE**, *et al*. Use of imaging in the management of malignant pleural mesothelioma *Clin Radiol* 2005;**60**:1237–47.
2. **O'Brien ME**, *et al*. A Randomised trial in malignant mesothelioma (M) of early (E) versus delayed (D) chemotherapy in symptomatically stable patients: the MED trial *Ann Oncol* 2006;**17**:270–5.
3. **NICE**. The diagnosis and treatment of lung cancer. February 2005. National Institute for Clinical Excellence.

P186 THE END OF THE LINE FOR ABRAMS PERCUTANEOUS PLEURAL BIOPSY? A SURVEY OF RESPIRATORY SPECIALIST REGISTRAR EXPERIENCE IN CLOSED PLEURAL BIOPSY

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Closed needle percutaneous pleural biopsy has traditionally been used to investigate exudative pleural effusion following non-diagnostic thoracocentesis when there is clinical suspicion of tuberculosis or malignancy. Diagnostic rates of 75% for tuberculosis and 57% for carcinoma have been reported (Tomlinson JR. *Semin Respir Med* 1987;9:30–6). Chakrabarti *et al* (*Chest* 2006;**129**;1549–55) reported low complication rates in all grades of medical staff performing the procedure in a UK hospital between 1997 and 2003.

More recently, CT-guided biopsy has been demonstrated to have diagnostic advantage over blind Abrams biopsy in cytology negative malignant pleural effusion (Maskell NA, Gleeson FV, Davies RJO. *Lancet* 2003;**362**:173). Thoracoscopy has a diagnostic sensitivity of 95% in malignant effusion, making it more sensitive than Abrams biopsy with the added advantage of performing therapeutic pleurodesis at the same procedure.

Increased use of image-guided and thoracoscopic biopsy, as well as an increase in the use of seldinger chest tube insertion without the opportunity for pleural biopsy while placing a surgical intercostal drain, has led to a reduction in the number of Abrams biopsies being performed with an inevitable effect on training.

An anonymous survey of experience in Abrams pleural biopsy was carried out among respiratory specialist registrars in the Wessex region of the UK (26 respondents). Over the last 2 years, on average, trainees had performed 2.5 procedures (11.5 total over the course of their training). 58% had received formal training; no respondents had undergone DOPS (direct observation of procedural skills) assessment in

the procedure. 62% of respondents felt competent in the procedure. 23% felt confident of obtaining pleural tissue. 22% felt they performed enough procedures to maintain competency.

Blind pleural biopsy remains of value in the investigation of exudative effusion following negative thoracocentesis. It may have health economic benefits in negating the need for image guided or thoracoscopic biopsy. However the infrequent use of the procedure may lead to difficulty in training future respiratory physicians and maintaining competency in those currently undertaking Abrams biopsy.

P187 ARE BLIND PERCUTANEOUS PLEURAL BIOPSIES STILL USEFUL IN THE DIAGNOSIS OF SUSPECTED MALIGNANT PLEURAL EFFUSIONS?

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Introduction: Thoracoscopic and CT guided pleural biopsies are now often used as the next diagnostic step in investigations of suspected malignant pleural effusions where a first diagnostic aspirate is cytology negative. They both have a higher diagnostic yield and lower complication rates compared to blind percutaneous pleural biopsy and in the case of thoracoscopy the ability to carry out therapeutic procedures. The Abrams' pleural biopsy needle is most commonly used in the UK. The yield compared with pleural fluid cytology alone is increased by only 7–27% for malignancy. Complications of Abrams' pleural biopsy include site pain(1–15%), pneumothorax (3–15%), vasovagal reaction (1–5%), haemothorax (<2%), site haematoma (<1%), transient fever (<1%) and, very rarely, death secondary to haemorrhage. If a pneumothorax is caused, only 1% require chest drainage. The aim of this project is too ascertain whether adequate pleural samples are obtained, the diagnostic rate and requirement for further diagnostic test aimed at obtaining histology and complication rates.

Methods: All patients who underwent day case Abrams Needle Pleural Biopsies for suspected malignant pleural effusion at a weekly ran Pleural clinic at the Respiratory Investigation Unit of the NNUH over a year's period (1/08/02–31/08/03) were included. All biopsies were done by a Respiratory Registrar or equivalent. Data which included demographic variables, lab results, and complications post procedure and further Diagnostic tests and Results were retrospectively collected from patients' case notes.

Results: A total of 20 pleural biopsies were taken. Adequate pleural samples defined as presence of pleura on biopsy sample adequate enough to generate a histological opinion, were obtained in 19 patients (95%). 11 malignant pleural effusions were diagnosed of which 6 (54.5%) were made on Abrams pleural biopsy samples. Diagnostic test which confirmed other malignancies and diagnosis were CT guided biopsies, Video assisted thoracoscopic surgical (VATS) biopsies and lymph node biopsies. Six mesotheliomas were diagnosed 2 (30%) with Abrams needle, the remaining were diagnosed in equal fashion by CT and VATS biopsies. In 8 out of 20 cases it was felt further test aimed at obtaining histology were necessary on clinical grounds. Complications: 1 patient had a pneumothorax which didn't require chest drainage. One patient had a vasovagal episode. There were no incidences of haemothorax, biopsy site heamatoma or infection.

Conclusion: Blind percutaneous pleural biopsies in experienced hands in the appropriate settings where CT guided or thoracoscopic biopsies are not easily available should be considered as a valuable approach in the diagnosis of suspected malignant pleural effusion.

P188 NINETY TWO PER CENT OF CURRENT RESPIRATORY SPECIALIST REGISTRARS THINK THAT TRAINING IN CHEST ULTRASOUND EXAMINATION FOR PLEURAL DISEASES SHOULD BE INCLUDED IN THEIR TRAINING CURRICULUM: RESULTS OF A NATIONAL WEB-BASED QUESTIONNAIRE SURVEY ON THE PRACTICE OF CHEST ULTRASOUND EXAMINATION IN THE UK

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Introduction: Chest ultrasound examination (CUS) has a well established role in the management of patients with plural effusions (PPE). In the UK CUS is mostly done in radiology departments (RD) where time and space constraints could lead to delays in clinical decision making. Opinion is growing favouring chest physicians (CP) performing their own CUS.[1, 2] Training in chest ultrasound forms part of the curriculum of Respiratory Medicine trainees in Europe. This is not the case in the UK, though the Royal College of Radiologists (RCR) has recently published CUS training guidelines for CPs. We wanted to ascertain the views of current respiratory specialist registrars (SpRs) of all grades with regards to CUS and training in CUS.

Methods: 512 SpRs whose email addresses were available on the British Thoracic Society contact database were invited electronically to participate in an on-line electronic questionnaire survey. There were 16 questions, with ''drop-down-menu'' (closed) choices, with the responses being automatically added to a database.

Results: Of the 512 invitations sent, 31 returned undeliverable. Data from 138 completed questionnaires (28.7% return-rate) were available for analysis.

Of the 138 respondents, 6 (4.3%) were first year SpRs (SpR-1) while 32 (23.2%), 32 (23.2%), 27 (19.6%), 21 (15.2%) and 20 (14.5%) were SpR-2, SpR-3, SpR-4, SpR-5, and SpR-6, respectively. At the time of survey (January 2006), 57 (41.3%), 19 (13.8%), and 62 (44.9%) of the respondents were working in District General Hospitals, Secondary Referral Teaching Hospitals, and Tertiary Referral Hospitals, respectively, with 39.2% and 25% of them working in firms seeing 5–8 PPEs and 9–12 PPEs per month, respectively. 119 (86.2%) of the respondents think that chest physicians should be performing their own CUS and 128 (92.7%) wanted CUS training included in the SpR curriculum. *Who has had formal training?* 20 (14%) of the SpRs have received formal training in CUS though only 13 (9.4%) had regular access to a CUS machine and a training mentor (as of January 2006). *Who has access to chest ultrasound machines?* 24 (17.4%) respondents had access to a CUS machine though 11 (7.8% of all respondents) would appear to be engaging in CUS with neither formal training nor a mentor. *Were SpRs aware of the RCR CUS training guidelines?* 128 (93%) of the SpRs were NOT aware.

Conclusions: The vast majority of current SpR who will be future CPs feel that training in CUS should be part of their curriculum. Apart from training in CUS, access to a CUS machine and a training mentor appear to be important issues that need addressing.

1. **Doelken**. *Chest* 2003;**123**:332.
2. **Guhan AR**. *Thorax* Dec 2004.

P189 SURVEY OF THE PRACTICE OF CHEST ULTRASOUND EXAMINATION (FOR PLEURAL EFFUSIONS) AMONG CHEST PHYSICIANS IN THE UK

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Introduction: Chest ultrasound examination (CUS) is an important investigation in the management of patients with pleural effusions (PPE). In the UK, this is commonly done in the Radiology Departments (RD) though opinion is growing favouring chest physicians (CP) performing their own CUS.The Royal College of Radiologists (RCR) has published guidelines on the training requirements for CPs acquiring CUS skills. The current CUS practice among CPs in the UK is unknown. A web based survey was conducted among all the consultant members of the British Thoracic Society (BTS) to clarify this.

Methods: All 869 consultant members of the BTS were invited by e-mail to participate in an online electronic questionnaire survey. There were 16 questions with ''drop-down-menu'' (closed) choices, with the responses being automatically added to a database.

Results: Of 869 invitations sent, 129 returned wrongly addressed. Data from 203 completed questionnaires (27.4% return-rate) were available for analysis.

97 (48%) were consultants in District General Hospitals, while 47 (23%) and 59 (29%) were in Secondary Referral Teaching Hospitals and Tertiary Referral Teaching Hospitals, respectively. 86 (42.4%) had 5–8 PPEs admitted to their firms per month, while 32 (16%) had 9–12 PPEs. 46 (22.7%) requested a CUS in 50% of their PPEs, while 42 (20.7%) requested a CUS in 30% PPEs. with 5% using CUS rarely. Majority (64%) of CUS requests were to localise loculated fluid collections. 189 (93%) of CUS were performed by the RD. 98 (48.3%) waited on average one day for a CUS after requesting one (range: 0 days (2%)–5 days (3.5%)).

Should CPs do their own bedside CUS? 129 (63.5%) positively supported this view. Other responses were ''Not sure'' (22.7%) and ''Perhaps'' (13.8%). However, 185 (91%) were unaware of the RCR training guidelines for CPs to acquire CUS skills. *Should CUS training be on the Respiratory Specialist Registrar (SpRs) curriculum?* Overall, 167 (82%) consultants positively supported this view. This view was supported by 74.6% of consultants in Tertiary Referral Hospitals and 85% of the consultants who were in District General and Secondary Referral Teaching Hospitals.

Conclusions: Majority (63.5%) of the chest physicians (CPs) in the UK prefer that they are skilled in bedside CUS in patients with pleural effusions (PPE). 20% of them requested a CUS in a third of their PPE, with a further 22% requesting this in 50% of their PPE; the vast majority (93%) of this is performed in the RD. More than four fifths of CPs think that CUS training should be included in the Respiratory SpR curriculum. Increased awareness of the Royal College of Radiologists' CUS training guidelines for CPs could be a potential impetus for this to be achieved.

P190 CLINICAL CHARACTERISTICS AND OUTCOMES OF EMPYEMA THORACIS IN 117 PATIENTS: A COMPARATIVE ANALYSIS OF TUBERCULOUS VERSUS NON-TUBERCULOUS AETIOLOGIES

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Background: Empyema thoracis remains a major problem in developing countries. Clinical outcomes in tuberculous empyema are generally believed to be worse than in non-tuberculous aetiologies because of the presence of concomitant fibrocavitary parenchymal disease, frequent bronchopleural fistulae and poor general condition of patients. We performed a prospective study over a two-year period with the objective of comparing the clinical characteristics and outcomes of patients with tuberculous versus non-tuberculous empyema
Methods: Prospective study of all cases of non-surgical thoracic empyema seen at a tertiary care centre in North India over a 2 year period. A comparative analysis of clinical characteristics, treatment modalities, and outcomes of patients with tuberculous versus non-tuberculous empyema was carried out. Factors associated with poor outcomes were analysed using multivariate logistic regression.
Results: One hundred and seventeen cases of empyema were seen in the study period of which 95 had non-tuberculous and 41 had tuberculous empyema. Malnutrition and bronchopleural fistulae (BPF) were more common and duration of symptoms longer in the tuberculous empyema group. Time to resolution of fever, duration of pleural drainage and pleural thickening >2 cm were significantly greater as well. Eight (10.5%) patients with non-tuberculous empyema and four (9.8%) with tuberculous empyema succumbed. Presence of a BPF was significantly associated with poor outcomes on multivariate logistic regression analysis.
Conclusions: Tuberculous empyema remains a common cause of thoracic empyema in India though it ranked second amongst all causes of empyema after community acquired lung infections in this study. Tuberculous empyema is associated with longer duration of symptoms, greater duration of pleural drainage and more residual pleural fibrosis.

P191 THE MANAGEMENT OF SPONTANEOUS PNEUMOTHORAX: ARE WE ADHERING TO BRITISH THORACIC SOCIETY GUIDELINES?

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There have been studies demonstrating the variability in the management of spontaneous pneumothorax and to this effect guidelines have been produced by the British Thoracic Society to clarify and standardise the management of spontaneous pneumothorax. The aim of this study was to assess whether current practices on the management of spontaneous pneumothorax conformed to these guidelines at five hospitals within the South Yorkshire region. A retrospective case note audit of 145 cases of spontaneous pneumothorax was performed (x primary and y secondary).

In the initial management of primary pneumothoraces simple aspiration was performed in 37 (38%) and chest drain in 45 (46%) cases. This finding did not comply with the BTS recommendation that simple aspiration should be the treatment of choice in all such patients. Only 36/98 (37%) of primary pneumothorax cases were managed according to the BTS guidelines. The initial management of secondary pneumothoraces however, faired better. Chest drainage was performed in 32 (68%) cases.

We also assessed whether management differed according to hospital type and size. 3 of the 5 hospitals are classified as district general hospitals and 2 classified as tertiary teaching hospitals. In the tertiary teaching hospital, 43% adhered to the BTS guidelines for the management of primary pneumothoraces compared to 36% in the DGH, and 87% and 71% respectively for the management of secondary pneumothoraces (p=NS).

Other differences in practice compared to BTS guidelines were delay in cardiothoracic referral. Only 33% (10/30) of referrals were made in the recommended 5 day period (mean 6.7 days, range 1–21 days). Reasons for these included the use of prolonged suction (5/20), placement of large bore tubes (4/20), delay in respiratory referral (2/20), and unknown (8/20).

This study highlights that there is significant scope to improve the management of this group of patients. The management of secondary pneumothorax on the whole fares better, however there seems to be some confusion as to the management of primary pneumothoraces. All initial management of spontaneous pneumothorax was performed by non-respiratory junior staff (27 (23%) by A+E, 51 (43%) by medical staff, and 3 (3%) by cardiothoracic surgical teams). It is our duty as respiratory physicians to provide a program of education and guideline dissemination so as to improve the management and provide a better standard of care for these patients.

P191A WHICH ASPECT OF CHEST DRAINAGE CAUSES MOST PAIN?

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Introduction: Chest tube drainage is painful. There are few data describing whether this pain is influenced by insertion technique (blunt dissection *v* guidewire), or tube size. Nor is it known whether these differences influence pain at tube insertion, while the tube is in place, or at tube removal.
Methods: 123 patients from 32 UK centres having chest tube drainage for pleural infection completed a self-administered categorical pain score (no pain, mild, moderate, severe pain) to describe how much pain they experienced at chest tube insertion, while the chest tube was in place, and at chest tube removal. These scores were summated to produce a summary score which was compared in patients having blunt dissection or guidewire insertion (primary analysis).
Results: Chest tubes inserted by blunt dissection were associated with more pain than those inserted by guidewire (dissection n=44, median pain score 7, IQR 5–8, guidewire n=79, med 5, IQR 4–7, p=0.006, Mann-Whitney). Average drain size was larger in the blunt dissection group (dissect 22 French, IQR 20–26, guide 12, IQR 12–12, p<0.0001, Mann-Whitney). However, within the insertion technique groups, drain size was not significantly associated with pain (p>0.1 Spearman's correlation, both groups). Pain at chest tube insertion or removal was not significantly different between the two insertion technique groups (χ^2 3df, p>0.1, both analyses). However, blunt dissection inserted tubes were significantly more painful while in place (χ^2, 3df=13.2, p=0.004).
Conclusions: We conclude that guidewire inserted tubes were less painful than blunt dissection inserted tubes. This difference was most marked while the tube is in place and appeared to be more strongly associated with insertion technique than tube size.

Cystic fibrosis: clinical management

P192 ECONOMIC IMPLICATIONS OF NEWBORN SCREENING FOR CYSTIC FIBROSIS: REDUCED THERAPY MAY OFFSET SCREENING COSTS

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Background: Compared to clinical diagnosis (CD), newborn screening (NBS) for cystic fibrosis (CF) associates with clinical benefit (Sims *et al. J Pediatr* 2005;**147**:S42) and reduced treatment (Sims *et al. J Pediatr* 2005;**147**:306). However NBS may not be introduced if resource costs are perceived to be prohibitive.
Aims: Using the UKCFD, we compared the cost of therapies received by NBS and CD patients and tested whether any savings accrued that could

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	2004 Scottish births	2004 Scottish costs	2002 Scottish costs	2002 UK births	2002 UK costs
Refused screening	42	–	–	514	–
Screened (IRT)	54,600	£143,154	£125,859	668,263	£1,641,719
DNA mutation screen	372	£157,744	£138,992	4557	£171,481
Patients diagnosed	28	£5634	£5346	343	£5286

offset the known costs of the new national NBS programme (Scotland), when scaled to the UK.
Methods: The cohorts of 184 NBS and 950 CD patients reported above, aged 1–9 years in 2002, were compared in a cost of illness retrospective, ''snapshot cohort'' study using a prevalence strategy. Costs of long term (LT; >3 months) drugs (including oral antibiotics and corticosteroids, and inhaled and nebulised medications) and home and hospital administered intravenous antibiotics (IV) were estimated. Costs (£) in 2004 of adding a two step (immunoreactive trypsinogen/DNA mutation) CF screening service to an established Scottish NBS service were estimated, adjusted to 2002 prices and applied to the UK.
Results: LT therapy costs per NBS patient were significantly lower when compared to a CD patient: mean (£4410 *v* £7326; 95% CI −4110 to −1237; $p<0.01$) and median (£215 *v* £1490; 95% CI −1169 to −110; $p<0.01$)). Assuming the CD cohort had been diagnosed by NBS and the disease progression was comparable to that of the NBS cohort, mean (£2,197,525) or median (£610,937) drug cost savings may have offset some or all of the estimated cost of a UK national CF NBS service (£1,813,200; see table).
Conclusions: Considering the drugs budget alone, in the first 9 years of life, diagnosis of CF by NBS could save 34% to 121% of the estimated costs of adding CF screening to an established national NBS screening service. Including indirect costs-savings, implementation of a NBS service may have wider benefits to families and society.

P193 AN AUDIT OF THE NEW EFLOW®RAPID SYSTEM IN THE PAPWORTH ADULT CF UNIT

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Introduction: The PARI GmbH eFlow®rapid is a new nebuliser that utilises a perforated oscillating membrane. It has several potential advantages over previous systems including being silent and offering faster inhalation times. It is also small, light and can be operated by battery or mains worldwide. Since July 2005 the Papworth Adult CF Centre has been converting patients from their conventional nebulisers to the eFlow®rapid.
Methods: In order to audit the impact of changing to the eFlow®rapid we asked 37 adult CF patients (18/36 male, 23/36 age 16–25 years, 8/36 age 26–35 years, 5/36 age older than 35 years) to complete two questionnaires, the first prior to, and the second two months after, starting the eFlow®rapid. The questionnaires were designed to assess nebuliser usage and adherence.
Results: 36/37 patients completed both questionnaires. The results of the first questionnaire showed that 33 patients were using established PARI nebuliser systems at the start of the audit. 31 (86%) patients performed two or more nebulisations per day. 8 (22%) patients reported being fully adherent with their nebuliser therapy, whilst the remaining 28 patients reported missing 1 to 17 nebulisations per week. 27 (75%) patients cited a time factor as the main reason for missing nebuliser treatment.

From the second questionnaire, 36/36 (100%) patients preferred the eFlow®rapid due to its speed, silence, and small size. The median inhalation time was reduced by 8 minutes for bronchodilators, 7 minutes for DNase, 14 minutes for antibiotics, and by 13 minutes for all therapies combined through using the eFlow®rapid (Wilcoxon signed rank test p values 0.042 for bronchodilators, <0.001 for all others). 12/36 (33%) patients reported being fully adherent to nebuliser therapy. 11 (31%) patients reported improved adherence, 8 (22%) reported less adherence and 17 (47%) patients reported no change in adherence using the eFlow®rapid. Full adherence with (a) DNase, (b) antibiotics and (c) all prescribed nebulised therapies (that is, DNase plus antibiotics plus bronchodilators) was not statistically significantly improved after the introduction of the eFlow®rapid (Binomial test p values (a) 0.312, (b) 0.500, (c) 0.312 respectively). The number of nebulisers missed per week with the eFlow®rapid ranged from 1 to 21. 18/36 (50%) patients continued to cite a time factor, and 6/36 (17%) patients cited forgetfulness, as the main reasons for missing their nebuliser therapy.
Conclusions: There was universal patient preference for the eFlow®rapid system due to its speed, silence and size. Despite this only 31% of patients reported improved adherence and 69% reported reduced or no change in adherence after changing to the eFlow®rapid.

P194 THE EFFICACY, PREFERENCE, AND SAFETY OF A NOVEL METHOD OF SPUTUM CLEARANCE, HYDRO ACOUSTIC THERAPY, ON ADULT PATIENTS WITH CYSTIC FIBROSIS

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Background: Daily airway clearance is an important part of management in cystic firbrosis (CF). Several methods are employed aiming to induce vibration in the airways, these are not well tolerated by patients.
Aim: To investigate the efficacy, safety, and patients' preference of a novel system that vibrates the lungs at their resonant frequency, to aid sputum clearance in CF. This system called Hydro Acoustic Therapy (HAT).
Method: Eighteen adult CF patients with an FEV1<70% predicted investigated during stable lung disease, received in a random order three techniques, HAT, Flutter, a placebo session which involved being sat in the bath without any sound waves. For HAT, sounds waves were generated underwater in a special bath to create a percussion effect on the lungs, aimed at dislodging bronchial secretions using the principal of chest percussion. The patient received therapy at three different resonant frequencies, each for 10 minutes. These frequencies ranged between 20–60 Hz with amplitude of up to 158 dB re1microPascal. Each therapy session lasted for 30 minutes. Oxygen saturation and heart rate was constantly monitored throughout each therapy session. We measured wet and dry sputum, and lung function parameters before and after each therapy session. At the end of the study patients completed a questionnaire about their preference to the type of physiotherapy received.
Results: The three methods resulted in similar production of sputum as measured by the weight of dry and wet sputum. There was fall in FEV1 after HAT therapy of 76 ml (95% CI 27–125 ml) $p<0.005$. The value of FVC, FEF25–75 did not significantly changed after HAT or other methods. The HAT therapy was described to be pleasant or very pleasant in 59% compared to 0% for flutter ($\chi^2=15.8$, $p<0.0001$). A total 70% of patients would prefer HAT as a physiotherapy method compared to 0% for flutter ($\chi^2=20.3$, $p<0.0001$). There were no procedure related complications in any of the three methods.
Conclusion: HAT is a novel system for sputum clearance. In a cohort of adult CF patients the technique was found to be safe, well tolerated and favoured by the majority of the patients to the conventional flutter device.

Sponsored by Aco-med Ltd, Dorset, UK.

P195 GLUCOCORTICOIDS AS AN ADJUVANT TREATMENT TO INTRAVENOUS ANTIBIOTICS FOR CYSTIC FIBROSIS PULMONARY EXACERBATIONS: A UK SURVEY

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Background: The use of glucocorticoids during pulmonary exacerbations (PX) of asthma and chronic obstructive pulmonary disease (COPD)

is well established. Their benefit during cystic fibrosis (CF) PX is less well defined, a Cochrane Review established the need for a prospective randomised controlled trial (RCT).[1] Additionally, attitudes of CF physicians towards glucocorticoid use have not been examined.
Objectives: To establish, among CF physicians, current practices and attitudes regarding the use of adjuvant glucocorticoid treatment in adult CF patients requiring intravenous (IV) antibiotics for a PX and to determine the feasibility of a prospective RCT.
Methods: A questionnaire was sent to all adult CF physicians in the UK. Questions addressed current usage of glucocorticoids, reasons for not using glucocorticoids and interest in participating in a prospective RCT.
Results: Out of 42 physicians, 34 (81%) completed and returned the questionnaire, 65% cared for more than 50 CF patients. A total of 64% of responders used glucocorticoids with IV antibiotics in their practice (63% occasionally, 26% regularly, 11% often). Of those who did not use glucocorticoids, 56% stated lack of convincing literature or lack of efficacy from personal experience and 44% cited potential side effects. Using Fisher's exact test there were no significant differences in responses from physicians in large (>50 patients) or small (<50 patients) units. Most responders (88%) agreed that a large prospective RCT is required and 75% would be willing to enter consenting patients into a potential RCT.
Conclusions: The majority of adult CF physicians in the UK agree that a prospective RCT of glucocorticoid use as an adjuvant to IV antibiotics is required and would be willing to participate in entering consenting patients. With the level of interest expressed, a prospective RCT could feasibly be undertaken.

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P196 *BURKHOLDERIA* SPECIES INFECTION AT THE MANCHESTER ADULT CYSTIC FIBROSIS CENTRE: CHANGING EPIDEMIOLOGY

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Introduction: All cases of *Burkholderia* species infection have been recorded at our centre since 1983. Microbiological surveillance of *Burkholderia* species has been performed at our cystic fibrosis (CF) centre since 1991. All isolates are sent to a single reference microbiology laboratory for strain typing. Patients with *Burkholderia* species infection were cohorted into different areas of the inpatient facility from 1991 onwards. Since 1993, patients with *Burkholderia* species infection have been cohorted to a different ward and outpatient clinics (complete cohort segregation). More recently, a policy of isolation has been introduced with patients infected with transmissible *B cenocepacia strains* being isolated when inpatients and attending separate outpatient clinics from other *Burkholderia* infected patients. In 2001, retrospective typing of previously stored isolates was undertaken. All subsequent new isolates since 2001 have been genomovar typed.
Methods: We reviewed the results of strain and genomovar typing of all available *Burkholderia* isolates at our center: 1983–2006.
Results: The incidence/prevalence of infection with *Burkholderia* species between 1983–90 was below 5%/9% each year. There was a rise in incidence/prevalence of *Burkholderia* species between 1991 and 1994 with a peak of 16.3%/31.2% in 1992. Following the introduction of complete cohort segregation, the incidence has fallen to below 3% for all but one year and the prevalence has gradually reduced to 9.3% in 2005. Currently, there is an increase in the prevalence to 10.6% for the first time since 1994, predominantly due patients with unique infections transferring into the unit from referring centres. The presence of unique strains now exceeds transmissible strains for the first time since 1991. Since full cohort segregation, within the centre, there have been 6 cases of new infection with transmissible B cenocepacia strains and 13 with unique strains of *Burkholderia* species. These included 2 cases of superinfection with a transmissible strain in those with a unique strain and patients who have not followed cohort segregation practices. For the past 6 years, there has been just 1 case of new infection with a transmissible *B cenocepacia* strain and 9 cases of new infection with unique strains of *Burkholderia* species among established patients.
Conclusions: Infection control measures including patient segregation have controlled spread of transmissible *B cenocepacia* strains, but not the acquisition of unique strains. Unique strains of *Burkholderia* species now account for the majority of new infections at the Manchester Adult Cystic Fibrosis Centre.

P197 INFLUENZA VACCINATION IN CYSTIC FIBROSIS: ANY ROLE?

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Background: The Department of Health in the UK recommends influenza vaccination should be offered to all patients with chronic obstructive pulmonary disease including cystic fibrosis (CF). Previous studies have shown that influenza infections cause worsening lung functions and disease progression in CF.[1] In addition, influenza infection may facilitate future bacterial colonisation. There is currently no evidence from randomised studies that influenza vaccine given to patients with CF is of benefit to them.[2] During the season 2003/04, trivalent influenza vaccine was used, the composition of which included: Influenza A (H3N2) and (H1N1) strains and influenza B.
Aims: To determine the vaccination coverage level for the 2003–04 influenza season in a paediatric CF population in South Wales and the factors associated with non-adherence with vaccination. Finally, to evaluate how many patients who were vaccinated against influenza subsequently acquired influenza infection.
Methods: The influenza vaccination status of 63 patients with CF enrolled for the study looking at the impact of respiratory viruses in CF was recorded. All these patients were older than 6 months of age on enrolment. Pernasal swabs from these patients were taken whenever they developed new upper respiratory tract symptoms and whenever they attended outpatient clinic for routine visit from October 2003 to April 2004. Influenza A and influenza B were detected using Nucleic Acid Sequence Based Amplification (NASBA).
Results: Of the 63 patients, 41 (65%) were vaccinated against influenza. For the 22 patients who were not vaccinated, 5 of them forgot, 7 were scared of needles, 1 was worried about side effects, 6 were too unwell to be vaccinated and 3 did not feel influenza vaccination was effective. Influenza virus was detected on 5 occasions; 3 influenza A (60%) and 2 influenza B (40%). 1 virus in the vaccinated group and 4 in the non-vaccinated were detected during the study period (p value = 0.046, using Fisher's exact test).
Discussion: Majority of the studied patients was vaccinated against influenza and the main reason for non-adherence was due to the fear of needles. Although the recent Cochrane review[2] has stated that the evidence to support routine influenza vaccination is lacking in CF, this study has shown that influenza vaccination may yet play a role in preventing its subsequent acquisition

1. **Collinson J**, Nicholson KG, Cancio E, *et al*. Effects of upper respiratory tract infections in patients with cystic fibrosis. *Thorax* 1996;**51**:1115–22.
2. **Tan A**, Bhalla P, Smyth R. Vaccines for preventing influenza in people with cystic fibrosis. *Cochrane Database Syst Rev* 2000;(2):CD001753.

P198 ASSOCIATION BETWEEN ABNORMAL HEPATIC ENZYMES, FATTY CHANGE IN THE LIVER, AND ACUTE PULMONARY INFECTION IN CYSTIC FIBROSIS

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Introduction: Liver disease complicating cystic fibrosis (CF) is well recognised in children and progresses to cirrhosis. In adults with CF abnormalities of hepatic enzymes are increasingly recognised, and usually attributed to infective exacerbations or drug therapy (for example, antibiotics). Liver ultrasounds (USS) have demonstrated either no abnormality or fatty change similar to that seen in diabetes.
Aim: To determine if elevated hepatic enzymes are associated with abnormalities on liver USS, and the impact of infective exacerbations and antibiotic therapy.
Methods: Retrospective review of medical records of 91 patients attending Adult CF Service at the London Chest Hospital. Data from both inpatient and outpatient attendances were recorded. Liver USS were performed and reported using a specific protocol (reporting presence of fatty change, portal vein flow, and splenic size). Data were analysed using Mann-Whitney U test with significance set at 0.05.
Results: Data were available for 91 patients (56 male), median age of 24 years (range 17–59), mean (SD) FEV1 2.4 (1.1) l, FVC 3.5 (1.3) l, BMI 22 (3.9). Hepatitis and autoimmune serology were negative in all

patients. 45 patients had had a liver USS; complete data were available for 44. 33/44 (75%) had a normal USS. Of the 11 abnormal scans, 2 had cirrhosis, and 9 had fatty change (20.5%); all were pancreatic insufficient. There was no significant difference in BMI between those with normal and abnormal USS (20.9 *v* 21.7). By far the most common abnormality in hepatic enzymes was an isolated elevation in alkaline phosphatase (ALP). The highest value of ALP was seen more commonly in inpatients receiving IV antibiotics for infective exacerbations (61%); peak inpatient ALP was 160 (107) iU/l, *v* 125 (52) iU/l for outpatients. *Inpatients*: In 34 inpatients with hepatic enzyme and USS data, 11 had a normal ALP; 2 had fatty change on liver USS. In the remaining 23 with an elevated ALP, 9 (39%) had fatty change on USS. There was no statistically significant difference in peak ALP between patients with or without fatty change on Liver USS (p = 0.19). *Outpatients*: In outpatients with stable CF, 40 patients had had a liver USS and of these 20 had a normal ALP; 3 had fatty change on USS. Of the 20 with an elevated ALP 8 (40%) had fatty change on USS. There was a trend to statistical significance in peak ALP between those with and without fatty change (p = 0.084).
Conclusions: Fatty change in the liver was more common than expected and did occurr despite a normal ALP. While peak ALP was higher in inpatients, the proportion of patients with fatty change was similar to outpatients, suggesting the elevation was secondary to infection and/or antibiotics. On these data ALP cannot be used to decide which CF patients should have a liver USS.

P198A ADULT CYSTIC FIBROSIS LUNG FUNCTION, NUTRITION, AND SURVIVAL AT THE ROYAL BROMPTON HOSPITAL COMPARED WITH UK AND US DATA

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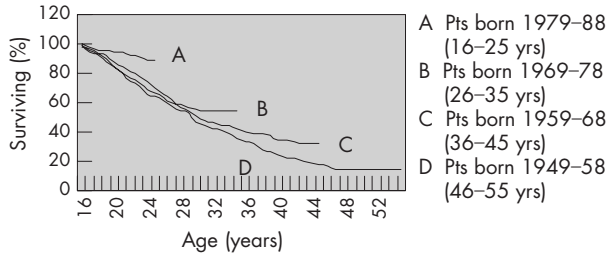
Introduction: Europe's first adult Cystic Fibrosis clinic was established at the Royal Brompton Hospital (RBH) in 1965. The centre records annual review data for each consenting patient. 1312 patients have been included since 1965, 595 of whom attended clinic or were inpatients at least once in 2004.
Method: The results of the RBH 2004 annual review data were compared with the national UKCF database Annual Report 2003 (UKCF).[1] Patient survival was compared to Cystic Fibrosis Foundation Annual Report from the US.[2]
Results: RBH patient age distribution is higher than that for the adult UKCF patients with 31% aged >35 years compared to 17%. The median FEV1 % predicted for RBH is 54.0%. UKCF specify a median in the range of 50–59%. Median RBH BMI is 21.76 compared to a UKCF median range of 19–20.9. Furthermore RBH has a higher proportion of patients with a BMI of 19 or over (81% compared with 77%) and therefore fewer patients with a BMI of 18.9 and under (19% compared with 23%). The US report a 50% median survival of 35.1 years. Survival curves for RBH patients born 1949–88 (n = 1095) demonstrate a 54% survival at age 35 for patients born 1969–78. Any patients who were lost to follow up were not included (n = 217). RBH accepts many referrals for transplant assessment for patients with end stage respiratory failure. If patients who died within 2 years of referral are excluded (n = 108), patient survival to 35 is 59%.
Conclusion: The RBH patient population includes sick and older patients, however, FEV1% predicted is comparable to data presented by UKCF and nutrition improved. Survival is shown to increase with every decade and exceeds median values reported in US data.

1. UK Cystic Fibrosis Database, Annual Data Report 2003. University of Dundee.
2. Cystic Fibrosis Foundation, Patient Registry 2004 Annual Report. Bethesda, USA.



Abstract P198A Survival from age 16 by year of birth.

Molecular mechanisms of lung disease

P199 ALKYLPURINE-DNA GLYCOSYLASE AND ALKYLGUANINE-DNA ALKYLTRANSFERASE REPAIR ACTIVITY IN PERIPHERAL BLOOD MONONUCLEAR CELL NUCLEI FROM LUNG CANCER CASES AND CANCER FREE CONTROLS

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Introduction: DNA damage, caused by tobacco smoke carcinogens, is a critical step for lung cancer development. APG and MGMT are DNA repair proteins that repair N3/7-alkylpurines and O^6-alkylguanines respectively, DNA damage that is induced by alkylating agents such as tobacco-specific nitrosamines present in cigarette smoke. Interindividual variability in APG and MGMT activity might therefore influence lung cancer susceptibility. To test this hypothesis we measured APG and MGMT activity in lung cancer cases and controls.
Methods: Repair activity was determined using two [^{32}P] based oligonucleotide cleavage assays in PBMC nuclei collected from 51 incident lung cancer cases and 88 cancer free controls, who were recruited from the Bronchoscopy Unit at Wythenshawe Hospital. APG activity was detected in all samples (range 1.37–8.43 fmole/μg DNA/hour) and MGMT in 114/119 samples (range 0.29–13.37 fmole/μg DNA). APG and MGMT repair activities were significantly correlated ($r^2 = 0.25$, p = 0.0009).
Results: Repair activity of either protein was not related to age or gender. MGMT activity was also unrelated to smoking or case status. There was evidence that APG activity was greater in ever smokers when compared to never smokers (3.81 (1.53) *v* 2.95 (1.04) fmole/μg DNA/hour, p = 0.07), there was no difference in activity between current and former smokers (p = 0.86). APG activity was significantly higher in cases than controls (4.21 (1.67) *v* 3.47 (1.35) fmole/μg DNA/hour) (p = 0.005). Ever smoking cases also had higher activity than ever smoking controls (p = 0.009). The study population was subdivided according to quartiles of APG activity in controls. The odds of lung cancer incidence in the highest APG activity quartile was four times that of the lowest quartile (OR 4.0, 95% CI 1.3–12.6, p = 0.02).
Conclusions: The increased expression of APG, by as yet unknown mechanism/s, may be a factor in smoking related lung cancer induction.
Project funded by the COLT foundation and Cancer Research UK.

P200 HUMAN SQUAMOUS CELL CARCINOMA CELL LINES CONTAIN A SELECTABLE SIDE POPULATION THAT IS CELL CYCLE DEPENDENT AND HAS CANCER STEM CELL-LIKE PROPERTIES

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Introduction: ''Side population'' (SP) cells are present in a number of adult tissues. These cells have a unique capacity to efflux lipophillic DNA binding dyes such as Hoechst 33342. In bone marrow and muscle, SP cells have been demonstrated to have stem cell characteristics; being able to self renew and have the capacity to form differentiated cells. The SP cell's high efflux capacity correlates with the elevated expression of drug-transporter proteins, including ABCG2. Hence these cells may be intrinsically resistant to a number of cytotoxic drugs and thereby contribute to tumour resistance and disease relapse. An SP has been identified in neuroblastomas and it has been suggested that they are a cancer stem cell population.
Aim: We examined a squamous cell carcinoma cell line (H357) for the presence of an SP cell fraction and proceeded to see if it demonstrated cancer stem cell characteristics.
Methods: H357 cells were incubated with Hoechst 33342, FACS sorted into SP and non-SP populations and subsequently used in proliferation, colony forming and drug resistance assays.
Results: SP cells can be repeatedly FACS sorted leading to a higher SP fraction in subsequent sorts. We show that the SP fraction is not a strict sub-population of cells but in fact Hoechst efflux is dependent on the cell cycle. SP cells show a higher rate of proliferation and colony formation

than non-SP cells. SP cells are more resistant than non-SP cells to chemotoxic drugs such as mitotraxone. Treatment with drug transporter inhibitors such as verapamil reduces the survival advantage of SP cells in the presence of mitotraxone.
Conclusion: Squamous cell cancers contain an SP population that is selectable. SP cells are more proliferative, have higher colony formation efficiency and have greater resistance to chemotoxic drugs than non-SP cells and hence have some properties of cancer stem-like cells.

This abtract has previously been presented at the American Society for Cell Biology Summer Meeting: Stem Cell Niches in Boston 15–18 July 2006

P201 CORRELATION BETWEEN THE THE EXPRESSION OF TOPOISOMERASE IIA AND THE THE INSTABILITY OF CHROMOSOME 17 IN THE INTRAOPERATIVE SPECIMENS IN NSCLC

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Introduction: Intraoperative imprints and FNAs offer a fast and accurate method of diagnosis and also a qualitative substrate for immunocyto-chemical and molecular studies—especially preserved samples by liquid phase cytology methods—because of the high conservation of the nucleus features. Aberrations of chromosome 17 are common in many cancers including NSCLC. Topoisomerase family which includes Topo I (20q11), Topo IIa (17q21), Topo IIb (3p24) is a class of enzymes in the nucleus of all living cells, which affect the topological structure of DNA. Cells die when Topoisomerase is inhibited and for this reason is a target of chemotherapy.
Materials and Methods: Using Tissue Microarray Technology (Chemicon TMArrayer ATA100), we created a 40 tumour TMA. 40 NSCLC (20 adenocarcinomas and 20 squamous carcinomas) and 10 normal lung epithelia (as control group) were obtained and embedded into a single paraffin block (core diameter: 1 mm). Immunohistochemical stain for anti-Topoisomerase IIa (Ki S1-DACO Corp) combined with CISH for the detection of chromosome 17 instability (Chr 17 Centromeric probe, Zymed kit) and specific gene status (Topo IIa Amplification probe Zymed kit) was performed in 2 and 5 μm sections and in intraoperative imprints. Finally using a semi-automated Image Analysis System we evaluated the nuclear features of number and optical density and the number of signals of chromosome 17 centromeres and gene copies per nucleus. Statistical analysis was performed by SPSS version 11.0 software.
Results: A significant proportion of NSCLC showed over expression of the marker (18/40) and CISH application showed Topo IIa amplification (high or low level) or deletion of one allele n 11/18 cases. Co-evaluating chromosome 17 instability we observed that 10/18 only amplification while the last 4/18 displayed deletion. We observed that chromosome 17 instability co-appearing with Topo IIa amplification correlates with low differentiation and poor prognosis ($p<0.001$).
Conclusion: The results indicate that Topo IIa amplification or deletion is a critical genetic event correlating with biological behavior in NSCLC and determining chemo sensitivity. Also intraoperative imprints and FNAs appeared to be more accurate at the evaluation of centromeric and specific gene signals because of the nucleus integrity.

P202 IL-13 MEDIATES PROINFLAMMATORY BUT NOT PROFIBROGENIC RESPONSES IN PRIMARY FIBROBLASTS

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Introduction: IL-13 has been implicated as a key cytokine associated with the asthmatic phenotype. Persistent inflammation in the airways leads to airway remodelling which is mediated by $TGF\beta_1$, a potent regulator of extracellular matrix formation and tissue remodelling. Given the previously reported increases in $TGF\beta_1$ and IL-13 in asthma we examined their ability to induce synergistic production of eotaxin in primary human fibroblasts.
Methods: Primary human fibroblasts were grown from endobronchial biopsies obtained from volunteers. Fibroblasts were treated with IL-4, IL-13, and/or $TGF\beta_2$ before αSMA and eotaxin mRNA was measured by RT-PCR and eotaxin release by ELISA.
Results: IL-13 alone induced significant amounts of eotaxin release from fibroblasts. A combination of IL-13 and $TGF\beta_2$ produced a significant synergistic increase in eotaxin production. $TGF\beta_2$ induced $TGF\beta_1$ release and αSMA expression but not eotaxin. IL-13 failed to induce a significant induction in αSMA mRNA.
Discussion: IL-13 was unable to induce significant profibrogenic responses from fibroblasts however IL-13 induced significant amounts of the eosinophil chemoattractant eotaxin which was synergistically increased in the presence of $TGF\beta_2$. Thus, it seems likely that the main effect of IL-13 on fibroblasts is to drive a proinflammatory response through recruitment of eosinophils. As eosinophils are a potent source of $TGF\beta_1$, this may represent an indirect method by which IL-13 contribute to toward airway remodeling.

P203 TNFα ACCELERATES THE TGFβ-INDUCED ''EPITHELIAL-MESENCHYMAL TRANSITION'' IN LUNG EPITHELIAL CELLS

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Background: Epithelial to mesenchymal transitions (EMT) play a critical role in tissue morphogenesis during embryogenesis, but aberrant induction of this process has been implicated in pathological processes such as cancer metastasis and fibrosis (Willis BC, *et al. Am J Pathol* 2005;**166**:1321–32. Lee JM. *J Cell Biol* 2006;**172**:973–81). In chronic lung diseases, inflammation usually accompanies fibrotic changes, therefore we hypothesised that inflammatory mediators such as TNFα may induce a stress response that acts in concert with TGFβ to promote an EMT. To test our hypothesis, we investigated the ability of TGFβ1 to induce an EMT in alveolar epithelial cells in the absence or presence of TNFα.
Methods: A549 alveolar epithelial cells were treated with 2.5 or 10 ng/ml TGFβ1 and absence or presence of 1 ng/ml TNFα, or with TNFα alone in low glucose DMEM medium with 0.1% BSA. The morphology of the cells was recorded from day 2 to day 6. Cells were harvested at 2 days and 6 days for RNA extraction. Expression of mRNA for MUC2, MMP9, Collagen I and α-SMA was analysed by quantitative RT-PCR.
Results: By day 2, morphological changes including loss of cell-cell contact and cellular elongation were observed in the cells treated with TGFβ1 alone, but these were more prominent in cells treated with both TGFβ and TNFα. TNFα alone had minimal effect on the epithelial morphology of the cells. From day 3 to day 6, the untreated cells or those treated with TNFα alone entered into a ''crisis'' with large scale cell death. Cell death was also observed in all cultures treated in the presence of TGFβ, however a significant number of cells survived. In all cases, the surviving cells were fibroblast-like and increased in number during the course of the experiment. The process of EMT induced by TGFβ was accompanied by reduced expression of the epithelial phenotypic marker MUC2, and stimulation of ''mesenchymal'' markers including collagen I and MM9. In contrast, α-smooth muscle actin expression showed only a transient increase at day 2 but was not different from control at day 6 suggesting an incomplete phenotypic switch. TNFα augmented the effect of low doses of TGFβ on MMP9 and collagen I expression, but did not affect αSMA expression. Although TNFα alone did not elicit a phenotypic change, it was able to induce MMP9 expression.
Conclusion: TGFβ1 signalling induces a phenotypic switch in alveolar epithelial cells that is reminiscent of an EMT and TNFα can facilitate this process. However, the absence of αSMA expression suggests that the EMT is incomplete. We speculate that TGFβ has induced a ''repair'' phenotype (that is, a migratory epithelial cell phenotype) rather than a ''pro-fibrotic'' (that is, myofibroblastic) phenotype.

P204 PREMATURE SENESCENCE OF AIRWAY EPITHELIAL CELLS: A POSSIBLE ROLE IN AIRWAY REMODELLING AFTER HUMAN LUNG TRANSPLANTATION

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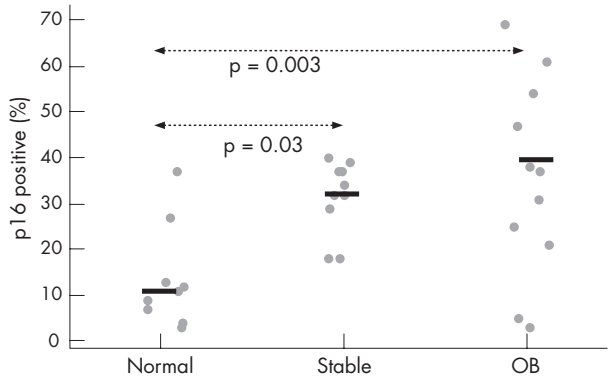
Introduction: Cells entering senescence lose their replicative capacity but remain biologically active for many months with a proinflammatory phenotype. This process is thought to contribute to the deterioration in



Abstract P204 Epithelial p16 staining in normal controls and lung allografts.

tissue function seen with aging. External insults such as oxidative stress can induce premature senescence in previously healthy cells in vitro, yet the contribution of senescence to organ dysfunction in vivo and specifically the lung is unclear. Therefore we investigated the expression of the cell cycle inhibitor p16, an ''in vivo'' marker of senescence, in the airway epithelium of lung transplant recipients.
Hypothesis: After transplant the airways are subject to numerous sources of external injury that may drive epithelial cells to premature senescence; the resulting lack of epithelial regenerative capacity and the proinflammatory mediators released by senescent cells may contribute to the development of obliterative bronchiolitis (OB) the main cause of chronic allograft dysfunction after lung transplantation.
Methods: Endobronchial biopsies were obtained from stable lung transplant recipients without evidence of OB (n = 10), patients with OB (n = 3) and from lungs explanted from OB affected patients at retransplantation (n = 8). ''Normal'' control samples were taken from lungs assessed for but not used in the lung transplant programme (n = 11). Paraffin embedded sections were stained for p16 and the level of airway epithelial staining quantified using an image analysis system. Results are expressed as a percentage of cells in the epithelium staining positive for p16.
Results: In ''normal'' biopsies the median level of p16 staining was 11% (3–37) and increased with subject age supporting its use as a marker of senescence. p16 staining was significantly increased beyond what would be expected with normal aging in allografts: stable patients 33% (range 18–40, p = 0.003), OB patients 38% (range 3–69, p = 0.03). There was no significant difference between the stable and OB groups.
Conclusions: The higher levels of p16 staining suggest a greater proportion of senescent cells in the allograft airway compared to normal controls; this may be both a cause and a consequence of this stressful environment. Further studies are needed to confirm the findings with alternative senescence markers, to link airway injury to the senescent phenotype and characterise the proinflammatory activity of senescent cells.

P205 INVESTIGATION OF CLARA CELL 10 KDA PROTEIN (CC10) POSITIVE SQUAMOUS EPITHELIUM IN LPS-CHALLENGED RAT LUNG

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Introduction: Clara cell 10 kDa protein (CC10, CCSP) is the major secretory protein of the Clara cell and is thought to play a protective role in the lung due to its anti-inflammatory properties. Studies have shown levels of CC10 decrease in BALF and plasma following lung inflammation. In humans, CC10-positive cells increase with progression down the bronchial tree but there is little information on the anatomical distribution of CC10 in rat lung.
Methods: We have used immunohistochemistry to determine the expression of CC10 along the tracheobronchial tree in control, saline-treated, and LPS-treated rats (once/day, 5 days).
Results: Control rats showed sporadic staining of CC10 in central airways and more frequent staining in bronchioles. In the transitional airways, many of the cells showed strong staining except for squamous cells. Following LPS challenge, there was a general reduction in staining in the upper airways but little change within bronchioles. There was increased staining in transitional airway squamous epithelia, which have been further characterised by immunohistochemistry for CC10 and pan-cytokeratins (fluorescent double staining), surfactant protein D and Ki-67 (standard light microscopy). The CC10-positive squamous cells co-stain for pan-cytokeratin and appear to co-localise with surfactant D-positive cells, indicating epithelial origin and function. There were Ki-67-positive proliferative cells within the TA, but only some of which appeared to be squamous cells.
Conclusions: These data show that diffuse inflammatory injury results in generalised loss of the CC10 phenotype in central airways. Conversely, there was an increase in expression in transitional airways, particularly in metaplastic squamous epithelial cells. Following LPS-challenge, the transitional airways showed evidence of a heterogeneous population of cells that included both CC10 and surfactant D-positive cells and we hypothesise that this is an attempt by the inflamed peripheral lung to increase surfactant levels and thus restore compromised alveolar compliance.

P206 SHOTGUN PROTEOMIC ANALYSIS OF HUMAN INDUCED SPUTUM

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Sputum is increasingly recognised as a biologically relevant sample of the environment of the airways when collected under controlled conditions. As such, it has been used for the analysis of bacterial load, tumour and inflammatory cell content, and of biomarkers of airways diseases such as cystic fibrosis, asthma and chronic obstructive pulmonary disease. While related biofluids such as broncho-alveolar lavage[1] fluid, nasal lavage fluid,[2] and in particular saliva[3] have been well-characterised using standard 2-D gel based proteomics, sputum has not. This is probably due to the presence of mucin glycoproteins that compromise the separation of proteins during the IEF stage of 2-D gel analysis, preventing good resolution.

We have used a combination of 2-D gel electrophoresis (fig 1B) and a multidimensional mass-spectrometric technique (GeLC-MS/MS) (fig 1A) to examine the proteome of induced sputum. 191 individual human proteins were confidently assigned using these techniques. In addition to expected components, several hitherto unreported proteins were discovered, including three members of the annexin family, kallikreins 1 and 11, and peroxiredoxins 1, 2, and 5. The resultant data represent the first detailed survey of the human induced sputum proteome and allow a comparison of the induced sputum proteome with other biologically related fluids such as broncho-alveolar lavage fluid and saliva. They also provide a platform for the future identification of biomarkers of airways disease.

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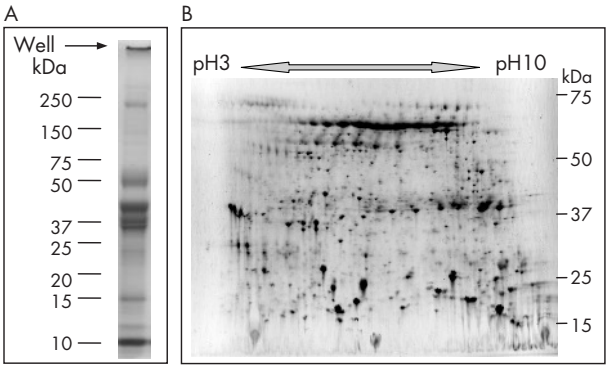

Abstract P206 Typical SDS-PAGE profiles of induced sputnum examined using (A) 1-D and (B) 2-D gels.

Clinical aspects of asthma

P207 IS THE PREVALENCE OF ASTHMA DECLINING?

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Background: Dramatic increases in the reported prevalence of asthma over the latter half of the last century have made asthma one of the most common chronic disorders globally. In recent years, however, there have been a number of suggestions that the prevalence of asthma is now declining, which, if true is important for health service planning and also because it offers the possibility to generate and test new aetiological hypotheses.
Objective: To examine recent trends in the international prevalence of asthma.
Review Methods: Systematic search of Medline, Web of Science, and Google Scholar databases for high quality reports of repeat cross-sectional studies, cohort studies and analyses of routine healthcare datasets.
Selection of Studies: We only included studies that presented data on estimates of asthma prevalence using comparable approaches for at least two time points during the period 1990–2006.
Output: Studies were categorised into two main groups: studies using the validated ISAAC questionnaire and other epidemiological studies.
Conclusions: The large volume of data identified indicates that there are, at present, no overall signs of a declining trend in asthma prevalence. On the contrary, asthma prevalence is in most parts of the world still increasing. The reductions in emergency healthcare utilisation being reported in some economically developed countries most probably reflect improvements in quality of care. There remain major gaps in the literature in relation to large parts of Africa, Asia, and South America.

P208 INCREASED PREVALENCE OF INFLAMMATORY BOWEL DISEASE IN PATIENTS WITH AIRWAYS DISEASE: 10 YEARS' EXPERIENCE IN A TEACHING HOSPITAL

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Lung disease is a recognised extra-intestinal manifestation of inflammatory bowel disease (IBD). The lung pathology is predominantly airways disease, but there are no consistent radiological, pulmonary, or airway inflammation abnormalities. We undertook a retrospective analysis of IBD prevalence in our respiratory clinic, to determine whether any pattern of airways disease or inflammation was associated with IBD. We identified 37 patients with IBD among 2192 patients with airways disease seen over 10 years by a single respiratory consultant. IBD was more prevalent (table) than expected in a similar sized general population cohort, using local IBD prevalence data (Stone *et al. Eur J Gastroenterol Hepatol* 2003;**5**:1275–80). This was true for both Crohn's disease (CD) and ulcerative colitis (UC) (OR 5.96, 95% CI 1.94 to 18.31 and OR 4.21 95% CI 1.71 to 10.41 respectively). Airways disease was categorised using standard criteria. IBD was more frequent in all patterns of airways disease except asthma; the association was particularly strong in airways disease associated with productive cough (table). All except 1 patient had established IBD; 24% had undergone colectomy before the onset of respiratory symptoms. There were no obvious radiological or pulmonary function differences between UC and CD cases. Induced sputum results showed a trend for a higher sputum lymphocyte count (3.7% *v* 0.5%, mean difference −3.25, 95% CI −9.1 to 2.6, p=0.2), and lower blood lymphocyte count (1.6 *v* 2.2, mean difference 0.5, 95% CI −0.2 to 1.3, p=0.15) in CD compared with UC. Sputum neutrophil count was also lower in CD (58.5% *v* 76.9%, mean difference 18.4, 95% CI −12 to 48.7, p=0.2).

Our findings support an association between airways disease and IBD, particularly non-asthmatic airways disease with productive cough. The pattern of airway inflammation seen may be different in CD compared with UC.

Abstract P208

Airways disease	Patients seen in clinic	IBD cases	OR observed/expected (95% CI of OR)
COPD	588	9	3.87 (1.19–12.62)
Bronchiectasis	215	7	8.38 (2.43–28.89)
Chronic cough	426	8	4.76 (1.43–15.90)
Chronic bronchitis	66	4	16.07 (3.92–65.76)
Asthma	893	9	2.54 (0.78–8.26)
Total	2129	37	4.26 (1.48–11.71)

P209 IS THERE A ROLE FOR INSPIRATORY FLOW RATE MEASUREMENTS PRIOR TO PRESCRIBING INHALED MEDICATIONS?

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Background: Inhalation as a route of drug delivery has been used for many years to administer medication to the lungs. Studies have shown that particle size, pattern of deposition of an inhaled drug, patient's inhaler technique and device employed, are important determinants upon drug delivery to the respiratory tract.[1] In practice however, whether the patient's inspiratory flow rate (IFR) lies within the range of optimum inspiratory flow rate (OIFR) at which an inhaler device will work most effectively is rarely considered when inhalers are being prescribed.[2, 3]
Aim: (1) To examine the suitability of prescribed inhaler device based on comparing the patient's IFR with the recommended OIFR for different inhaler devices. (2) To determine if there is a role for IFR measurement prior to prescribing patients inhalers.
Method: Over a 3 month period, an unselected random sample of inpatients and outpatients with asthma and COPD were assessed for the suitability of their prescribed inhalers on the basis of comparing their measured IFRs with the recommended OIFRs for different inhalers (Clement Clarke International (CCI), 2003). The patients' IFRs were measured using the CCI ''in-check dial'' inspiratory flow meter. Peak expiratory flow rate (PEFR) and spirometry were also recorded.
Results: Seventy eight patients (51 female) were assessed. 46 patients (mean age 77.5 years, range: 53–94 years) had COPD. These patients had a mean FEV1 of 43% predicted normal (range: 9–87%). 32 patients (mean age 64 years, range 23–87 years) had asthma with a mean PEFR of 283 l/min (range 50–510 l/min). The asthma group had higher values of IFR than those with COPD (mean values 82.5 l/min and 64.2 l/min respectively). In the asthma group, 24 patients (75%) were prescribed at least one inappropriate inhaler based on comparing their IFRs with the OIFRs. In the COPD group, 32 patients (69%) were prescribed at least one inappropriate inhaler. The asthma group tends to have IFRs higher than the upper limit of the OIFR for some devices whereas COPD patients tend to have IFRs below the lower limit of the OIFRs for some devices. Neither FEV1 or PEFR showed any correlation with IFR.
Conclusions: (1) This study has shown that prescribing inhalers without considering IFR measurement leads to a high number of inappropriate inhalers being used. (2) The severity of disease based on FEVI and/or PEFR could not predict the patients' IFRs. (3) IFR measurements may have a valuable role to play prior to prescribing inhaled medications.

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P210 EVIDENCE-BASED ASTHMA TRAINING IMPROVES ASTHMA MANAGEMENT SKILLS IN GENERAL PRACTICE: A COMMUNITY-BASED SURVEY

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Background: The BTS/SIGN Asthma Guideline provides evidence-based recommendations for the diagnosis and treatment of asthma. Although easily accessible online, the guideline alone may not be sufficient to change practice, and community-based health professionals may benefit from an educational package linking the guideline to practice. Here we assess the effects of accredited asthma training, based on the guideline, on clinical practice in primary care.
Methods: 526 primary care nurses enrolled on an accredited (Education for Health) diploma level asthma module received a postal questionnaire at the start (baseline) and the end of course (6 months). Nurses' self-reported confidence in their abilities and frequency of performing key components of the guidelines were measured on a Likert scale where

1 = poor confidence or low frequency and 5 = high confidence or high frequency. Enhanced practitioner role was assessed using a Likert scale where 1 = not enhanced and 5 = greatly enhanced. Paired data were analysed using McNemar's test.
Results: 303 paired sets of data were suitable for analysis (58% overall response rate). The proportion of the respondents who reported they were ''usually confident'' or ''very confident'' in their ability to provide appropriate asthma care and education to patients rose from 10% to 84%. There was a significant increase from baseline in frequency of taking a structured respiratory history (''most times''/''always'' 38% to 80%; $p<0.0001$); using bronchodilator reversibility testing for diagnosis (36% to 76%; $p<0.001$) and measurement of peak expiratory flow (65% to 92%; $p<0.0001$). Frequency of checking of inhaler technique (58% to 91%; $p<0.0001$) and checking adherence to treatment (62% to 92%; $p<0.0001$) also increased from baseline as did advice given to patients and/or prescribers on inhaler device selection (25% to 74%; $p<0.0001$). 57% respondents reported enhancement of their clinical role and 54% reported enhancement of their professional education role in their workplace.
Conclusion: In this study, nurses who completed a BTS/SIGN Guideline-based accredited asthma module reported an increase in the management skills associated with improved diagnosis and treatment of asthma. Training a nurse within the practice can encourage knowledge sharing among colleagues and therefore aid local dissemination of the key points of the guidelines.

P211 THE EFFECTIVENESS OF SPEECH AND LANGUAGE THERAPY IN VOCAL CORD DYSFUNCTION

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Introduction: Vocal cord dysfunction (VCD) is a condition where the vocal cords adduct during inspiration, resulting in inspiratory wheeze and stridor. It is often associated with, and misdiagnosed as asthma. The aetiology, symptom triggers and concomitant conditions are not well defined. There is anecdotal evidence of the benefits of Speech and Language Therapy (SLT) in management of VCD. A protocol was developed to define the VCD population in terms of diagnosis, aetiology, triggers, associated conditions, and treatment.
Method: Fifty patients (41 females, 9 males, mean age 47.1, range 20–79) consecutively referred to the VCD clinic at Heartlands hospital, were put through the protocol. They were assessed by SLT using nasendoscopy and full lung function tests. Established cases of VCD received 4 therapy sessions of SLT and treatment effectiveness was assessed by baseline and post treatment self-rated symptoms questionnaire (scored out of 25).
Results: The diagnosis of VCD was confirmed by nasendoscopy (''paradoxical vocal cord movement'') in 19/50 (38%). A further 23 (46%) patients had symptoms suggestive of VCD, but nasendoscopy was not conclusive. VCD was excluded in 8 (16%) patients who were alternatively diagnosed with globus pharyngeus. Of the 19 confirmed VCD cases, the most commonly associated conditions were oesophageal reflux (15, 79%) and asthma (14, 74%), though rhinitis and dysphonia were also prevalent (10, 53%). The most commonly reported triggers were stress (18, 95%), cough (18, 95%), exertion (16, 84%), heartburn (15, 79%), and smoke (14, 74%). 15/19 patients completed a course of SLT. A significant reduction in patient-reported symptoms was noted post SLT. Wilcoxon Rank Test pre therapy mean 17.6, SD 3.8, post therapy mean 10.0, SD 4.3, $Z=-3.4$, $p=0.01$. A similar improvement in symptoms scores was also seen in ''suggestive VCD cases''.
Conclusion: VCD is a complex condition though there are a common range of concomitant factors and triggers. SLT can play a role in symptom management.

P212 SIMVASTATIN AS A POTENTIAL THERAPEUTIC ANTI-INFLAMMATORY AGENT IN ASTHMA

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Rationale: Statins effectively lower cholesterol, and have also been shown to exhibit anti-inflammatory properties. Recent preliminary in-vitro and animal studies have suggested they may be useful for the treatment of a number of inflammatory conditions including asthma.
Objectives: To evaluate the in vivo therapeutic potential of simvastatin as a novel anti-inflammatory agent in asthmatics.
Methods: Any potential signal from treatment effect was optimised by initially withdrawing all anti-inflammatory treatment for the duration of the study. Thereafter, participants received one month of simvastatin and one month of placebo in a randomised double blind, crossover trial, with 16 patients completing per protocol.
Measurements: Airway and systemic asthmatic inflammation and was evaluated by measuring exhaled tidal nitric oxide (the primary outcome), alveolar nitric oxide, induced sputum eosinophil count, airway hyperresponsiveness to methacholine, salivary eosinophilic cationic protein, high sensitivity CRP, and peripheral eosinophil count. Dynamic and static lung volume measurements were made as was estimation of cholesterol.
Results: Compared with placebo simvastatin led to a 0.86 geometric mean fold difference (95% CI 0.7 to 1.04, $p=0.154$) in exhaled nitric oxide, and a −0.178 doubling dilution shift (95% CI −1.90 to 1.55, $p=1.0$) in methacholine hyperresponsiveness. Similarly, there were also no significant differences in other inflammatory outcomes, lung volumes or airway resistance between simvastatin and placebo. Treatment with simvastatin did as expected lead to significant reduction ($p<0.005$) of total and LDL cholesterol.
Conclusion: Despite theoretical in vitro potential for use of statins in asthma, there is no evidence to suggest they have a therapeutic role in patients.

This paper was entered into the BALR young investigator competition at the 2006 summer meeting.

P213 THE RESPONSE TO METHOTREXATE IN REFRACTORY ASTHMA

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Introduction: Methotrexate is a well established steroid sparing immunosuppressive agent used in the management of refractory asthma. The therapeutic response to methotrexate varies widely and little is known about the factors predicting a favourable outcome.
Methods: We identified 41 patients with refractory asthma attending the Glenfield Hospital refractory asthma clinic who had either a past or current history of methotrexate treatment for asthma control. The cohort represents 12.8% of the total number of refractory asthma patients on the clinic database (n = 320) and 34.7% of all the patients on regular maintenance oral corticosteroid therapy (n = 118). Sufficient data were obtained from 35 of the patients for further analysis.

In all patients, methotrexate prescription followed a period of treatment with maintenance oral corticosteroids for at least 6 months that failed to achieve satisfactory symptom control and/or control of underlying eosinophilic airway inflammation. When tolerated, methotrexate was prescribed at a dose of 15 mg weekly for at least 3 months before an assessment of response was made. A positive response was defined as a sustained fall in maintenance oral corticosteroid dose, improvement in daily symptom control or improvement in lung function when compared with control in these parameters for the 6 months prior to starting therapy.
Results: Patients started on MTX were on a significantly higher dose of maintenance prednisolone at baseline compared with the population on maintenance oral steroid therapy not started on methotrexate (mean 17.7 mg *v* 9.6 mg, $p=0.03$). The mean duration of therapy with methotrexate following commencement was 12.2 months (SE 1.62). 11 of the 35 patients have remained on long term methotrexate. Side effects (derangement in liver function tests, rash, gastrointestinal symptoms, and constitutional symptoms) occurred in 6 patients that had methotrexate stopped (17%). 49% (n = 17) showed a positive response to methotrexate. 50% of this cohort had a positive response in all the specified criteria and a further 25% showed improvement in symptoms together with a fall in maintenance oral corticosteroid dose. A 52% reduction in the dose of maintenance prednisolone was achieved in responders. Five patients were able to withdraw oral corticosteroid therapy completely. Six of the responders subsequently had to stop therapy due to side effects or loss of efficacy. In those patients that developed impaired efficacy, the mean duration of efficacy was 13.8 months with no patient showing ongoing responsiveness to methotrexate beyond 24 months. Non-responders (n = 18) had a mean duration of therapy of 8.5 months. There was no significant difference between responders and non-responders in any measured clinical or inflammatory variables.
Conclusions: Our results are consistent with previous publications and indicate that methotrexate is a valuable steroid sparing agent in a small minority of refractory asthma patients. However, factors predicting a response remain unclear.

P214 ELIGIBILITY FOR TREATMENT WITH OMALIZUMAB AMONG PATIENTS ATTENDING THE GLENFIELD HOSPITAL REFRACTORY ASTHMA CLINIC

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There is a pressing need for novel therapeutic agents in the management of patients with refractory asthma. The humanised monoclonal anti-IgE antibody, Omalizumab, has recently been introduced as add-on therapy for patients with severe atopic asthma. Omalizumab is licensed for use in patients with a positive skin prick test or specific IgE to a perennial aeroallergen, reduced lung function (FEV1<80% of predicted) along with frequent symptoms or nocturnal awakenings and multiple severe exacerbations despite regular inhaled corticosteroids plus a long acting beta-2 agonist. In addition patients with a low (<30 iU/ml) or markedly elevated total IgE should not be dosed with an upper limit for treatment of 700 iU/ml or lower dependant on body weight. We aimed to determine what proportion of patients referred to our refractory asthma clinic would be eligible for treatment with Omalizumab according to the above criteria. We assessed 251 consecutive patients attending our refractory asthma clinic with uncontrolled asthma symptoms and recurrent severe asthma exacerbations. We recorded body weight (kg), spirometry as FEV1 % of predicted, symptoms using the Juniper Asthma Control score, total serum IgE (iU/ml) and skin prick tests to common aeroallergens. Only 34 (13.5%) patients met all of the criteria for treatment. 148 patients had no evidence of persistent airflow obstruction (FEV1>80%). 58 patients had negative skin prick tests to all common aeroallergens, 45 patients had a total IgE <30 (of which 16 had positive skin prick tests) and 53 patients had a total IgE >700 iU/ml. A further nine patients had a total IgE greater than the maximum recommended for dosing in relation to their body weight. Although Omalizumab offers an additional therapeutic option for patients with severe asthma, its use is likely to be limited to a small proportion of patients. Further studies are needed to determine its efficacy in patients with a total IgE outside the recommended range for optimal dosing. There remains a high unmet need for novel treatments for patients with severe asthma.

P215 ASSOCIATION BETWEEN CONTROL OF ASTHMA AND GASTRO-OESOPHAGEAL REFLUX DISEASE SCORE

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Gastro-oesophageal reflux disease (GORD) is more common in patients with asthma compared to controls. There is evidence that the presence of GORD is associated with more severe asthma. The mechanism for the increased prevalence of GORD in asthma is unclear. We set out to determine the relation between a validated GORD score (Manterola *et al. J Clin Epidemiol* 2002;**55**:1041–5) and asthma characteristics in a cohort of 113 patients with well characterised disease. Asthma characteristics investigated were the modified Juniper Asthma Control Questionnaire (JAC) consisting of the response to symptom questions only, JAC score for daily bronchodilator use, dose of inhaled corticosteroid, FEV1 as % predicted, induced sputum eosinophil differential and neutrophil count, exhaled nitric oxide concentration (F_ENO) and the results of a methacholine inhalation test (PC_{20}). A multiple independent linear regression model was used to predict the reflux score. The model coefficients are given in the table. For the total model $r^2=0.362$, $p=0.003$. Poorly controlled asthma symptoms, as assessed by the modified JAC, are associated with a higher reflux score. The reflux score was not related to use of inhaled corticosteroids or bronchodilator use. Neither the pattern of airway inflammation, nor the degree of airway hyperresponsiveness was associated with the reflux score.

Abstract P215

Variable	Coefficient	Standard error	p Value
Modified JAC score	1.42	0.37	0.000
FEV1 as % predicted	0.02	0.02	0.208
Bronchodilator use score	0.17	0.34	0.614
Dose of inhaled corticosteroid (mg)	−3.52	0.001	0.968
Log sputum eosinophil count (%)	−0.21	0.46	0.646
Log sputum neutrophil count ($\times10^6$/g of sputum)	−0.38	0.37	0.310
Log Pc20 (mg/ml)	0.10	0.25	0.699
Log F_ENO	−0.38	−0.57	0.689
BMI (kg/m^2)	0.05	0.04	0.908

P216 SEVERE ASTHMA IS ASSOCIATED WITH TIDAL BREATHING CLOSE TO RESIDUAL VOLUME

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Introduction: Our hypothesis is that a proportion of patients with severe asthma tidal breathe at a volume close to residual volume (RV); a feature which may causes a worsening of symptoms. We aimed to confirm the presence of this pattern of breathing in patients with severe asthma and whether it bears any correlation to hyperinflation.
Methods: We recruited 32 subjects: 10 normal, 10 severe asthmatics (BTS step 4 or greater), 7 mild asthmatics (BTS steps 1 or 2), and 5 patients with COPD and known hyperinflation. Using body plethysmography to determine functional residual capacity, and using slow vital capacity maneuvers, we were able to determine all lung volumes in the different subject groups.
Results: Mean expiratory reserve volume (ERV) was significantly reduced in the severe asthma group (mean ERV=0.66 l) compared to normals (1.55 l, $p<0.001$) and mild asthma (1.24 l, $p=0.009$), and in the COPD group (0.82 l) compared to normals ($p=0.004$). In the COPD group, all subjects were hyperinflated with high values of RV % predicted (mean 207%). A subgroup of severe asthma patients had ERVs lower than those in the COPD group, but with normal RV % predicted (fig 1).
Discussion: These results support the earlier data[1] that some subjects with severe asthma appear to tidal breathe at a volume close to RV. The reasons for this are unknown, but our results show that hyperinflation is not uniquely the cause. This may represent a distinct clinical phenotype of severe asthma. Alternatively it may represent an acquired form of dysfunctional breathing. So far no evaluated treatment for this pattern exists, but it may revolve around techniques that aim to increase lung volumes.

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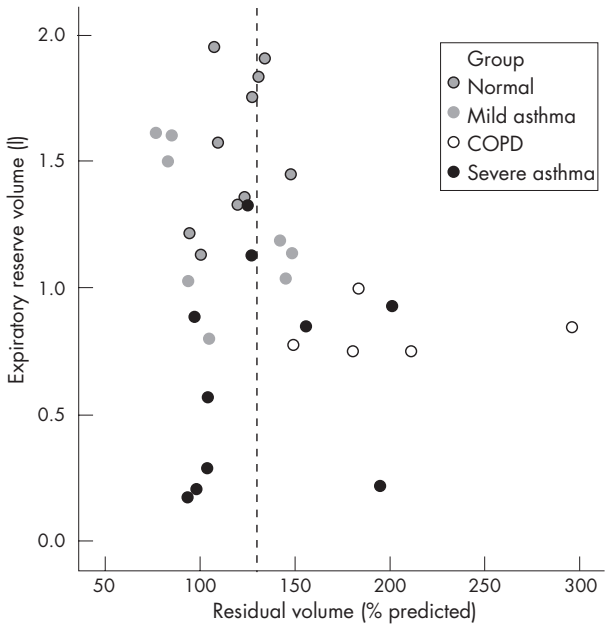

Abstract P216 Scatter plot of ERV against residual volume. Broken reference line lies at 130% predicted (values greater than which indicate hyperinflation).

P217 VALIDATION OF A MULTIDETECTOR CT SCANNER TO MEASURE PROXIMAL AND DISTAL AIRWAY WALL VOLUME

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Background: Multidetector CT has emerged as a useful tool to non-invasively measure cross-sectional proximal airway wall dimensions in airways disease. However we and others have found that there is a systematic error in the measurement of distal airways. This is most likely due to the effect of partial volume averaging of captured CT image. We sought to validate and improve the accuracy our Siemens Sensation 16 slice MDCT scanner to measure airway wall area and volume.
Methods: A phantom model of 9 plastic tubes of varying airway wall dimensions (Range wall area (WA) $\pm$2SD normal and asthmatic airways (2.42–47 mm^2)) embedded within a polystyrene block was constructed. The polystyrene had a mean attenuation (SEM) of -965 (2.4)HU, similar to the density of inflated lung tissue. Gold standard measurements were made to the nearest 20 μm by imaging both faces of each tube with a stereomicroscope and the length by Vernier callipers. CT scanning was performed at 16$\times$0.75 mm collimation, 120 kV, and 50 mAs with a table feed of 13.5/0.5 s scanner rotation. Images were reconstructed at 0.75 mm spacings using a B70-f very sharp aligorithm at 139 mm field of view with a 512$\times$512 matrix. Cross sectional measurements were made at a face designated the leading face using Ray Casting (Harvey Coxson VA) and the full-width half-maximum technique by 3-blinded observers. Volumetric measurements were made using a commercial platform (Mimics, Materialise). To minimise the error in the measurement of smaller airways, we varied the threshold measurement for tubes 5–8 to achieve the % width maximum of the grey level across the tube wall that produced $<$5% error in wall volume when compared to the gold standard. A plot of threshold versus wall volume was generated. We tested the validity of this relationship by examining whether we were able to predict the % maximum threshold required to produce $<$5% error in wall volumes of tubes 1–4.
Results: Ray casting was highly reproducible amongst observers (ICC = 1 for wall area (WA), luminal area (LA) and %WA), and between observers and the steromicroscope (ICC = 1 for %WA tubes 6–9, LA &WA tubes1–9). Plots of the mean interobserver LA and WA versus % error followed a second order polynomial relationship (LA $r^2 = 0.96$, WA $r^2 = 0.90$). There was an excellent correlation between Vernier calliper tube lengths and reconstructed CT 3D tube length ($r^2 = 1$, absolute mean error = 1.63%). For tubes 5–8 there was a close linear relationship between wall volume and the % maximun wall threshold ($r^2 = 0.98$). This allowed us to predict the thresholds required to measure tubes 1–4 and reduced the mean (SD)% error from 49.3 (13.9)% (50% maximum wall threshold) to 5 (3.9)%.
Conclusions: The measurement of tubes corresponding to proximal and distal airways (generation 3–8) by CT is reproducible and absolute measurements can be made accurately.

P218 THE NIJMEGEN QUESTIONNAIRE DOES NOT APPEAR TO PREDICT HYPERVENTILATION IN SUBJECTS WITH SEVERE ASTHMA

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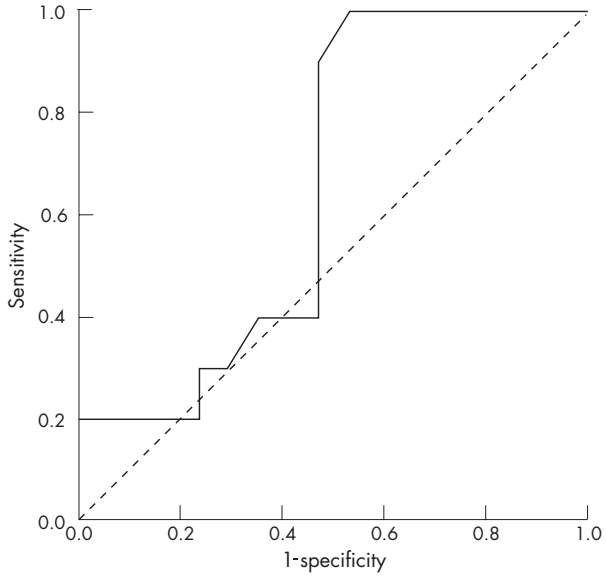
Introduction: The Nijmegen questionnaire was originally validated to predict hyperventilation in the absence of chest disease.[1] Its use has subsequently been extended to predict hyperventilation in the presence of chest disease despite never having been validated in this context.
Methods: Twenty seven subjects with severe asthma were recruited. Nijmegen questionnaires were completed prior to spirometry and then an incremental shuttle walk test with concomitant continuous end tidal partial pressure of carbon dioxide ($P_{ET}CO_2$) monitoring. $P_{ET}CO_2$ values were taken as the mean of 10 consecutive breaths at one minute prior to starting exercise, and over the last 10 breaths before exercise tolerance was reached. Subjects were considered to hyperventilate if a) resting $P_{ET}CO_2 < 30$ mmHg (chronic hyperventilation; CH) or b) $P_{ET}CO_2$ fell with exercise (acute exercise induced hyperventilation; AEIH). Multiple stepwise logistic regression was performed to identify the 3, 4, 5, 6, 7, and 8 best predictive items within the questionnaire.
Results: 10/27 subjects (37%) were classed as hyperventilating (5 CH, 5 AEIH). The mean Nijmegen score for the whole cohort was 22 (normal $<$23). There was no significant correlation between Nijmegen score and either CH or AEIH. A receiver operator characteristic plot (fig) showed that Nijmegen score was not significantly better than chance at predicting hyperventilation (area under curve 0.659 sig = 0.175). At a threshold of greater or equal to 22.5, the Nijmegen score had a sensitivity of 70% and a specificity of 53%. Similar results were achieved when the Nijmegen questionnaire was used to predict either CH or AEIH alone. Using only the best predictive items from the questionnaire also failed to improve the predictive value to an acceptable level.
Discussion: The original Nijmegen validation had a sensitivity of 91% and specificity of 95. The questionnaire does not appear valid in the prediction of hyperventilation in subjects with severe asthma. Our definition of hyperventilation is open to discussion, however probably reflects the original gold standard: a diagnosis of hyperventilation ''made on the basis of the complaints pattern''.[1] A number of the items within the questionnaire refer to symptoms that are commonly experienced in asthma which may explain both the high mean scores and the inability of the questionnaire to identify patients with both severe asthma and hyperventilation.



Abstract P218 ROC plot with Nijmegen score as test variable and presence of hyperventilation as a positive result. Broken diagonal line denotes predictive value of guessing.

1. **van Dixhoorn J**, Duivenvoorden HJ. Efficacy of Nijmegen Questionnaire in recognition of the hyperventilation syndrome. *J Psychosom Res* 1985;**29**:199–206.

P219 ADIPOSITY PREDICTS ASTHMA AND PULMONARY FUNCTION IN A YOUNG ADULT POPULATION

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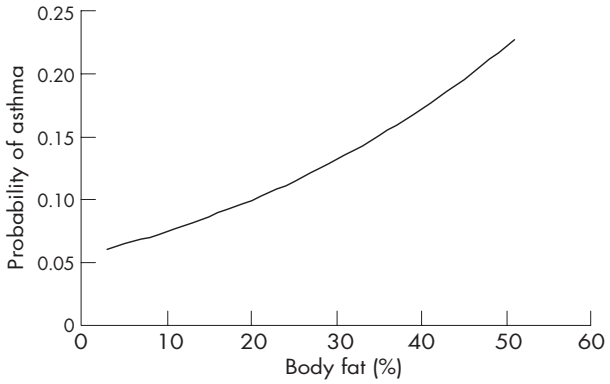
Background: A concurrent rise in the prevalence of asthma and obesity in recent decades has led to speculation on obesity as a causal factor in asthma. To further elucidate the role of obesity, we examined measures of central obesity (waist circumference, WC) and percentage body fat (%BF) in addition to body mass index (BMI) with relation to asthma prevalence and lung function in a population of young adults.
Methods: A prospective cross sectional study (n = 1614) was performed in a population of adults aged 18–30. Validated questionnaires provided data on doctor-diagnosed asthma and atopic disease. Measurements included height, weight, WC, %BF and morning spirometry.
Results: BMI, WC, and %BF were all associated with current asthma ($p<0.01$). BMI was significantly associated with asthma ($p<0.001$) such that a 5 unit increment in BMI reflects a 41.5% increase in asthma risk. %BF was significantly associated with asthma ($p = 0.001$) such that a 5% increase in %BF reflects a 16% increase in asthma risk (fig 1). %BF was also significantly associated with current eczema (OR 1.03, $p = 0.001$). BMI predicted frequency of symptoms over the last 3 months, such that each unit rise in BMI equated to an 8.7% risk of having more frequent symptoms—for example, ''continuous'' rather than ''daily'' ($p<0.05$). BMI also predicted daily inhaled bronchodilator volume in a subgroup of male smokers ($p<0.05$). BMI, WC, WHR, and %BF were positively associated with FEV1, FVC, PEF across normal adiposity ranges but



Abstract P219 Probability of asthma by percentage body fat (%BF).

inversely associated once higher adiposity levels were reached ($p<0.001$). A similar pattern was seen for BMI and %BF with % predicted FEV1 and PEF ($p<0.05$). For instance, % predicted FEV1 increased with BMI until a BMI of 29, with % FEV1 declining thereafter. BMI, WC and WHR were inversely associated with FEV1/FVC ($p<0.001$).
Conclusion: Adiposity indices were associated with asthma and this was also true for %BF, a more direct measure of adiposity than BMI. In this general population of young adults, adiposity indices showed non-linear associations with lung function, with positive associations seen across normal ranges of adiposity and inverse associations seen at higher levels. Adiposity was inversely associated with FEV1/FVC, suggesting an increasing degree of airflow obstruction in more adipose individuals. Examining the relation between %BF and asthma phenotypes is likely to further elucidate the role of obesity in asthma.

P220 A MECHANISM WHEREBY A PROPENSITY TO WHEEZE MIGHT BOOST EXERCISE CAPACITY

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Introduction: Airway hyperresponsiveness is common in elite athletes and may reflect environmental exposures during training.[1] Casual observation suggests that wheeze is common amongst competitors at junior events as well. Thus it might confer a competitive advantage. A possible mechanism could be that mild wheeze encourages a slow deep pattern of breathing as is promoted by physiotherapists. A newly developed model shows that this breathing pattern is associated with a reduced level of ventilation during submaximal exercise.[2] We now report the same pattern among 15 male subjects who were referred on account of work related wheeze. Their average features were: age 45 years, post bronchodilator FEV1 77% predicted and reversibility 16%.
Measurements: Lung function was obtained by standard methods.[3] Exercise was after inhalation of a bronchodilator aerosol; it was progressive on a treadmill and standardised indices were obtained by interpolation. Exercise ventilation ($\dot{V}$E,St) and CO_2 output were at an O_2 uptake of 45 mmol/min (1.0 l/min); breathing frequency and tidal volume were at a ventilation of 30 l/min (fR30 and Vt30 respectively, where fR30 = 30/Vt30). Reference variables were: for FEV1 age and stature,[3] for $\dot{V}$E,St the CO2 output and fR30[2] and for Vt30 the FVC.[3] Differences were assessed by paired t test.
Results: The mean values for $\dot{V}$E,St and Vt30 were 26.1 l/min and 1.74 l; these exceeded the reference values of 22.5 l/min and 1.51 l respectively ($p<0.05$). Compared with the reference values the depth of breathing was increased (Vt30 difference 0.23 l $p<0.05$). However in 6 of the 15 subjects the difference was quite small (<0.2 l) whereas in 5 subjects it exceeded 0.4 l. These subgroups did not appear to differ with respect initial spirometry or reversibility.
Discussion: The chosen work level was on average less than 50% of the symptom limited maximum and the subjects felt comfortable with it, so the slow deep breathing pattern was not a response to stress. Comparison with other occupational disorders suggested that the response was associated with wheeze. Here it was well developed only in some subjects. In these men the model indicates that $\dot{V}$E,St would have been reduced by up to 3 l/min, but the benefit appears to have been obscured by $\dot{V}A/\dot{Q}$ inequality since the $\dot{V}$E,St was on average slightly increased. Had the airway obstruction been fully corrected (as would seem to be necessary for a wheezy athlete to be successful) the model predicted that the same breathing pattern would have reduced the ventilation and associated breathlessness. Is this why a disproportionate number of athletes have a tendency to wheeze?

1. **Langdeau J-B**, *et al. Am J Respir Crit Care* 2000;**161**:1479–84.
2. **Cotes JE**, Reed JW. *Proc Physiol Soc* 2006;**3**:C39.
3. **Cotes JE**, *et al. Lung function: physiology, measurement and application in medicine*, Sixth edition. Blackwell Publications, 2006.

P221 ADRENAL FUNCTION OF PATIENTS WITH BRONCHIECTASIS AND ASTHMA WHO TAKE INHALED CORTICOSTEROIDS

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Introduction: Asthmatic patients who take inhaled corticosteroids (ICS) have been shown to have reduced basal serum and urine cortisol levels (Donnelly. *AJRCCM* 1997;**156**:1746). However, no work has addressed the ability to produce cortisol following a stimulus in patients who have been taking long term ICS commonly used in the UK Bronchiectasis is associated with increased airway inflammation and following an index case of complete adrenal shut down due to ICS, we examined the dynamic adrenal function in patients with bronchiectasis and asthma who have taken ICS for more than 1 year.
Method: Twenty nine subjects underwent serum cortisol, ACTH, and fasting glucose measurement prior to intramuscular administration of 250 μg synacthen. Serum cortisol was repeated after 30 minutes. Subjects were diagnosed as suppressed if the 30-minute cortisol was <550 nmol/l. Concomitant medications, symptoms and signs of adrenal dysfunction, St George's Respiratory Questionnaire (SGRQ) and Short-Form 36 (SF-36) scores were compared for those who had adrenal suppression and those who did not.
Results: See table.
Conclusion: 48% of patients with bronchiectasis and asthma who take licensed doses of ICS long term have biochemical evidence of dynamic adrenal suppression. Significantly more of those who are suppressed have symptoms of being light headed on standing, nausea, and abdominal pain.

Abstract P221

	Suppressed	Not suppressed	p Value
n	15	14	
Mean daily dose of ICS (BDP equiv)	1828 (SD 851.6)	1640 (SD 530.2)	0.64
On beclamethasone (n=)	2	0	0.48
On budesonide (n=)	1	2	
On fluticasone (n=)	11	13	
Had nasal steroid over last year (n=)	4	3	0.56
Had oral steroid over last year (n=)	4	7	0.32
Total dose oral steroid last year (mg)	313	659	0.32
Lightheaded on standing (n=)	8	4	0.048
Nausea	8	3	0.020
Abdominal pain	6	1	0.031
Vomiting	5	1	0.070
Postural hypotension at 1 or 3 mins	3	5	0.682
Fasting glucose	5.13	4.91	0.470

Tuberculosis: epidemiology and treatment

P222 INCREASES IN TUBERCULOSIS IN THE UK-BORN IN NORTH EAST LONDON AND THE LONDON BOROUGH OF HACKNEY

T. Sanghera, G. H. Bothamley. *NE London TB Network, Homerton University Hospital, UK*

Introduction: The proportion of tuberculosis (TB) in those born outside the UK has steadily increased nationally and also within NE London. We wanted to know whether the number of TB cases in the UK-born was stable or not and the contribution of the outbreak strain to the increase locally.
Methods: The NE London Tuberculosis Network receives notification data from all boroughs within the sector. These were analysed according to country of birth and whether UK-born or not for the period 1998–2005. In one borough there appeared to be a significant increase in TB. The importance of travel to a country where TB was common and a number of risk factors for adherence (alcoholism, psychiatric treatment, illegal drug use, prison experience, homelessness, and being a member of the isoniazid-resistant outbreak) were documented.
Results: TB cases in the UK born have shown an increase since 1998, this can only be partially explained by the introduction of a more robust reporting method. Two hundred and four UK-born TB patients living in Hackney were identified. A third of these (n = 67) had traveled or stayed with relatives in a country where the incidence of TB was high. The isoniazid-resistant outbreak contributed significantly to the observed increases in UK-born TB. The complexity of cases increased during the period of study, measured by the number of risk factors per adult patient.
Conclusions: TB in the UK-born has increased due to travel and the isoniazid-resistant outbreak. These factors should be addressed vigorously to prevent an increase in tuberculosis in the UK-born.

This study was funded by the NHS Culyer allocation and the NE London TB Network.

P223 THE PERSISTENT LINK BETWEEN TUBERCULOSIS AND POVERTY IN LIVERPOOL ILLUSTRATES THE INABILITY TO IMPROVE HEALTH INEQUALITIES IN ENGLAND

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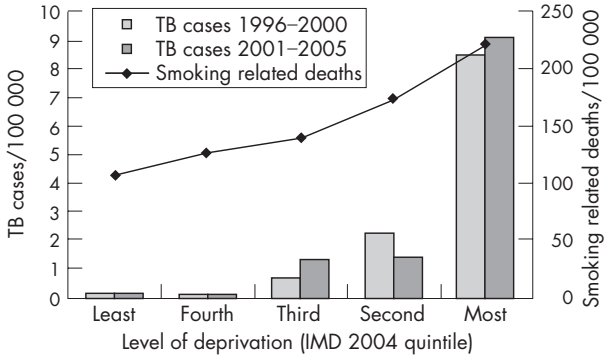
Aim: To compare health inequalities today with the recent past.
Background: A previous study showed that tuberculosis (TB) rates across Liverpool are related to poverty.[1] With a commitment to reduce health inequalities, cities with the lowest life expectancy should show improvement in patterns of a curable disease like tuberculosis.
Design: An ecological study of geographic patterns of TB and respiratory disease.
Methods: TB notifications, mortality and hospital data (1996–2005) were analysed against ward-level measures of deprivation.
Results: TB rates in 1996–2000 and 2001–05 had virtually exactly the same correlation with deprivation as observed in 1985–91. There were almost no TB cases in the most affluent areas; 2 per 100 000 in moderately deprived areas; and over four times this rate in the most deprived wards. Other respiratory diseases and mortality from conditions related to smoking show the same geographical pattern across Liverpool and are also likely to have not changed from historic distributions.
Conclusion: The persistent pattern of tuberculosis across the city of Liverpool illustrates that health inequalities, inextricably linked with poverty, have not reduced in the last 20 years. The ban on smoking in public places may help to reduce some inequalities in respiratory diseases, but tuberculosis control policies do not appear to be improving its distribution across the city of Liverpool.

1. **Spence DPS**, Hotchkiss J, Williams CSD, *et al.* Tuberculosis and poverty. *BMJ* 1993;**307**:759–61.



Abstract P223.

P224 INCIDENCE OF TUBERCULOSIS IN THE GREENWICH BOROUGH OF LONDON FROM 1993 TO 2005: AN OVERVIEW

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Background: We experienced a rise in tuberculosis (TB) notifications in Greenwich in 1998, of which we attempted to examine the epidemiology.
Design: Clinical and demographic data on all patients diagnosed with TB were obtained from the in-patient records, the microbiology department, chest clinic/radiology records and notifications made to the Director of Public health. Co-infection with HIV in adult patients with TB was estimated from the chest clinic data.
Results: There were a total of 874 notifications, of which 175 notifications (20.6/100 000/year) were in the period 1993–1996, compared to 699 (47.41/100 000/year) for 1998–2005.The notification rate for the white population rose from 5/100 000 to 12.9/100 000 (mean 11.93, SD 2.96). However, the rates are higher for patients of Asian (168.7 to 329.89/100 000 mean 241.91, SD 50.89), Black African (98.02 to 278.42/100 000 mean 174.13, SD 63.11) and other Black (10 to 118.43/100 000, mean 55.41, SD 40.14) origins. 64.51% of all cases were culture positive for Mycobacterium tuberculosis of which 3.2% were multi-drug resistant. In both periods the age distribution, sex ratio, and principal sites involved were unchanged.

Abstract P222

		London Borough of Hackney residents						
Year	NE London UK born TB	Adults	Adult Travel	Risk factors/ adult	Child	Child travel	Contact (all patients)	Outbreak related (all patients)
1998	96	21	11	0.72	0	0	0	1
1999	98	13	3	0.62	1	1	0	0
2000	82	23	10	0.48	1	0	0	1
2001	87	19	8	0.63	0	0	0	4
2002	161	24	6	0.71	8	5	3	7
2003	191	27	4	1.52	5	1	2	9
2004	168	30	5	1.67	6	2	4	11
2005	186	19	7	1.74	7	4	4	4
Total (mean)	1069	176	54	(0.98)	28	13	13	37

Three of the most deprived wards are responsible for most of the rise in TB. The estimated HIV co-infection rose from 5.6% to 7.58%. The principal sites of disease in each ethnic group was also determined.
Discussion: Notification rates were particularly high in certain ethnic groups. However; the ethnic distribution seems dynamic with a disproportionate increase in TB rates in certain ethnic groups. The geographical distribution seems uneven with the most deprived areas having higher rates. The study could not determine whether this was due to new infection, reactivation or infected immigrants gravitating to these areas. TB in patients co-infected with HIV makes an increasingly important contribution. A successful population-based TB control strategy shall need to accommodate this geographical and ethnic variability and adapt accordingly.

An earlier part of this study was previously presented at the European Society of Mycobacteriology annual meeting, July 2006.

P225 AN AUDIT OF PATIENTS WHO DIED WHILE ON TREATMENT FOR TUBERCULOSIS

A. S. Collett, E. Togun, M. Ogedengbe, A. Nundloll, V. A. L. Graham, R. D. Barker. *Kings College Hospital, Camberwell, London SE5 9PJ, UK*

Background: Tuberculosis (TB) notifications are increasing in the UK particularly in London. Published mortality varies from 5% (USA) to 29% (Afghanistan). At Kings College Hospital 5.8% of tuberculosis patients die. We wanted to make a quantitative estimate of risk factors for death and a qualitative look for possible preventable causes.
Methods: Outcomes are reported for all patients who started treatment for TB between January 2000 and June 2005. Case records for all patients who died while on treatment for TB were reviewed. Information was retrieved from our TB clinical database, the paper notes and the hospitals electronic patient record. We looked quantitatively at age, sex, drug resistance, inpatient or outpatient at diagnosis, HIV status and qualitatively at hepatitis, treatment interruption and delayed diagnosis in hospital as risk factors for death.
Results: Thirty five (6.5%) of 611 patients died. These were subclassified as shown in the table. In univariate analyses men were more likely to die than women odds ratio (2.2 95% CI 1.0 to 4.9). Those who died were older (mean 57 v 34 years p = 0.000). Mortality in the 8th decade was 35% and 40% in the 9th decade. Patients diagnosed with TB as an in-patient were much more likely to die (OR 28.5, 95% CI 6.7 to 119.9) than those diagnosed as out patients. Sixteen (46%) of the patients who died had HIV tests, (compared to an overall offering rate of 93% and testing rate of 68%). Death was not associated with being HIV positive (OR 2.1 95% CI 0.7 to 5.8). Of the 35 patients who died, only 3 had drug resistance. Death was not associated with drug resistance (OR 0.7 CI 0.2 to 2.5). One patient, with hepatitis C related cirrhosis, died with a severe hepatitis. Treatment interruptions and delayed diagnosis in hospital did not appear to be significant factors. In multivariate analyses only age and being an in-patient at diagnosis significantly predicted death.
Conclusion: Dying, with tuberculosis as the sole cause, is quite uncommon in our hospital. Drug resistance, drug induced hepatitis and delayed diagnosis in hospital did not appear to contribute significantly to mortality. Few patients diagnosed in clinic die but elderly TB patients, with multiple comorbidities, are at high risk of dying.

Abstract P225

Outcome	Number (total 35)
Died - TB cause	7 (1.1%)
Died - TB contributed	12 (2.0%)
Died - TB incidental	13 (2.1%)
Died - TB influence unknown	3 (0.5%)

P226 CHARACTERISTICS OF PATIENTS DYING WITH TUBERCULOSIS

J. A. Fitton, I. Patel, H. J. Milburn. *Department of Respiratory Medicine, Guy's & St Thomas' Foundation Trust, London, UK*

Patients reported to the London TB Register are classified as dying with tuberculosis (TB) if they die within 1 year of the start of treatment. We examined the medical records of patients from Guy's and St Thomas' Hospitals (GSTT) who died with TB from 2002 to 2005 in order to describe their characteristics.

19 patients died with TB at GSTT during this period. 654 patients were treated during the same period, giving a case mortality rate of 2.9%. (National mortality rate 7.9% in 2002.) The characteristics of this group are summarised in the table. Numbers in brackets represent percentages of the whole group.

A subcategory of 13 patients (68.4) for whom TB caused or contributed to death were further analysed; their characteristics were broadly similar except for age (median 48 years), suggesting co-morbid conditions caused death in older patients.
Conclusions: Patients dying with TB tended to be older and most had pulmonary TB. No particular ethnic group predominated and most immigrants to the UK had been in the country for many years. The majority had co-morbidity, most frequently respiratory conditions. Risk factors such as social deprivation, HIV infection and non-compliance occurred in only a minority, several of whom demonstrated more than one such risk. A sizeable minority were not managed primarily by a chest physician although all were eventually referred.

Abstract P226

Gender	Male 13 (68.4); female 6 (31.6)
Age	Range 17–86 years; median 61 years
Ethnicity	Indian, Bangladeshi, Pakistani 6 (31.6); Black African 5 (26.3); White British 4 (21.1); Black Caribbean 2 (10.5); other 2 (10.5)
Time spent in UK	12 patients (63.2) were immigrants to UK. Of these, time ranged from 0.1 to 47 years, median 14 years
Previous TB?	4 patients (21.1) previously diagnosed with TB
Social factors	Unemployed 3 (15.8); homeless 3 (15.8); alcoholics 3 (15.8); 4 not recorded
Other risk factors	HIV-positive 4 (21.1); drug-resistant TB 1 (5.3); non-compliance 5 (26.3)
Comorbid conditions	Primary conditions were respiratory 6 (31.6), cardiovascular 3 (15.8), renal 2 (10.5), GI 2 (10.5), HIV 2 (10.5), haematological malignancy 2 (10.5)
n = 17 (89.5%)	
Site of TB	Pulmonary 16 (84.2); extra-pulmonary 3 (15.8)
Primary doctor	11 (57.9) managed primarily by chest physician
Duration of symptoms	Range 4–730 days; median 44 days
Time on treatment	Range 4–450 days; median 23 days

P227 REVIEW OF ADVERSE EFFECTS AND TREATMENT ALTERATIONS IN 100 PATIENTS TREATED WITH ANTI-TUBERCULOSIS MEDICATION

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Background: Anti-tuberculosis (anti-TB) therapy is associated with abnormalities in liver function tests (LFTs) in 10–25% of cases and clinical hepatitis in 3–5%.
Aim: To review the incidence of abnormal LFTs and other complications leading to treatment alterations.
Methods: Retrospective case note review of 100 patients on anti-TB therapy at Nottingham University Hospitals between January 2005 and March 2006.
Results: Of 100 patients, 60% of the 86 adults were men. Standard quadruple chemotherapy initiated in 87 and chemoprophylaxis in 13, of which 9 (62%) were children. 26 patients developed complications. 18 had abnormal LFTs (6 drug induced hepatitis (DIH), 2 rifampicin hypersensitivity and abnormal LFTs, 10 rise in LFTs but stable with

regular monitoring), 5 developed a rash, 1 joint pain, 1 drug fever, and 1 rifampicin hypersensitivity. Treatment alterations occurred in 18 patients; 3 were short term interruptions due to nausea/vomiting/rash followed by successful full treatment within a week, treatment stopped in 3 (1 admitted to ITU with cavernous sinus granuloma, bilateral empyema and transferred elsewhere, 1 diagnosed malignancy, 1 empirical therapy for presumed tuberculosis but treatment stopped as she developed rash and joint pain). Sequential re-introduction of therapy occurred in 12. Of these 2 (17%) were unsuccessful: 1 treatment started as a prerequisite for anti-TNF therapy but as unable to tolerate rifampicin the patient deferred anti-TNF therapy and TB medication, 1 developed DIH while on chemoprophylaxis and treatment withdrawn.
Conclusion: Complications due to anti-TB therapy occurred in 26% of patients on full treatment and 23% on chemoprophylaxis. A relatively high incidence (6%) of hepatotoxicity noted. Overall, treatment withdrawn in 5 (5%) of patients.

P228 PATIENTS LOST TO TREATMENT FOR TUBERCULOSIS

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Introduction: Treatment outcomes are routinely reported in England and Wales, but there are no reporting structures to describe factors that may contribute to a patient being lost to follow up.
Methods: The NE London TB Network receives outcome data from all boroughs within the sector. The cases found to be lost to follow up for the period 2003–05 were identified from the treatment outcome returns. A review of the medical and nursing notes provided information on lifestyle and treatment variables. These patients were compared to the overall caseload for the same period.
Results: Lost to follow up patients (n = 54) can be placed into two groups: those who cannot be found after becoming lost to follow up (n = 26) and those that would regulalrly reconnect and disconnect from the TB service after becoming lost to follow up (n = 28). The percentage of patients with drug misuse, alcohol misuse, housing problems, prison history and umemployment were higher in the lost to folow up group. Registration with a GP was more common in the overall caseload.
Conclusions: Lost to follow up TB patients are more likely to have social factors likely to affect their ability to comply with therapy, be unemployed, and have worse access to primary care services. A thorough needs assessment, when the patient with tuberculosis is first identified may improve adherence.
This study was funded by the NE London TB Network.

P229 TREATMENT SUCCESS IN A COHORT OF PATIENTS WITH TUBERCULOSIS FROM AN INNER LONDON HOSPITAL. WHAT HAPPENED TO THE PATIENTS WHO TRANSFERRED OUT?

A. S. Collett, J. M. Garland, E. Togun, A. Nundloll, M. Ogedengbe, R. D. Barker. *King's College Hospital, Camberwell, London SE5 9PJ, UK*

Background: The increased incidence of tuberculosis in London has raised concerns about poor treatment outcomes as a possible cause. The London Regional Office of the National Health Service has set a target treatment completion rate of 90% for tuberculosis, whilst the millennium development goals (MDG) target for successful treatment is 85%. The MDG target is derived from a calculation that suggests that a case detection rate of 70% and successful treatment rate of 85% will lead to a decrease in incidence and prevalence of tuberculosis (Dye, *et al. JAMA* 2005). At our hospital we thought our 89.5% successful treatment outcomes was satisfactory, but we were concerned that patients in the ''transferred out'' category might be concealing adverse outcomes. We decided to obtain more detailed outcomes for our patients who had transferred out and to combine them with existing data to obtain a true measure of treatment success.
Methods: Outcomes are reported for all patients who started treatment for TB between January 2000 and June 2005 at King's College Hospital. Patients were identified from our TB database, which includes clinical notes from the medical team and the TB nurses. Outcomes for patients, initially designated as ''transferred out'', were obtained from by contacting their destination TB units.
Results: Outcomes were obtained for 34 of 48 patients initially designated as transferred out. The remaining 14 had left the UK.
Conclusion: Detailed analysis of transfers out increased the lost to follow up rate by 2.2% and increased treatment completion by 2.9%. This analysis did not alter the relationship of our successful treatment outcomes to MDG targets, which we met. We are still missing the London target by a small margin.

Abstract P229

	Outcomes from original data	Outcomes after detailed analysis of ''transfers out''
Complete	501 82% (CI 79 to 85)	519 84.9% (CI 82.1 to 87.8)
Transferred out	48 7.9% (CI 5.7 to 10)	14 2.3% (CI 1.1 to 3.5)
Death	35 5.7% (CI 3.9 to 7.6)	36 5.9% (CI 4 to 7.8)
Lost to follow up	24 3.9% (CI 2.4 to 5.5)	37 6.1% (CI 4.2 to 7.9)
Still on treatment	3 0.5% (CI −0.1 to 1)	3 0.5% (CI −0.1 to 1)
Treatment success*	89.5% (CI 86.9 to 92)	87.7% (CI 85 to 90.3)

*(complete/(complete + death + lost to follow up))*100%.

P230 CHARACTERISTICS OF PATIENTS NON-COMPLIANT WITH TUBERCULOSIS THERAPY IN LONDON

I. S. Patel, J. A. Fitton, H. J. Milburn. *Department of Respiratory Medicine, Guy's & St Thomas' Foundation Trust, London, UK*

A proportion of patients with tuberculosis (TB) fail to complete the appropriate course of treatment because of poor compliance with medication or inconsistent attendance at hospital appointments. This difficult group is a cause for concern as they run the risk of disease relapse and increased drug resistance. We assessed the rates of non-compliance at Guy's and St Thomas' Hospitals (GSTT) from 2002–05 and compared the characteristics of these patients with our previously presented data from 1999–2000.

Abstract P228

	Patients lost to follow up			
	Patients with no contact with TB service after lost to follow up (n = 26)	Patients who persistently reconnect and disconnect with TB services after lost to follow up outcome (n = 28)	Total lost to follow up cases (n = 54)	TB caseload 2003–05 (n = 1645)
GP registration	50%	40%	48%	59%
Drug misuse	0%	28%	15%	3%
Alcohol misuse	15%	25%	20%	5%
Mental health problems	0%	18%	9%	Unavailable
Prison history	4%	18%	11%	3%
Unemployed	38%	57%	48%	25%
Directly observed therapy	25%	25%	28%	5%
Housing problems	8%	14%	11%	5%
Part of Isoniazid resistant cohort	4%	25%	15%	2%

The total number of patients with TB who were lost to follow up or non-compliant at GSTT from 2002–05 was 14/654 treated in total (2.14%). This is an improvement from 14/169 or 8.3% in 1999–2000.

The characteristics of these patients were as follows: 8 (57%) males, 6 (43%) females; age range 17–49 (median 29) years with 79% aged from 20–39; 9 (64%) Black African of whom 4 were Somali; 3 (21%) White British; 2 (15%) of other ethnicity. Only 3 (21%) were refugees with the majority having resident status in the UK. However for 8 patients (57%) English was not the first language and was poor. Social deprivation, and drug and alcohol dependence were a prominent feature of these patients as 7/14 (50%) were unemployed, 6/14 (43%) were homeless, 4/14 (28%) were alcoholics, 2/14 (14%) had a mental illness and 1/14 (7%) was an intravenous drug user. 2/14 (14%) were HIV positive. 8/14 (57%) patients had pulmonary TB and 4/14 (28%) patients received directly observed therapy (DOT).

Eight patients (57%) were originally managed by non-chest physicians or encountered delay in referral to the TB team. The median time on treatment before default was 83 days, or 36% of the appropriate duration of therapy for their disease and organism sensitivity. None encountered serious side effects, which might have affected compliance.

In conclusion numbers of non-compliant TB patients at GSTT have fallen since 1999 on a background of increasing numbers of cases. Young black African men with poor English remain the most vulnerable group in this context, as shown in our previous audit. Patients tend to become non-compliant with TB therapy after completing approximately 36% of their time on treatment, which, we postulate, may correspond with improvement in symptoms. TB teams need to address this by improving communication and focusing on these patients at this critical time. Delay in referral to the TB team may prevent the early establishment of the rapport needed to facilitate this process.