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Age period cohort analysis of mortality due to lobar and pneumococcal pneumonia in the 20th century

G MARKS, P BURNEY *Department of Public Health Medicine, UMDS, London* From 1938 to 1939 mortality due to lobar pneumonia fell by 32%. This was attributed to the commencement of widespread use of sulphonamides during 1939. However, this dramatic short-term reduction is small compared to the 100-fold reduction in mortality from this condition in young adults during the course of this century. The decline in mortality from lobar and pneumococcal pneumonia has continued well beyond the time when the use of antibiotics became widespread. We examined the role of cohort factors in this decline using the OPCS' historical mortality data files. Age and sex specific death rates for lobar pneumonia (ICDs 2 to 7, 1911 to 1967) and pneumococcal pneumonia (ICDs 8 and 9, 1968 to 1990) were plotted by year of death (period) and year of birth (cohort) for subjects aged 15 to 64 years. Age-period-cohort analysis using iteratively reweighted least squares regression showed that there were significant independent risks attributable to age, period and cohort effects (all $p < 0{\cdot}0001$). The period-by-age plots showed a decreasing risk of death over time in all age groups, with higher death rates and a slower rate of decline in the older age groups. The cohort-by-age plot, however, showed that this apparent interaction between age and period may represent a cohort effect. Plots of mortality rate by year of birth for each age group all declined steeply and were superimposed on each other. Since age at death, period of death and cohort of birth are linearly related, analysis cannot distinguish an effect due to an age-period interaction from a simple cohort effect, however, the latter is a more parsimonious explanation. The presence of a cohort effect implies that developmental or environmental factors which influence the risk of acquiring or succumbing to lobar or pneumococcal pneumonia have played an important part in reducing mortality from this disease. [Data for this analysis were provided by OPCS.]

Reliability of the sputum Gram film

CM PARRY, C CONNELL, J CORKILL, R CUNNINGHAM, E RIDGWAY, A RIGBY, R WHITE *Department of Medical Microbiology, Royal Liverpool University Hospital, Liverpool* A Gram film of expectorated sputum may provide a clue to the bacterial aetiology of a lower respiratory tract infection, although contamination with upper respiratory tract material can make interpretation difficult. The criteria for evaluating specimens include estimating numbers of neutrophils (N) or squamous epithelial cells (SEC) per low power field and noting the association of a particular organism, such as Gram positive diplococci (GDPC) or Gram negative coccobacilli (GNCB), with a purulent area of the film. To assess the reliability with which these features are recorded, Gram films were prepared from 70 routine sputum samples. The films were coded and scored by five microbiologists (experience range 6–23 years) according to numbers of N (<>25/LPF), SEC (<>10/LPF), GPDC or GNCB (<>15/HPF) and whether the Gram film suggested infection (purulence with an associated organism—INF). The films were randomly recoded and read again by each rater. Intrarater and interrater agreement was assessed by the kappa statistic with a kappa value >0·6 suggesting reasonable agreement.

	Intrarater (rater no)					*Interrater*
	1	*2*	*3*	*4*	*5*	*All*
N	0·47	0·47	0·63	0·56	0·51	0·32
SEC	0·40	0·53	0·74	0·45	0·85	0·49
GPDC	0·64	0·37	0·60	0·72	0·69	0·66
GNCB	0·47	0·34	0·36	0·44	0·49	0·55
INF	0·89	0·74	0·46	0·60	0·61	0·69

The association of purulence with a predominant organism and the scoring of significant numbers of GPDC were the most reliably recorded features of the sputum Gram film.

C-reactive protein in pneumonia

RP SMITH, BJ LIPWORTH *Departments of Respiratory Medicine, King's Cross Hospital and Clinical Pharmacology, Ninewells Hospital, Dundee* C-reactive protein (CRP) is an acute phase protein synthesised by the liver in response to a number of stimuli including infection and inflammation. The purpose of the present study was to evaluate whether CRP levels are a useful marker of parenchymal lung sepsis in patients with pneumonia. Serum concentrations of CRP were measured on day 1 of admission in 40 patients with uncomplicated pneumonia (age 64(3) years) and in 20 patients with an infective exacerbation of chronic obstructive pulmonary disease (COPD) without pneumonia (69 (2) years). Pneumonia patients had a higher temperature (37·7 (0·2) *v* 36·6 (0·1)°C) and WBC count (13·7 (1·1) *v* 10·7 (0·6) × 10^9/l). CRP concentrations were appreciably raised to above 70 mg/l in all cases of pneumonia and were above 100 mg/l in all but two cases. In COPD there were no cases with a CRP above 70 mg/l, and only seven out of 20 had concentrations above the normal range (<10 mg/l). Mean (SEM), range, lower/upper quartiles for CRP were: (pneumonia) 217(16), 73–494, 130/275; (COPD) 18 (3), 10–61, 10/18. A CRP above 70 mg/l in pneumonia on day 1 occurred in association with a WCC <12 in 45% of cases, and with a temperature <37·0°C in 32%. Measurements of CRP were repeated after 3–7 days of antibiotic treatment in 21 cases of pneumonia: (pre) 213 (21), 104–494, 138/270; (post) 31 (5), 10–96, 17/47 ($p < 0{\cdot}00001$); 95% CI for difference 141–221. Thus a CRP >100 mg/l will clearly separate patients with parenchymal lung infection from those with endobronchial infection. There was a pronounced fall in CRP in response to treatment of pneumonia. This suggests that CRP may be a useful adjunctive test in the management of patients with pneumonia.

The value of microbiological investigation of community acquired pneumonia in relation to disease severity

N FRENCH, C PARRY, R WONG, CRK HIND *Department of Medicine and Microbiology, Royal Liverpool University Hospital, Liverpool* To examine the value of routine microbiological investigations of community acquired pneumonia (CAP) in relation to disease severity, all patients admitted to the RLUH between 1 January 1992 and 30 April 1992 with CAP were identified and their notes reviewed. The recording and presence of severity markers (respiratory rate >30, diastolic BP <60, urea >7 mmol/l, confusion, Po_2 <8 kPa, extremes of white cell count, age >60, albumin <30 g/dl) and results of microbiology investigations were related to antiobiotic treatment and clinical outcome. 111 patients were identified, median age 72

(range 17–92) years, 54% men. Six or more markers of severity were recorded in 102 (92%) of patients. 15/61 (25%) patients with one or more of the first three markers of severe disease died or required ventilation compared with 1/50 (2%) who did not have those markers ($p < 0.01$). The number of microbiological investigations and their yield was not related to disease severity, except that pneumococcal bacteraemia was commoner in those with severe disease. An aetiology was established in 31 (28%) of patients. The empirical antibiotics chosen were confirmed as appropriate in 22 (20%). Antibiotic treatment was changed as a result of the microbiological result in only one patient with a penicillin resistant *Streptococcus pneumoniae*. Confirmation of the correct antibiotic choice is particularly important in severe pneumonia. Intensive microbiological investigations should concentrate on patients with markers of severe CAP.

Factors other than severity of pneumonia associated with increased mortality from lower respiratory tract infection

R CHAN, L HEMERYCK, J FEELY, L CLANCY *Departments of Therapeutics and Respiratory Medicine, St James's Hospital, Dublin* We prospectively studied patients with a clinical diagnosis of community acquired lower respiratory tract infections (LRTI) requiring hospital admission over a one year period. Patients were classified as severe and excluded if they required admission into the intensive care unit, ionotropic support, respiratory stimulants, or exhibited signs of septicaemia. Details of age, sex, previous exposure to antibiotics, vital signs, basic laboratory, microbiological investigations and chest *x* ray films were recorded during admission. Each patient was followed up until discharge or death. We obtained 542 patients, mean age 64·3 (range 14–94) years, of which 52·3% were males, 83% smokers, and 34% were already on an antibiotic on admission. Chest radiological changes consistent with acute infection were present in 206 (42·2%) patients. Sputum and blood cultures were obtained from 301 (55·7%) and 137 (25·3%) patients, respectively. At least one pathogen was isolated in 31·2% and 8·7% of the respective samples; *Haemophilus influenzae* (33%), *Streptococcus pneumoniae* (28%), *Pseudomonas aeruginosa* (10%), and *Moraxella catharrhalis* (9%). The average duration of stay in hospital was 8·78 (range one to 52) days and 34 (6·3%) patients died during their hospital stay. Factors associated with increased mortality were age >60 years ($\chi^2 = 7.53$, $p < 0.01$), urea >7mmol/l ($\chi^2 = 9.472$, $p < 0.01$) and chest *x* ray films consistent with cardiac failure ($\chi^2 = 20.102$, $p < 0.01$). Acute infective changes on chest radiographs and culture positivity were not statistically significant factors. Our figures suggest that the British Thoracic Society and the Public Health Laboratory Service findings (*Q J Med* 1987;**62**:195–220) on severity can identify further high risk patients who may benefit from special medical attention in LRTI. [This work was supported by the Health Research Board.]

Pneumonia after stroke: a prospective study

DS RENWICK, DG SMITHARD, R ENGLAND, PA O'NEILL *Departments of Medicine for the Elderly, University Hospital of South Manchester and Manchester Royal Infirmary* Pneumonia is a common complication of acute stroke: a recent retrospective survey reported an incidence of 33% (Walsh *et al. Thorax* 1992;**47**:874). Patients with swallowing problems secondary to stroke may be especially at risk. We report a prospective study of the incidence of lower respiratory tract infection (LRTI) and swallowing problems in patients with acute stroke. 121 consecutive patients with acute stroke were included (median age 79, range 40–93 years, 69 women). All patients were examined within 24 hours of stroke onset, and then monitored for evidence of infection (pyrexia, inspiratory crackles, tachycardia, or tachypnoea). Chest *x* ray films were taken on days 1 and 7. Swallowing was assessed clinically on admission, and by videofluoroscopy (VF) before day 4 in all patients except those with a reduced conscious level. Results were analysed by χ^2 tables. 40 patients (33·1%) developed LRTI by day 7. Of these, 23 underwent VF: six (15%) had aspiration of barium, seven (17·5%) had penetration of barium into the larynx, and 10 (25%) had no evidence of aspiration (difference NS). Only three patients developed LRTI between days 7 and 28; of these, two had aspiration on VF. Mortality was higher in patients developing LRTI (16/40, 40%) than in those without infection (17/81, 21%; NS). Mortality was also higher in patients with VF evidence of aspiration or laryngeal penetration (17·1%) than in those with normal VF (8·8%; NS). Our data confirm the high incidence of LRTI in acute stroke, but do not suggest that this is a result of aspiration.

Is penicillin the drug of choice in human immunodeficiency virus (HIV) positive patients with community acquired lobar pneumonia?

AA JEFFREY, D KESSEL, NM FOLEY, RF MILLER *Department of Medicine, UCLMS, and Department of Imaging, Middlesex Hospital, London* The British Thoracic Society recently updated their recommendations for treatment of pneumonia (*Br J Hosp Med* 1993;**49**:346–50). It is suggested that lobar pneumonia is best treated with penicillin. In this study we have questioned whether these guidelines apply to patients immunosuppressed by HIV infection. 33 HIV positive patients (all homosexual men) aged 23–58 years (21 smokers, two ex-smokers) presented with radiographic lobar pneumonia (confirmed by DK) between 1987 and 1993. Fever was present in 21 patients (>38°C in 14) and 11 had purulent sputum expectoration. A bacteriological diagnosis was made in 17 patients and revealed *Streptococcus pneumoniae* in eight (including two with copathogens), *Pneumocystis carinii* in five (one also had *Staphylococcus aureus*, one *Enterobacter cloacae*, and another *Salmonella typhimurium*), *S aureus* in two (one also had group A *Streptococcus*), *Pseudomonas aeruginosa* in two (one had coinfection with *Fusobacterium nucleatum* and *Enterobacter cloacae*). Ten of these 17 patients were bacteraemic (including six patients with *Str pneumoniae*). Antibiotic sensitivity testing showed that in seven of the 15 episodes of bacterial infection (excluding the two pure *P carinii* infections) there were organisms resistant to penicillin (all *Str pneumoniae* isolates were sensitive). All those with *P carinii* had longer histories (> seven days) and normal peripheral blood white cell counts, otherwise no features were associated with a particular organism. Three patients died, six developed pleural effusion, three pulmonary cavitation, and two had pulmonary abscesses. In conclusion a wide variety of organisms produce lobar pneumonia in HIV positive patients. Whereas penicillin should be used, we suggest that additional broad spectrum antibiotics are also given. Patients should be rigorously investigated to identify a causative organism.

Activity of single agent gemcitabine in non-small cell lung cancer

N THATCHER, H ANDERSON, M RANSON, B LUND, F BACH, H HANSEN *Manchester Lung Tumour Study Group, Wythenshawe Hospital, Manchester, UK; Rigshospitalet, Copenhagen, Denmark; Herlev Hospital, Copenhagen, Denmark* Gemcitabine is a pyrimidine antimetabolite with proved antitumour activity. Eighty two patients with unresectable stage IIIa-IV non-small cell lung cancer received weekly gemcitabine by 30 minute infusion for three weeks, followed by a week of rest. Courses of treatment were repeated every 28 days. The first 54 patients were treated at a starting dose of 800 mg/m², subsequent patients at 1000 mg/m². Dose escalation was permitted after course 1 if WHO toxicity was $\leqslant 1$. Patients were evaluable for response when they had received two courses. Independently validated partial responses were observed in 16/68 response evaluable patients (24%, CI 14–35%), with a median duration of seven months. Overall median survival was seven months. Gemcitabine was well tolerated, WHO grade 3 and 4 toxicities by patient were: anaemia 5%, thrombocytopenia 1%, leucopenia 7%, neutropenia 22% (no WHO 3 and 4 infections), transaminases 12%. Two patients developed transient WHO rises in serum creatinine. Two patients developed acute renal failure associated with microangiopathic haemolytic anaemia, four and six weeks after their last dose of gemcitabine. This was of uncertain aetiology. There was no WHO grade 4 symptomatic toxicity, WHO grade 3 toxicity was: vomiting (easily controlled without the use of 5HT3 antagonist antiemetics) in 38%, alopecia 1%, other toxicities were very mild; flu like symptoms in 44%, (WHO 3 fever in 1%), and ankle oedema not associated with cardiac failure in 40%, transient lethargy in 38%, and dyspnoea in 17%. Gemcitabine is an active new agent in the treatment of non-small cell lung cancer and the favourable profile is such that it warrants further investigation in other malignancies and in combination with other agents.

Late BCNU lung fibrosis: severity and survival are influenced by age at treatment

BR O'DRISCOLL, S KALRA, HR GATTAMANENI, AA WOODCOCK *Wythenshawe and Christie Hospitals, Manchester* We have previously reported that 35% of patients treated with BCNU (6 of 17) who survived childhood brain tumours had died of pulmonary fibrosis between two and 13 years after treatment (*N Engl J Med*

1990;323:378–82). Of eight patients studied in 1989 (13–17 years after treatment), all had physiological and biopsy or radiological evidence of pulmonary fibrosis. Between 1989 and 1992, two further patients had died of pulmonary fibrosis giving an overall mortality of 47%. Of the eight patients who died of pulmonary fibrosis, the median age at treatment was 2·5 years whereas the nine long term survivors had a median age at treatment of 10 years. All five patients treated below the age of 5 years died of lung fibrosis. Analysis by the standard survival curve method indicated that patients treated at age $\leqslant 6$ years were more likely to die than those treated at age $\geqslant 7$ years ($p = 0·03$). Of the nine survivors, seven were observed over a further three years. Six had a gradual decline in FVC from 2·12 litres to 1·98 litres (50% predicted to 47% predicted) and TLC fell from 60% predicted to 54% predicted. One patient (age 16 at treatment) has a stable FVC at 72% of the predicted value. We conclude that the severity of BCNU lung fibrosis is related to age at treatment. All patients treated in infancy have died of pulmonary fibrosis. The survivors all have pulmonary fibrosis. This is progressing slowly in all cases except one patient treated at age 16. Therefore adult patients are probably at less risk of pulmonary fibrosis.

A review of the process of management of lung cancer

J PREWITT, A WILCOCK, R HUBBARD, J MACFARLANE, J BRITTON *Respiratory Medicine, City Hospital, Nottingham* Between 1 November 1991 and 31 October 1992, 379 cases of lung cancer were diagnosed histologically in our hospital. 176 (121 males) Nottingham residents referred directly to the hospital were studied. Histological cancer types included squamous (62), large cell (42), small cell (37), adenocarcinoma (25), other/unspecified (10). 84 were referred to respiratory physicians (RPs), 33 direct to thoracic surgeons (TSs), and 59 to other consultants (OCs), including 21 to geriatricians. Bronchoscopy was performed a median of three days after referral to RPs, eight days for TSs and 10 days for OCs. Other investigations performed included (% cases for RPs; TSs; OCs): fine needle aspirates (FNAs) (19%, 21%, 13%), pleural biopsy (19%; 21%; 19%), sputum cytology (13%, 0%, 29%). FNAs were arranged a median of 20 days after referral for RPs, 12 days for TSs, and 72 days for OCs. 49% and 45% of cases seen by RPs and TSs respectively were discussed with an oncologist a median of 14 days and 21 days after referral compared with 27% of those seen by OCs, a median of 50 days after referral. 13% of cases seen by both RPs and OCs were referred to TSs on a median of 22 days and 55 days after referral. We conclude that a significant proportion of lung cancer cases are seen initially by non-respiratory specialists with whom investigations and specialist referral occur more slowly.

Palliative care and lung cancer

SA GOMM, K FORBES, GD CORCORAN *St Gemma's Hospice and St James's Hospital, Leeds* Lung cancer has a poor prognosis and is rarely curable; hence the role of symptom control is paramount. A study was undertaken to assess the frequency and type of symptoms, palliative treatment undertaken, and prognostic influence of symptoms on survival for 80 patients with lung cancer admitted to a hospice over a period of eight months. There were 42 male and 38 female patients with a median age of 70, range 36–89 years. Tumour type: 14 small cell lung cancer, 54 non-small cell lung cancer, and 12 unknown histology. Seven patients (9%) were alive at the end of the study. 73 patients were admitted for terminal care of whom 12 had two or more previous admissions. The overall median number of symptoms was 10 (range 5–15). The commonest symptoms were poor mobility 83%, fatigue 82%, dyspnoea 78%, pain 75%, and anorexia 74%. Analysis of symptoms according to performance status score, Eastern Co-operative Oncology Group (ECOG) scale from 0 (no change from baseline) to 4 (completely unable to self care and bed bound) showed no significant relation, although the median number of symptoms (10) was higher in patients (ECOG score 3 and 4) compared with seven in patients (ECOG score 2). Commonest forms of symptomatic treatment were strong opiates 82%, benzodiazepines 76%, aperients 73%, antibiotics 64%, corticosteroids 54%, bronchodilators 44%, and antifungal compounds 43%. Oxygen was used infrequently (11%). Adjuvant pain controls were non-steroidals 26%, anticonvulsants 13%, TCNS 9%, nerve blocks 5%, and radiotherapy 5%. In the terminal phase, drugs were given by syringe driver in 47/80 patients (59%) using diamorphine in 47, midazolam in 35 (44%) and hyoscine in 26 patients (33%), respectively. Overall median survival was 17 days (range 1–72), which decreased with worsening of respiratory score (rs; MRC Lung Cancer Working Party 1979). 19 patients without dyspnoea (rs = 1–2), median survival 22 days; 20 patients (rs = 5), median survival 13 days. 14 patients died within 72 hours of whom 13 had an rs of 3–5. Symptoms are prognostically important in cancer; this study supports the requirement of accurate assessment of symptoms for treatment needs and outcome.

Audit of the work of a hospital based Macmillan nurse with an interest in lung cancer

M CAMPBELL, A WILCOCK, J MACFARLANE, R CORCORAN *Respiratory Medicine and Hayward House Macmillan Palliative Care Unit, City Hospital, Nottingham* In early 1992 we appointed a full time hospital based Macmillan nurse specialist (MN) with a responsibility primarily for patients with intrathoracic cancer. We review progress here over the year. 303 patients have been seen (243 lung cancer, 60 oesophageal/GI cancer); 81 as outpatients (OPs), 222 as inpatients/day cases (IPs); the numbers having nearly doubled between the first and last three month periods. During 162 lung cancer IP stays, patients were seen for psychological support (56%—including relatives), pain/symptom control (37%), and 7% for advice on discharge/services. Action taken included referral to community MNs in 63, to district nurses (DNs) in 22, hospice day care (DC) in 13, and social services (SS) in 3. Transfer was suggested/arranged for palliative radiotherapy in 11 and to two local hospices in 11. 26 deaths (16% of admission episodes) occurred in hospital. The MN took 33 teaching sessions for medical/nursing staff and frequent ward based informal discussions and accompanied doctors breaking bad news. For the 81 OPs, there were 146 contacts within a special combined lung oncology clinic during 41 clinic attendances by the MN. 46% patients were referred on to community MNs, DNs, SSs and hospice DC. 170 follow up phone calls were received from OPs (37), relatives (54), or made to patients/relatives (41) and various community services (38). OPs most requested psychological/physical support, relatives also wanted further information about diagnosis/prognosis. We conclude that the first year has uncovered an enormous need and work load for an MN with an interest in thoracic cancer in a general hospital.

Dietary sodium intake and the risk of atopy and hyperreactivity in a general population sample

J BRITTON, I PAVORD, K RICHARDS, A KNOX, A WISNIEWSKI, I WAHEDNA, S WEISS, A TATTERSFIELD *Respiratory Medicine Unit, City Hospital, Nottingham, and Harvard Medical School, Boston, USA* We have tested the hypothesis that dietary sodium intake is a risk factor for atopy and airway hyperreactivity in a cross sectional study of a random sample of adults aged 18–70 from an administrative district of Nottingham. Of 2633 subjects who took part in a survey of diet and respiratory symptoms, we were able to estimate dietary sodium intake from a 24 hour urine collection in 1879 subjects, of whom 945 (50%) were female, 370 (20%) were current smokers and 937 (50%) were lifelong non-smokers, and 781 (42%) were defined as atopic on the grounds of at least one positive response to allergen skin prick testing with *D pteronyssinus*, grass pollen, or cat fur. Methacholine PD_{20} FEV_1 was measured in 1702 subjects, of whom 222 (12%) were reactive to 12·25 μmol or less. Geometric mean 24 hour excretion of sodium was higher in men and in ex-smokers and current smokers compared with never-smokers. It also declined significantly with age. 24 hour sodium excretion was also significantly higher among subjects with at least one positive allergen skin test, by 10·8 (95% CI 4·7–17·2) mmol, and after adjustment for confounding by age, sex, smoking and 24 hour creatinine excretion in a multiple logistic regression, the odds of having a positive allergen skin test were increased independently by a ratio of 1·97 (95% CI 1·02–3·8, $p = 0·043$) per $\log_{10}$ unit increase in 24 hour sodium excretion. There was no difference, however, in sodium excretion between hyperreactive and non-reactive subjects, either before or after adjustment for sex, smoking, atopy, or age. Our study does not therefore support previous reports that dietary sodium intake is a risk factor for airway hyperreactivity, but does indicate that dietary sodium may be an important environmental determinant of the expression of atopy in the adult population.

Effect of factors operating in pregnancy and early childhood on the occurrence of wheezing up to age 16

S LEWIS, D RICHARDS, N BUTLER, J BYNNER, J BRITTON *Respiratory Medicine Unit, City Hospital, Nottingham, and Social Statistics Unit, City University, London* Maternal smoking during pregnancy and in early childhood, low birth weight, premature birth, low maternal age, and cessation of breast feeding have all been implicated in the aetiology of wheezing in childhood. These effects, however, have all been shown to be interrelated, and in particular to be confounded by smoking. We have estimated the relative independent importance of these effects on the occurrence of wheezing up to 16 in 15 712 subjects from a British national birth cohort of children born in one week of April 1970, and followed up at ages 5, 10, and 16. Relevant perinatal information was established by the midwife at birth, and at each age mothers provided information on the child's wheezing history and a number of family and social factors, including quantified maternal consumption of cigarettes. We found a cumulative reported prevalence of wheezing up to 16 of over 30%. Univariate comparisons of prevalence revealed an association with maternal smoking, both during pregnancy and in the first five years of childhood, low social index, a birth weight of less than 2000 g, low maternal age, and absence of breast feeding, and showed that social index, birth weight, maternal age, and breast feeding were all significantly associated with maternal smoking, both during and after pregnancy. In a multivariate regression, wheezing was most closely related to maternal smoking in pregnancy in a dose response manner (adjusted OR for 15+ cigarettes/day = 1·330, 95% CI 1·182–1·496), and independently related to low birth weight (adjusted OR for birth weight <2000 g = 1·362, 95% CI 1·001–1·853). After adjustment for maternal smoking in pregnancy and birth weight, there was no additional significant effect of social index, maternal age, or breast feeding, indicating that the univariate associations with these variables arose from confounding by maternal smoking. These data show that maternal smoking in pregnancy and low birth weight are the major independent predictors of childhood wheezing.

Association of virus infections with hospital admissions for asthma: a time trend analysis

S JOHNSTON, M CAMPBELL, P PATTEMORE, S SMITH, G SANDERSON, S MYINT, D TYRRELL, S HOLGATE *University Medicine and Medical Statistics and Computing, Southampton, MRC Common Cold Unit, Salisbury, and Department of Microbiology, University of Leicester* Many asthmatic subjects on admission to hospital give a history of a cold in the days preceding the exacerbation, but attempts to prove an association between virus infections and asthma exacerbations have foundered as a result of inadequate virus identification techniques. Using the polymerase chain reaction to identify rhinovirus (RV) and coronavirus (C), we have recently shown that viruses are the major trigger of asthma-like episodes in susceptible children in the community; however many of the children were not diagnosed as asthmatic, and none of the episodes was of sufficient severity to lead to a hospital admission. Hospital admissions are known to be the major risk factor for asthma mortality and identifying the major cause of such admissions is essential to target future preventive strategies. We have therefore carried out a time trend analysis to examine the possible association between virus infections and hospital admissions for asthma. During a prospective community based study between 1 April 1989 and 31 March 1990, in the Southampton area, 108 children (9–11 years) kept a diary card of daily upper and lower respiratory symptom scores and twice daily peak expiratory flow (PEF) recordings. On reporting an episode (identified by a fall in PEF of <50 l/s or if the child developed upper or lower respiratory symptoms) children were visited at home within 24–48 hours and samples taken for virus identification. The fortnightly virus identification rates were then compared with fortnightly hospital admission rates for asthma (ICD code 493) for the same time period, for the Southampton District Health Authority (SDHA), and the Wessex Region Health Authority (WRHA) for both paediatric and adult age groups. Regression analysis was carried out. A Durbin-Watson test failed to show any significant serial correlation of the residuals. Strong correlations were found between virus identification rates and hospital admission rates for asthma in children, $r = 0{\cdot}55$; $p = 0{\cdot}003$ (SDHA) and $r = 0{\cdot}66$; $p < 0{\cdot}001$ (WRHA) and in adults $r = 0{\cdot}46$; $p = 0{\cdot}013$ (WRHA). This study shows that virus infections (which in this study were 66% rhinovirus and 13% coronavirus) are strongly associated with exacerbations of asthma requiring hospital admission in all age groups, and suggests that efforts be intensified to find an effective treatment for these virus infections.

Role of virus infections in exacerbations in children with recurrent wheeze or cough

S JOHNSTON, P PATTEMORE, S SMITH, G SANDERSON, F LAMPE, L JOSEPHS, S MYINT, D TYRRELL, S HOLGATE *University Medicine, Southampton; MRC Common Cold Unit, Salisbury; Department of Microbiology, University of Leicester* Previous studies in exacerbations of asthma or "wheezy bronchitis" have identified virus infections in only 10–40% of episodes due to difficulties in identifying rhinovirus (RV) and coronavirus (C) infections, which are responsible for causing the most common colds. We conducted a 13 month prospective community based study with standard virological techniques and the polymerase chain reaction (PCR) to identify RV and C infections. 108 children (9–11 years), identified by questionnaire as having wheeze and/or troublesome cough, kept a diary card of daily upper and lower respiratory symptom scores and twice daily peak expiratory flow (PEF) recordings. On reporting an episode (identified by a fall in PEF of >50 l/s or if the child developed upper or lower respiratory symptoms) children were visited at home within 24–48 hours. A capillary blood sample, and a nasal aspirate (NA) were taken, and a convalescent blood sample two weeks later. Viral identification methods were culture of NAs for three passes in Ohio HeLa, Hep2, C16, and MDCK cells; immunofluorescence (IMF) for respiratory syncytial (RS) virus, influenza virus (Flu) type A, parainfluenza virus types 1–3 (PF), and adenoviruses (Ad); ELISA for RS, Flu, PF, Ad and C; and PCR identifying PV (PV = RV and enterovirus) and C RNA in NA samples. Viruses were identified in 228 of all 292 (78%) reported episodes (2·5/child/y). Data were computerised and analysed: PEF episodes were defined as two or more days in which morning PEF was below the 10th centile, preceded by one day above the 10th centile and followed by two days at or above the median; respiratory symptom episodes for cough and/or wheeze (LRT), wheeze (W) and cold (URT) symptoms were defined as two or more days with scores above the median, preceded by one day and followed by two days at or below the median. Viruses were identified in 81% of LRT, 80% of PEF, 81% of W episodes, and in 83% of URT/LRT/PEF episodes: viruses identified were 147 PV (50% of episodes), 38 C (13%), 21 Flu (7%), 21 PF (7%), 12 RS (4%), and five others (2%). Of the 147 PVs 84 were characterised as RV by further tests, it is likely that most of the remainder are RV rather than EV which cultures readily, thus about 66% of viruses identified are likely to be RV. PV was identified in 12% of the children when symptom free. This study suggests that viruses are the major trigger of asthma-like episodes in susceptible children.

Gastro-oesophageal reflux in patients with brittle asthma

JF MILES, K NOBLE, HR MATTHEWS, RM CAYTON, JG AYRES *Chest Research Institute, Oesophageal Laboratory, Birmingham Heartlands Hospital, Birmingham* As part of the West Midlands Brittle Asthma Register, 40 patients with peak expiratory flow (PEF) variability (amp % max) of greater than 40% for more than three hours out of every six despite considerable medical treatment (mean inhaled steroid dose 1975 μg/day) have been identified. Age, sex, and inhaled steroid matched asthmatic controls exhibiting PEF variability of 25% or less for a similarly continuous period have subsequently been recruited. Twenty brittle asthmatic patients have undergone oesophageal manometry and 24 hour pH monitoring. Six of the controls agreed to be studied and their results were compared with all 20 brittle asthmatic patients by the z test for two sample means. All control patients used only PRN short acting bronchodilators, 12 of the 20 patients were on continuous subcutaneous infusions of terbutaline, and the other eight on salmeterol. 19/20 (95%) of the brittle group had symptoms suggestive of reflux as did all six controls; 15 of the brittle group had abnormal manometry compared with only two controls ($p = 0{\cdot}06$). Herniation of the LOS was noted in 14 out of the 20 brittle asthmatic patients and in no controls ($p < 0{\cdot}02$). In severe asthma LOS pressure may be lowered either by changes in transdiaphragmatic pressure or by differences in bronchodilator use causing sphincter relaxation and thus facilitating reflux. We suggest that gastro-oesophageal reflux occurs in severe asthma as a result of the disease or its treatment as opposed to acid reflux causing worsening asthma.

	Age (y)	FEV_1%	TLC%	RV%	LOSP	%RT
Brittle (mean; n = 20)	42	66·7	94·2	132·9	7·63	8·4
Non-brittle (mean; n = 6)	41	72·5	106·4	153·3	12·7	4·2
z test (p value)	NS	<0·01	<0·001	<0·001	<0·001	<0·001

LOSP—lower oesophageal sphincter pressure (normal 12–25 mm Hg); %RT—percentage reflux (normal <4·0%).

Comparison of bone density in asthmatic patients taking inhaled budesonide and beclomethasone dipropionate

GE PACKE, O ROBB, DM REID, JG DOUGLAS *Departments of Thoracic Medicine and Rheumatology, City Hospital, and Department of Radiology, Aberdeen Royal Infirmary, Aberdeen* We have previously shown that vertebral bone density (VBD) is reduced in asthmatic patients taking high dose inhaled beclomethasone dipropionate (BDP) and intermittent systemic corticosteroids (*Thorax* 1992;47:414–7). The object of the present study was to examine VBD in a group of similar asthmatic patients taking inhaled budesonide (BUD). VBD was measured by quantitative computed tomography in 20 patients with a mean (SD) age of 36 (7) years. Median dosage of BUD was 800 μg. All had taken this treatment for more than one year, and had not previously taken BDP. None were taking regular oral steroids. 13 female patients were premenopausal. VBD in the patients taking BUD was 139·5 (28·6) mg/ml. This was significantly lower ($p < 0·05$, unpaired t test) than the VBD of 160 (27) mg/ml in a group of mild asthmatic patients studied earlier who had never taken inhaled or systemic steroids. Our previous study showed that VBD in patients taking BDP in a median dosage of 1000 μg daily and intermittent corticosteroids was 128 (23) mg/ml. This value was lower than that seen in the patients taking BUD but not significantly so ($p = 0·1$). Differences between BUD and BDP were even less apparent when bone density values were adjusted for dose of inhaled steroid (covariate analysis). Seven patients taking BUD had not previously taken systemic steroids; VBD was 148 (35) mg/ml compared with 135 (25) mg/ml in the 13 patients who had taken intermittent steroids ($p = 0·4$). VBD is reduced in asthmatic patients taking inhaled BUD. This reduction in VBD is similar in magnitude to that seen in patients taking inhaled BDP.

Withdrawal of fenoterol and the end of the asthma mortality epidemic in New Zealand

J CRANE, C BURGESS, R BEASLEY, N PEARCE *The Wellington Asthma Research Group, Wellington School of Medicine, Wellington, New Zealand* A series of epidemiological and experimental studies have implicated the high dose preparation of fenoterol as a major factor in the second New Zealand asthma mortality epidemic. These studies led to the warning from the New Zealand Department of Health, in 1989, that fenoterol should not be used by patients with severe asthma, and then to the withdrawal of fenoterol from the drug tariff in New Zealand in 1990. These regulatory moves led to a large reduction in the sales of fenoterol from a stable 30% of the β agonist market during 1983–88 to 6% in 1990. During the same period, the mortality fell from an average of 2·3 (range 1·9–2·6) per 100 000 in the 5–34 year age group to 1·1 in the second half of 1989, and to 0·8 in 1990. The 1990 figures represent the lowest New Zealand mortality for more than 25 years. Thus the end of the New Zealand asthama mortality epidemic occurred during the period of the withdrawal of fenoterol in 1990, in a similar way as the epidemic commenced when fenoterol was introduced in 1976. By contrast, the increased use of β agonist drugs as a class occurred after the epidemic began, with sales continuing to increase during the period when mortality fell. Data on time trends should be assessed with considerable caution; nevertheless, it is useful to note that the time trends are consistent with other epidemiological and experimental evidence indicating a major role of fenoterol, but not β agonist drugs as a class, in the second mortality epidemic in New Zealand.

Therapeutic response to oxygen supplied from a complex polymer membrane

CB COOPER, JM STRAKOVA, LS WILKINSON, JR COLTHURST *UCLA School of Medicine, Los Angeles, California, USA* For therapeutic purposes, it has been assumed that an O_2 supply should be 100% (or nearly 100%) to be effective. Membrane separator technology currently produces lower concentrations of O_2 but these concentrations might produce an adequate therapeutic response in some patients with chronic hypoxaemia. We evaluated a prototype membrane separator made of complex polymer straws differentially permeable to O_2 and N_2. When fed with compressed air at 7 bar, this membrane produced 47% O_2, fully humidified, up to flow rates of 10 l/min. We studied 10 subjects (three men, seven women) of mean (SD) age 58 (11) years with chronic hypoxaemia (breathing room air, Pao_2 was 53·2 (10·3) mmHg and $Paco_2$ was 47·1 (7·3) mmHg). Eight had obstructive lung disease, one restrictive lung disease, and one obesity hypoventilation syndrome. All subjects had received domiciliary oxygen treatment and four had transtracheal catheters. We compared the membrane separator (SE) at flow rates of 4, 6, and 8 l/min with a PSA molecular sieve (SI) at 1, 3, and 5 l/min. Also we compared three types of O_2 delivery: standard nasal cannulae (NC), occluding nasal cannulae (OC), and transtracheal catheters (TC). Seven subjects had arterial catheters for sequential blood gas measurements. Oxyhaemoglobin saturation (Spo_2) was measured by pulse oximetry with an ear probe. Using SE with nasal cannulae, for the whole group, mean values of Pao_2 increased from 54 to 76 mm Hg and Spo_2 from 82 to 92%. Using SE with transtracheal delivery, in four subjects, Pao_2 increased from 41 to 71 mm Hg and Spo_2 from 69 to 93%. We found greater increases in Spo_2 and Pao_2 with the SI. All changes were significant ($p < 0·05$). The complex polymer membrane supplying 47% O_2 produced adequate increases in oxygenation in selected patients with chronic hypoxaemia. Membrane technology for therapeutic O_2 supply has the advantages of high flow capability, humidification, bacterial filtration, and the possibility of miniaturisation.

Role of oxygen during recovery from exercise in patients with chronic obstructive pulmonary disease

IJ WILLIAMSON, CJ CLARK *Department of Respiratory Medicine, Hairmyres Hospital, East Kilbride* During pulmonary rehabilitation programmes, patients with chronic obstructive pulmonary disease (COPD) frequently become breathless due to exercise hyperpnoea and reduced ventilatory reserve. Oxygen can improve exercise tolerance in these patients but its role during recovery is less clear. This study investigates the effect of administering oxygen placebo during recovery from exercise of moderate intensity. Eleven patients with COPD attending the pulmonary rehabilitation programme, who were known not to desaturate on exercise, were entered. The study used a randomised, single blind, cross over, placebo controlled protocol. After a 90 second warm up period, the patient performed steady state exercise, at 75% of a previously determined maximum work load, on a bicycle ergometer for the same time in each test. During recovery they breathed either air or 60% oxygen and measurements of heart rate, respiratory rate, minute ventilation, dyspnoea (Borg) score, Vo_2 and transcutaneous gas tensions were recorded. The second test was performed after a minimum rest period of 30 minutes. Eleven patients (three women) completed the study (age 58 (4) years, FEV_1 (%pred) 58 (19), FEV_1/FVC ratio 53 (12), and resting Po_2 9·56 (0·8) kPa (mean (SD)). The two exercise tests performed by each patient were comparable with no significant differences in variables measured. During recovery on oxygen the mean Po_2 rose from 9·86 to 21·3 kPa. These returned to baseline during the 30 minute rest period between tests. The recovery time (Borg score fall back to baseline) was on average 20 seconds shorter when breathing oxygen ($p < 0·05$, paired Student's t test). The area under the curve for Borg score decay on 60% oxygen was not, however, significantly different from placebo, nor were any of the other variables measured during recovery including minute ventilation. This study found little evidence to support the use of oxygen supplementation during recovery from exercise in patients with moderate COPD.

Nasal ventilation in acute exacerbations of chronic obstructive pulmonary disease (COPD): effect of ventilator modes on arterial blood gases

DJ MEECHAM JONES, EA PAUL, C GRAHAME-CLARKE, JA WEDZICHA *Department of Thoracic Medicine, The London Chest Hospital, Bonner Road, London* Acute hypercapnic respiratory failure due to exacerbations of COPD is associated with a high mortality despite advances in medical treatment. Several recent studies have reported

the successful use of nasal positive pressure ventilation in this condition. We have examined the acute effect of four different modes of nasal ventilation on arterial blood gas tensions in 12 patients (11 men) median age 69 (range 49–79) years within 16 hours of admission with acute exacerbations of COPD. At the start of the study, mean (SD) FEV_1 was 0·59 (0·13) l, FVC 1·44 (0·33) l, Pa_{O_2} 6·00 (1·18) kPa, Pa_{CO_2} 8·10 (0·93) kPa (air). Each patient underwent four one hour periods of nasal ventilation in randomised order; three with the BiPAP ventilator: (a) pressure support (PS) 18 cm H_2O (IPAP), (b) PS 18 cm H_2O + PEEP 6 cm H_2O (IPAP + EPAP), (c) CPAP 8 cm H_2O, and one period using the volume cycled BromptonPAC ventilator (d) adjusted to deliver the maximum calculated minute volume that the patient could tolerate. There was an interval of at least one hour between treatment periods to allow blood gases to return to baseline. There was no significant change in baseline blood gas concentrations during the course of the study. Arterial blood samples were obtained from a radial arterial line immediately before each period of ventilation and at one hour. Oxygen treatment at the same flow rate was continued throughout the whole study. All modes of ventilation produced a significant improvement in Pa_{O_2}; however, repeated measures analysis of variance showed no difference between modes. Mean (SD) changes in Pa_{O_2} (kPa) were (a) IPAP +2·5 (2·27), (b) IPAP + EPAP +0·82 (2·34), (c) CPAP +1·35 (2·24), (d) Brompton PAC +2·34 (1·51). For the 12 patients, mean changes in Pa_{CO_2} were: (a) IPAP −0·29 ((0·74) kPa, (b) IPAP + EPAP −0·24 (1·09), (c) CPAP +0·25 (0·67), (d) Brompton PAC +0·04(0·83). None of these changes were statistically significant. When patients were subdivided into those with starting Pa_{CO_2} above or below 8 kPa, however, there was a significant difference between the two groups: Pa_{CO_2} fell in those with Pa_{CO_2} <8 kPa, but rose in those with Pa_{CO_2} > 8 kPa ($p = 0·014$). This pattern was not found in changes in Pa_{O_2}. Although the Pa_{O_2} improved in all patients, the change in Pa_{CO_2} depends on the initial degree of hypercapnia. This suggests that in patients with severe hypercapnia, nasal ventilation may not be sufficient to reduce Pa_{CO_2}, but will control further rises in Pa_{CO_2} allowing safe controlled oxygen treatment. [This work is supported by The British Lung Foundation.]

Nasal intermittent positive pressure ventilation in advanced progressive chronic respiratory failure due to chronic obstructive pulmonary disease

DJ MEECHAM JONES, GM BRAID, JA WEDZICHA *Department of Thoracic Medicine, The London Chest Hospital, Bonner Road, London* Long term oxygen treatment (LTOT) is beneficial to patients with chronic respiratory failure due to chronic obstructive pulmonary disease (COPD). Nasal intermittent positive pressure ventilation (NIPPV) has been used increasingly to treat patients with chronic respiratory failure due to COPD, but the criteria for starting NIPPV in these patients have not been established. Also, the effects of treatment with NIPPV in patients with advanced COPD have not been evaluated. We report the effect of domiciliary nocturnal NIPPV in a group of nine patients (five men, four women, median age 60 years, range 48–68) with advanced chronic respiratory failure due to COPD and long standing peripheral oedema. All were established on domiciliary LTOT (median duration 59, range five–85 months). Eight of the nine had refractory hypoxaemia with resting Pa_{O_2} less than 8 kPa while on supplemental oxygen and all had symptomatic hypercapnia that limited further oxygen treatment. All patients had shown clinical deterioration in the three month period immediately before starting NIPPV. At initiation of NIPPV, mean (SD) FEV_1 was 0·58 (0·11) l, FVC 1·6 (0·39) l, mean Pa_{O_2} (room air) 5·34 (0·73) kPa, and Pa_{CO_2} 8·04 (1·17) kPa. On oxygen, the mean Pa_{O_2} was 7·37 (1·58) kPa, and Pa_{CO_2} 8·63 (1·16) kPa. The patients were followed up for a period of four–19 months (median nine) and LTOT, diuretics, and all other appropriate treatments were continued. Six month follow up blood gases are available for six patients. In this group the mean Pa_{O_2} fell from 5·61 (0·76) to 4·91 (1·26) kPa, and Pa_{CO_2} rose from 8·00 (1·38) to 8·52 (1·22) kPa, five of the six patients showing a deterioration in blood gases. Five patients died during follow up (range 4–14 months) during exacerbations of cor pulmonale. The four surviving patients were followed up for six–19 months (median 11): at six months mean Pa_{O_2} (room air) fell from 5·75 (0·94) to 5·41 (1·14) kPa and Pa_{CO_2} rose from 7·76 (0·96) to 8·37 (0·61) kPa. Symptomatic hypercapnia was still present in all patients and all required further admissions to hospital with cor pulmonale. In these patients with advanced and progressive COPD, the addition of NIPPV to LTOT and standard treatment produced no improvement in clinical condition or blood gases. In COPD, studies have shown that despite an initial fall in mortality with LTOT, mortality rises later due to an irreversible deterioration in airflow obstruction. We suggest that to be clinically effective, NIPPV should be added to LTOT at an earlier stage in the natural history of the disease, before rapid clinical deterioration occurs. [This work is supported by The British Lung Foundation.]

Non-invasive inspiratory pressure support and exercise tolerance in patients with severe chronic airflow limitation (CAL)

SEJ KEILTY, TA FLEMING, J MOXHAM *Department of Thoracic Medicine, King's College School of Medicine and Dentistry, London* Patients with chronic airflow limitation (CAL) commonly present with dyspnoea limiting exercise tolerance. We have studied the effects of non-invasive inspiratory pressure support (IPS), continuous positive airways pressure (CPAP), and O_2 on exercise in six patients with CAL, mean (SD) FEV_1 0·73 (0·21) l, complaining of disabling dyspnoea. Patients walked on a treadmill until their sensation of dyspnoea, scored at one minute intervals, reached level 5 (severe) on the modified Borg Scale (Borg GAV. *Med Sci Sports Exercise* 1982;**14**:377–81). Studies were performed with IPS (mean airway pressure 15 cm H_2O), CPAP at 6 cm H_2O (with a full face mask), and O_2 at 2 l/min (with an oxygen mask) in random order on three separate days. Each of these was compared with walking with a sham circuit (breathing air via an oxygen mask at 2 l/min from an unlabled cylinder) and with no support. On cessation of exercise, distance achieved and leg fatigue score were recorded. No patients stopped walking due to leg fatigue, only stopping when their breathlessness score had reached level 5. Non-invasive IPS improved median walking distance when compared with sham: median increase 97% (139, range 14 to 533 metres, $p = 0·036$, $n = 6$). Compared with no support IPS increased walking distance in five out of six patients: median increase 42% (140, range −10 to +382 metres, $p = 0·059$, $n = 6$). Neither CPAP nor O_2 significantly improved walking distance in the six patients studied. We conclude that walking with non-invasive IPS may improve exercise tolerance in patients with CAL.

Cough reflex sensitivity decreases with successful treatment of chronic cough

F O'CONNELL, VE THOMAS, RW FULLER, NB PRIDE *Departments of Clinical Pharmacology and Respiratory Medicine, Royal Postgraduate Medical School, Du Cane Road, London* We prospectively evaluated effects of specific treatment on cough severity measured by visual analogue score (VAS) and cough sensitivity to inhaled capsaicin (log concentrations required to elicit two (C2) and five (C5) coughs) in 87 consecutive unselected referrals with chronic cough. A specific cause of cough was successfully treated in 48 (55%) patients. In 11 patients with rhinitis, VAS was less ($p = 0·014$) after treatment with intranasal steroids and anticholinergics. Log C2 and C5 were greater after treatment but the differences were not significant. In nine patients with gastro-oesophageal reflux (GOR), VAS was less ($p = 0·009$) and log C2 ($p = 0·02$) and C5 ($p = 0·015$) greater after antireflux treatment. Six patients with rhinitis and GOR had lower VAS ($p = 0·04$) and higher log C2 ($p = 0·04$) and C5 ($p = 0·05$) after treatment. Twenty two patients with asthma ($n = 9$), postviral ($n = 9$), or ACE inhibitor cough ($n = 4$) also had lower VAS and higher log C2 and C5 values after treatment. All remaining 39 (45%) patients had negative histamine challenge tests. Twenty had rhinitis and/or GOR. In eight of these patients (a) the symptoms of PND/GOR cleared with appropriate treatment whereas the VAS, log C2, and log C5 showed no change. Treatment of PND/GOR failed in the other 12 patients (b) and there was no change in VAS, log C2, or log C5 (table). Nineteen patients in whom no specific cause of cough was found showed no change in VAS or capsaicin responses after empiricial trials of treatment for PND and GOR. Enhanced capsaicin cough sensitivity in patients with chronic cough returns to normal with successful treatment of the cough.

	VAS		log C2		log C5	
	(pre)	(post)	(pre)	(post)	(pre)	(post)
Treatment success:						
Rhinitis	61 (7)	12 (4)	0·8 (0·2)	1·1 (0·2)	1·6 (0·3)	2·0 (0·2)
GOR	69 (5)	20 (5)	0·6 (0·3)	1·0 (0·2)	0·8 (0·3)	1·4 (0·3)
Rhinitis + GOR	56 (8)	17 (6)	0·4 (0·2)	0·9 (0·1)	0·5 (0·2)	1·6 (0·3)
Asthma	50 (7)	15 (7)	0·4 (0·3)	0·8 (0·2)	0·7 (0·3)	1·7 (0·2)
Postviral	48 (2)	3 (1)	0·3 (0·2)	0·9 (0·2)	0·9 (0·3)	1·6 (0·2)
Treatment failure:						
PND/GOR (a)	68 (6)	66 (6)	0·4 (0·2)	0·0 (0·2)	0·5 (0·3)	0·3 (0·3)
PND/GOR (b)	69 (7)	64 (8)	0·9 (0·2)	0·8 (0·2)	1·2 (0·3)	1·1 (0·2)
Idiopathic	61 (4)	60 (5)	0·2 (0·1)	0·3 (0·1)	0·5 (0·2)	0·6 (0·2)

(a) Treatment of PND/GOR successful but of cough unsuccessful; (b) treatment of PND/GOR and cough unsuccessful.

Levels of antibody to the mycobacterial 30 kD protein in sarcoidosis

HM FIDLER, GAW ROOK, N MCI JOHNSON, C O'CONNOR *Department of Medical Microbiology, UCL Medical School, London* We have recently shown the presence of *M tuberculosis* DNA in a subgroup of sarcoidosis tissues (Fidler HM *et al. BMJ* 1993;**306**:546–9). The form in which these organisms exist remains mysterious, and serological responses to mycobacteria may reflect interesting properties of this unusual infection. Raised titres of antibody to the secreted mycobacterial antigens, designated the antigen 85 complex, seem to be a marker of active, multibacillary disease with live mycobacteria (Espitia C *et al. Clin Exp Immunol* 1992;**87**:362–7). We therefore used an ELISA to measure levels of the antibody in serum to the 30 kD antigen of this complex in 136 sarcoidosis patients and 38 matched control sera. No difference was found between these groups, or between sarcoidosis patients' spouses, early and late disease patients, and controls. The lack of an antibody response to this strongly immunogenic antigen is at first surprising. It suggests either that the organisms are present in very low numbers or that most of the genome is inactive, with minimal synthesis of antigen.

Subject	*No of patients*	*30 kD antibody level* (SD)*
Sarcoidosis	136	42·8 (20)
Controls	38	39·4 (21·5)

*Mean optical density expressed as a % of a positive control serum.

Sequential analysis for *M tuberculosis* with the polymerase chain reaction technique in lavage fluid from patients and bronchoscopes

D NOONE, M GLENNON, T SMITH, F GANNON, H MOORE, JJ GILMARTIN *National Diagnostics Centre/Bioresearch Ireland, University College Galway, Ireland, and Department of Respiratory Medicine, University College Hospital, Galway, Ireland* The polymerase chain reaction (PCR) technique is a recent exciting development with initial encouraging results in the diagnosis of tuberculosis using bronchoalveolar fluid (BALF). In a pilot study we were concerned at possible contamination of samples either in the bronchoscopy suite or in subsequent sample handling. We therefore undertook an analysis of 56 sequential samples obtained at diagnostic bronchoscopy (26) or simulated lavage (30). BALF was obtained from the lingula or right middle lobe with saline heated to body temperature in patients with suspected tuberculosis, sarcoidosis, or cancer of the bronchus. Control samples were obtained by a mock lavage through the bronchoscope of saline or saline with a known concentration of killed *M tuberculosis* bacteria. All samples were AFB culture negative on the Bactec system. After PCR amplification with IS 6110 all samples were further tested using a probe specific for *M tuberculosis* bacteria. All negative samples were tested for the presence of factors that would inhibit PCR by amplification of IGF-1 DNA in the sample. The positive controls indicated a sensitivity of 5 organisms/ml. Nine clinical samples exhibited the presence of inhibitors leaving 17 analysable of which six were PCR positive. Three of four patients with sarcoidosis had positive results whereas two other patients with positive results had no other evidence of tuberculosis. Further doubts on the relevance of these positive results was the finding of positive samples from the mock lavage from the bronchoscope giving a false positivity rate of 6/47. These data indicate the need for stringent control samples such as we have included when using the PCR in BALF.

Inactivation of a_1 protease inhibitor in cystic fibrosis: a post-sampling effect?

CM O'CONNOR, K MCQUAID, M HAYES, J HAYES, MX FITZGERALD *Department of Medicine, University College, Dublin; The Adult Cystic Fibrosis Centre, St Vincent's Hospital, Dublin* Neutrophil elastase (NE) is thought to play a significant part in lung destruction in cystic fibrosis (CF). Treatment of CF patients with aerosolised a_1 protease inhibitor (a_1PI), an inhibitor of NE, has been suggested for attenuating lung damage. Several studies suggest, however, that endogenous a_1PI is inactivated in the CF lung. Thus the efficacy of a_1PI treatment is questionable, as the administered inhibitor would be inactivated in the same manner as the endogenous protein. Evidence for the inactivation of a_1PI in CF comes largely from studies that show the presence of an inactive, "truncated" form of a_1PI in bronchopulmonary samples from CF patients and the absence of a_1PI-NE complexes in the same samples, despite the presence of active NE. In a recent study, we noted that addition of serine protease inhibitors to sputum samples after collection altered the electrophoretic protein profile of the samples, suggesting that degradation of protein can occur subsequent to sample collection. The aim of the present study was to examine the effect of postsampling proteolysis on a_1PI in sputum from CF patients. Sputum samples, collected from 14 CF patients, were extracted in the presence or absence of serine protease inhibitors (PMSF and DIPF) and/or metallo-protease inhibitors (EDTA and phenanthrone). Samples were examined by electrophoresis and immunoblotted *v* an antibody specific for a_1PI. Quantification of the a_1PI positive bands was performed by laser densitometry. Results indicated that the preservation of complexed a_1PI was best achieved by addition of both serine- and metalloprotease inhibitors to sputum samples on collection. Although the major form of a_1PI present in all aliquots corresponded to a "truncated" form of the protein, significantly lower amounts of this form and larger quantities of native a_1PI were present in aliquots containing both serine- and metalloprotease inhibitors ($p < 0.05$). These results indicate that significant proteolysis of a_1PI-NE complex and a_1PI can occur in CF sputum samples following collection in the absence of added protease inhibitors. In the light of these findings, reports suggesting that a_1PI is inactivated in vivo in the CF lung may have to be reassessed.

C-reactive protein and plasma cytokines in cystic fibrosis

PH BROWN, SP MATUSIEWICZ, M GORDON, K LIDDLE, AP GREENING *Adult Cystic Fibrosis Unit, Western General Hospital, Edinburgh* Circulating markers such as C-reactive protein (CRP) and tumour necrosis factor-α (TNF) may be useful in monitoring the host inflammatory response to chronic bronchial sepsis in cystic fibrosis (CF) (*Thorax* 1991;**46**:91). We measured plasma TNF and granulocyte-macrophage colony stimulating factor (GM-CSF), together with total white cells (WCC) and serum CRP in 15 adults (17–44 years, 10 men) with CF. Samples were taken before and after 17–21 days of intravenous antibiotics and when patients were in a stable state. Exacerbations of bronchiectasis were defined clinically by increase in sputum volume and purulence accompanied by reduction in FEV_1 and vital capacity. Samples for cytokines were taken into aprotinin-supplemented EDTA, spun at 4°C, and stored at −80°C until batch assay with in house sandwich ELISA (detection limit 15 pg/ml for both TNF and GM-CSF). After antibiotics (AB) there were increases ($p < 0.001$; paired *t* tests) in mean (SE) FEV_1 (1·56 (0·16) to 2·05 (0·21) l), vital capacity (2·8 (0·26) to 3·4 (0·27)), and body weight (53·4 (2·1) to 55·3 (1·8) kg). WCC fell from 13·1 to $10 \times 10^9/l$ ($p < 0.001$). The table shows the results for CRP, TNF, and GM-CSF. TNF was detectable in only three patients before AB and changes in TNF and GM-CSF were not significant. Although CRP fell ($p < 0.001$, Wilcoxon) after AB, seven of the 15 patients had normal values before treatment. WCC was $>11 \times 10^9/l$ in 11 patients and was increased after AB in three. Measurements of CRP and TNF are of limited value in exacerbations of CF bronchiectasis.

	CRP (g/l)	*TNF (pg/ml)*	*GM-CSF (pg/ml)*
Pre-AB	18 (<10-204)	<15 (<15-460)	45 (<15-459)
Post-AB	<10 (<10-18)	<15 (<15-335)	<15 (<15-428)
Stable	<10 (<10–23)	<15 (<15–220)	25 (<15–200)

Values are medians (range).

Effects of seasonal exposure to allergen on nasal cytokine immunoreactivity and its modulation by fluticasone propionate

P BRADDING, IH FEATHER, S WILSON, ST HOLGATE, PH HOWARTH *Immunopharmacology Group, Southampton General Hospital, Southampton* Seasonal allergic rhinitis is associated with tissue infiltration by eosinophils and activation of mast cells. These events seem to be under the control of certain cytokines including IL-4, IL-5, and IL-6. In this study we have employed immunohistochemistry with specific anticytokine mAbs to investigate the effects of natural seasonal exposure to allergen on the cellular distribution of IL-4, IL-5, and IL-6 in nasal mucosa and the effects of treatment with the topical corticosteroid fluticasone propionate (FP). 26 grass pollen sensitive subjects with a previous history of seasonal rhinitis were randomised double blind to six weeks treatment with either FP nasal spray or placebo, with nasal mucosal biopsies taken preseason and after six weeks of treatment. Biopsies were processed into GMA and sequential 2 μm sections immunostained for IL-4, IL-5, IL-6, tryptase, ECP, and CD3. Positive cells in the submucosa and epithelium were expressed as cells/mm^2 and cells/mm respectively. There was a significant seasonal increase in the number of submucosal eosinophils in the placebo group ($p = 0{\cdot}003$), which was prevented by treatment with FP, but no change in the number of submucosal mast cells. Most IL-4 and IL-6 immunoreactivity was localised to mast cells, whereas IL-5 was localised to both mast cells and eosinophils. With the mAb 3H4, which may detect secreted IL-4, there was a seasonal increase in +ve cells in the placebo group that did not reach statistical significance ($p = 0{\cdot}08$) and a decrease from baseline on the FP group ($p = 0{\cdot}08$). When these seasonal changes were compared between the two groups there was a significant difference ($p = 0{\cdot}014$). Cells +ve for mAb 4D9, which detects stored IL-4, decreased significantly in the FP group ($p = 0{\cdot}016$) but were not altered on placebo ($p = 0{\cdot}68$), but comparing the two groups the difference for mAb 4D9 was not significant ($p = 0{\cdot}07$). No significant differences were found in cells +ve for IL-5 or IL-6. These results do not show a clear seasonal increase in the number of cytokine +ve cells present in the nasal mucosa but do suggest that IL-4 expression in vivo is suppressed by topical corticosteroids.

Intrinsic variability of asthmatic airways

I RICHMOND, H BOOTH, GE PRITCHARD, C WARD, PA CORRIS, EH WALTERS *William Leech Centre for Lung Research, Freeman Hospital, Newcastle upon Tyne, and Department of Respiratory Medicine, Alfred Hospital and Monash University, Victoria, Australia* This study examines the intrasubject variability of inflammatory cell numbers in airway biopsies with lobe examined (upper *v* lower) and with time. A standard fibreoptic bronchoscopy was performed on 12 patients with mild asthma (eight men and four women, median age 31·5, range 18–53 years; five receiving beclomethasone dipropionate up to a maximum daily dose of 400 μg and the remainder on inhaled β agonists as required). Endobronchial biopsies were taken from third generation carinae of both right upper and right lower lobes. The procedure was repeated one month later. There had been no change in active treatment, lung function (mean % predicted FEV_1 94·6(14)%) or airway responsiveness to methacholine (geometric mean 21·1(4)). On each occasion the biopsies were snap frozen in liquid nitrogen at -196°C after immersion in cold isopentane. Standard 7 μm step sections were taken from each sample and stained with monoclonal antibodies against T lymphocytes (CD3), T lymphocyte subsets (CD4 and CD8) and eosinophils (EG2). Quantitative analysis was used to obtain submucosal counts (mm^2) to a depth of 150 μm. All counts were made by one observer (IR) and interobserver coefficients of variation for measurement and counting functions were <5% and <8% respectively. There was no significant difference between upper and lower lobe counts for any of the markers. Large intrasubject variations for both T lymphocytes and eosinophils were apparent, however, with time (CD3 median difference 185·0, range of differences 109·9–426·3/mm^2; CD4 91·5, range 67·7–202·1/mm^2; CD8 167·7, range 71·0–322·9/mm^2, and EG2 12·3, range 0·9–110·1/mm^2). This may support the view that the asthmatic airway is in a constant state of flux with regard to inflammatory cell numbers and types, or may reflect difficulties in the sampling technique.

Nerves containing calcitonin gene related peptide are increased in bronchial epithelium of patients with chronic idiopathic cough

F O'CONNELL, A MORADOGHLI-HAFTVANI, DR SPRINGALL, P CLARKE, RW FULLER, NB PRIDE, JM POLAK *Departments of Clinical Pharmacology, Histochemistry, Medical Physics, and Medicine, Royal Postgraduate Medical School, Du Cane Road, London* With an anatomical diagnostic approach similar to that of Irwin *et al* (*Am Rev Respir Dis* 1981;**123**:413–7) we excluded specific causes of cough in 16 patients with persistent cough for a minimum of one year by history, physical examination, spirometry, home PEFR monitoring, histamine bronchial challenge, skin tests for common aeroallergens, chest, and sinus *x* ray films, barium swallow, and oesophageal pH monitoring. In addition all patients failed to respond to empirical two month courses of topical intranasal corticosteroids and anticholinergic agents and of aggressive antireflux treatment including diet, postural measures, alginate, and high dose H_2 antagonists or omeprazole. We compared cough sensitivity to inhaled capsaicin and endobronchial biopsies in these 16 patients (P) with six normal healthy volunteers (H). Cough sensitivity was enhanced in P compared with H (log C2 (concentration required to elicit two coughs) H = 2·6 (0·2), P = 1·4(0·1), $p = 0{\cdot}003$ and C5 (concentration required to elicit five coughs) H = 3·5 (0·1), P = 1·7 (0·2), $p = 0{\cdot}001$). At fibreoptic bronchoscopy under local anaesthesia, endobronchial biopsies were taken from the carina between the right main bronchus and the bronchus intermedius and a subsegmental bronchus of the right lower lobe. Biopsies were fixed immediately in Zamboni's solution. Frozen sections were stained by indirect immunofluorescence for the anatomical nerve marker PGP9·5 and for the sensory neuropeptide calcitonin gene related peptide (CGRP). Immunoreactive nerves were quantified in airway epithelium by image analysis to measure the fluorescent area as a percentage of epithelial area. The overall weighted percentage for each marker in two sections from each site was calculated for each subject and compared between patients and controls. Total nerve density (PGP9·5 staining) was greater in patients (mean 2·46%, range 0·27–10·09) than controls (1·24%, 0·31–2·9) but the difference was not significant ($p = 0{\cdot}59$). CGRP immunoreactive nerve density was significantly greater in patients (1·27%, 0·09–5·08) than in controls (0·12%, 0·0–0·44) ($p < 0{\cdot}003$). Staining for CGRP as a fraction of PGP9·5 was also greater in patients than controls ($p = 0{\cdot}001$). Either an increased number or functional changes of sensory nerves in airway epithelium may be responsible for upregulation of cough sensitivity in patients with chronic idiopathic cough.

Increased expression of the monocyte chemoattractant protein 1 in asthmatic bronchial epithelium

AR SOUSA, SJ LANE, J NAKHOSTEEN, T YOSHIMURA, TH LEE, RN POSTON *UMDS, Guy's Hospital, London, Augusta Teaching Hospital, Boshum, Germany, and NIH, Bethesda, MD, USA* The presence of monocyte chemoattractant protein 1 (MCP-1), a member of the chemokine low molecular weight cytokine family, was assessed in the bronchial wall, in vivo, on frozen bronchial biopsies from 12 asthmatic and 12 normal subjects. MCP-1 was detected by immunohistochemistry with a highly specific monoclonal antibody (clone F9). A mouse myeloma protein (MOPC21) without antibody specificity was used as a control immunoglobulin to ensure specificity of the staining. Hue-saturation intensity (HSI) colour image analysis was used to quantify epithelial staining of both the test and control antibodies. The epithelium of the bronchial biopsies of asthmatic subjects stained strongly with MCP-1 antibody, with 51·8 (3·7)% (mean (SE)) of the epithelium being reactive, whereas the epithelium of normal individuals stained significantly less with only 6·39 (1·89)% of the epithelium being stained ($p < 0{\cdot}0001$). There was no overlap between the groups. Increased staining was also present in blood vessels and macrophages of asthmatic biopsies. There was negligible staining of the bronchial wall with the control MOPC21 antibody. A polyclonal antibody against MCP-1 gave similar positive results. These data show upregulation of MCP-1 in the asthmatic bronchus, suggesting that MCP-1 may play an important part in the immunopathology of bronchial asthma.

Airway eosinophil infiltration in fatal asthma

M SYNEK, R BEASLEY, W ROCHE, D GOULDING, L HOLLOWAY, ST HOLGATE *University Medicine, Southampton General Hospital, Southampton, and Wellington School of Medicine, New Zealand* The degree of eosinophil infiltration of the bronchial mucosa was compared in 28 asthmatic patients who died of asthma with 11 mild to moderate asthmatic patients who died of unrelated causes. Lung tissue sections 4 μm thick were cut from paraffin embedded blocks taken at postmortem. The resting and activated eosinophils were

detected by monoclonal antibodies (EG1 and EG2) with the streptavidin-biotin horseradish peroxidase technique. The size of the airways was determined by measurement of basement membrane length. Eosinophils within the airway wall were counted per mm² of airway wall area. All airways regardless of their size were evaluated first. Then large airways (>2 mm) and small ones (<2 mm were studied separately. There was no overall significant difference in the degree of airway eosinophil infiltration between the group of asthmatic patients who died from asthma and those who died from unrelated causes. Cell densities in the airway wall were 52·1 *v* 46 cells/mm² for EG1 and 94·4 *v* 87·9 cells/mm² for EG2 (all NS). In the airways >2 mm, however, there was significantly higher eosinophil infiltration of the airway wall in asthma deaths. The figures were 49·4 *v* 6·8 cells/mm² (p = 0·01) for EG1 and 101·1 *v* 19·7 cells/mm² (p = 0·01) for EG2. In small airways (<2 mm) no significant differences between the two groups were found. This study suggests a role of eosinophil infiltration in large but not in peripheral airways in fatal asthma.

Regular inhaled salbutamol may exacerbnate bronchial inflammation in patients with mild asthma

RJ DAVIES, CJ TRIGG, JH WANG, N MANOLITSAS, A MACAULAY, N JHALLI, S HAMILTON *Department of Respiratory Medicine, St Bartholomew's Hospital, London* β_2 agonist use may worsen asthma control when administered regularly or in high dose. In this study, regular salbutamol (200 μg four times a day) was compared double blind with nedocromil sodium (4 mg four times a day) and placebo. All subjects received intermittent inhaled salbutamol as required. Histamine bronchial provocation, bronchial biopsies, and bronchoalveolar lavage (BAL) were performed before and after four months of treatment in 38 non-smoking patients with mild asthma aged 18-45 years who had received only intermittent inhaled β_2 agonist in the preceding six months. There was a non-significant trend towards improvement in bronchial responsiveness in the nedocromil treated group but no clinical deterioration in the placebo and regular salbutamol groups. Mast cell numbers were not affected by treatment but activated (EG2) eosinophils increased significantly on regular salbutamol compared with a reduction on nedocromil sodium. ECP and tryptase levels in BAL were not significantly affected. These data suggest a deleterious effect of regular inhaled β_2 agonists on bronchial inflammation in mild asthma. Similar trends have been found in comparison of intermittent and regular β_2 agonists with inhaled steroids (our experience; also Laitinen *et al. J Allergy Clin Immunol* 1992;**90**:32–42).

Treatment	*Pre*	*Post*
Nedocromil sodium	(n = 9) 143·8	104·9
Regular salbutamol	(n = 11) 127·5	211·4*
Placebo	(n = 12) 119·0	121·0

*p < 0·05, Wilcoxon test; n = number of viable biopsies.

Placebo controlled trial of long term inhaled beclomethasone dipropionate (BDP) in asthma: effect on bronchial mucosal inflammation

CJ TRIGG, JH WANG, N MANOLITSAS, MA CALDERON, A MACAULAY, MJ HERDMAN, J DUDDLE, RJ DAVIES *Department of Respiratory Medicine, St Bartholomew's Hospital, London* The effect of long term inhaled BDP on bronchial inflammation has not previously been studied in a placebo controlled double blind trial. 25 non-smoking patients with mild asthma received either beclomethasone dipropionate (BDP) (500 μg twice daily) or placebo double blind for four months. None of the subjects received antiasthma treatment other than intermittent inhaled β_2 agonist in the preceding six months. Histamine bronchial provocation, fibreoptic bronchoscopy with biopsy, and bronchoalveolar lavage (BAL) were performed before and after treatment. There was a non-significant trend towards improvement in lung function and bronchial responsiveness. Tissue mast cells, total (EG1), and activated (EG2) eosinophils were all significantly reduced in the BDP group. There was also a trend towards reduced BAL eosinophils and ECP level. No change in CD4 or CD25 T lymphocytes was seen. The results compare well with the response to six weeks BDP and three months budesonide.

	Viable biopsies			*Active*	
	Before	*After*		*Before*	*After*
EG1 (n = 8)	136·7	197·2	(n = 11)	141·3	54·1**
EG2 (n = 8)	120·4	156·0	(n = 11)	122·1	66·7**
Mast (n = 7)	42·0	48·2	(n = 9)	80·4	31·6*

*p < 0·05; **p < 0·01; values are geometric mean cells/mm².

Symptomatic asthma unresponsive to corticosteroids

AE REDINGTON, J MADDEN, R DJUKANOVIC, J WILSON, ST HOLGATE, PH HOWARTH *Immunopharmacology Group, University of Southampton* Although corticosteroids are an effective form of treatment in most cases of asthma some patients remain unresponsive to their effects. We have studied the endobronchial biopsy and bronchoalveolar lavage (BAL) findings in 16 patients (five male, 17 female; mean age 41·1 (15·9) years) who, despite high dose inhaled (n = 13) and/or oral (n = 11) corticosteroids, have persistent symptoms, peak flow variability (period maximal diurnal variation median 37·4%) and airflow obstruction (mean FEV_1 74 (22·4)% predicted) (SU group) and compared these findings with those from 10 asthmatic patients (five male, five female, mean age 25·5 (4·3) years) who are well controlled on inhaled corticosteroids (SR group) as indicated by their symptoms, peak flow variability (median 14·3%), and FEV_1 (mean 103·8 (12·5)% predicted). Immunostaining was performed on biopsies by means of specific monoclonal antibodies against mast cells (AA1), eosinophils (EG2), and T lymphocytes (CD3, CD4 and CD8). BAL fluid was analysed for T lymphocyte subsets (CD4, CD8) and activations status (CD25 and HLA-DR). The biopsy findings did not differ significantly between the SU and SR groups with respect to submucosal mast cells (median cells/mm² 21·1 *v* 28·5), eosinophils (5·7 *v* 3·5), or T lymphocytes (52·6 *v* 45·5). Similarly, there were no significant differences between the two groups in the proportion of CD4+ cells (median 54·9% CD3 *v* 57·9) or CD8+ (33·0 *v* 24·4), nor in the activation markers CD25 (2·2 *v* 3·0) and HLA-DR (4·8 *v* 3·4). These findings suggest that either non-inflammatory mechanisms contribute to disease expression in corticosteroid unresponsive asthma or, alternatively, that proximal airway biopsies may not reflect events either in the distal airways or deeper within the airway wall.

Bronchial mucosal inflammation in patients with corticosteroid sensitive (CS) and corticosteroid resistant (CR) chronic asthma

SP MATUSIEWICZ, PH BROWN, WAH WALLACE, E RAMAGE, SEM HOWIE, GK CROMPTON, AP GREENING *Respiratory Unit, Western General Hospital and University Department of Pathology, Edinburgh* Bronchoscopic procedures have increased our understanding of asthma immunopathology, but most studies have looked at patients with mild asthma. Such studies have tended to show increased numbers or activation of lymphocytes and eosinophils (Eos). Our aim was to examine, with immunohistochemical staining, bronchial mucosal biopsies from severe chronic asthmatic patients. We have bronchoscoped a group of non-smoking, clinically stable patients with severe asthma and chronic daily symptoms despite high dose inhaled (800–3200 μg/day) steroids ± systemic steroids (mean age 51 years; histamine PC_{20} < 1 mg/ml; FEV_1 62% predicted). Asthmatic patients were defined as relatively corticosteroid resistant (CR) (by a failure of FEV_1 or mean PEF to improve by >15% after two weeks of prednisolone despite a >15% response to β_2 agonist (*Am Rev Respir Dis* 1991;**144**:1016)) or corticosteroid sensitive (CS). Normal non-smoking volunteers were used as controls. Coded cryostat sections from frozen mucosal biopsy material were acetone fixed and stained by a standard ABC immunohistochemical technique for a panel of cell surface markers. Positive cells were counted by eye with light microscopy and an image analysis system (HOME) and quantified as number of +ve cells/mm² submucosa (group mean data (SE)). No differences were seen between the

groups for leucocytes (CD45), cells (CD3), or type II MHC antigens. Corticosteroid resistant asthma was associated with reduced submucosal CD4 counts compared with CS asthma and increased NK cells compared with normal controls.

Marker	*Control (n = 7)*	*CS asthma (n = 9)*	*CR asthma (n = 6)*
CD4	28 (8)	†43 (6)	†16(5)*
CD8	35 (9)	41 (8)	71(22)
Eosinophil	7 (2)	28 (8)	14(6)
NK cell	†4 (2)	10 (4)	†26(7)*

*$p < 0.05$ (ANOVA); †$p < 0.05$ (*t* test)

Airborne inhalable dust and fungi in homes of asthmatic patients and matched controls

A MACLEAN, I HOGG, E CORNER, G MORRIS, K ANDERSON *Department of Respiratory Medicine, Western Infirmary and Department of Environmental Health, University of Strathclyde, Glasgow* Indoor air is the major source of inhalable material in winter, the constitution of which is determined by heating, ventilation, and predominant use of a particular room. We studied the indoor environment of 49 homes under varying circumstances to establish a local range of measurements for airborne dusts and fungi. Our homes contained 12 subjects with asthma who lived in nine different houses and nine similar houses for comparison. The other houses were selected for study under circumstances that we considered would be the dustiest conditions possible during occupation—in homes undergoing renovation, and in moderately dusty circumstances during a house removal. The asthmatic patients were volunteers who attended the chest clinic in the hospital and did not perform any specific dust lowering manoeuvres. Airborne samples were taken with low volume cyclone samplers for dust and SAS samplers for fungi. The highest dust and fungal counts were in the houses undergoing renovation where fungal counts were higher than could be recorded in 6/15 (>5600 colony forming units/m³) and higher during than after renovation in all the other homes. Respirable dust was also significantly lower (mean 0·6 (0·37) *v* 0·11 (0·07) mg/m³). A similar, less pronounced pattern was found during and after house moving. Serial dust and fungi samples were taken from December to February. The measurements in the control homes remained similar during the three months of study but were significantly different from those in homes containing asthmatic patients during February (living room inhalable dust mean 4·7(1·3) *v* 1·12(1·13) mg/m³, $p < 0.001$; bedroom dust mean 5·03 (0·99) *v* 0·59 (0·57), mg/m³, $p < 0.001$). Fungal counts were higher in the asthmatic patients' living rooms (mean 149 *v* 51 cfu/m³, $p < 0.01$) but not in the bedroom. Our results show the possible range of dust and fungal concentrations within houses. They also suggest that the indoor environment of the asthmatic patient who does not have a specific dust control regime may result in a significantly different pattern of exposure to indoor inhalable materials, which could be improved.

Method of quantifying dampness in homes

I WILLIAMSON, G MCGILL, C MARTIN, R MONIE, A FENNERTY *Department of Respiratory Medicine, Southern General Hospital, Glasgow and Healthy Homes Ltd, Glasgow* Damp housing is thought to aggravate respiratory symptoms, but methodological difficulties make an objective measurement of dampness in homes difficult. Previous methods include identifying dampness and mould growth by questionnaire or detecting dampness with an electronic meter. Neither are reliable for quantification purposes. We describe a quick, semiquantitative method of assessing dampness in homes. The important measure of dampness is the excess free moisture within a material that is available to support mould growth. By trapping a small volume of air exposed to the surface of a material, water evaporating from the material will raise the relative humidity (RH) of the air until both are in equilibrium. We measured RH after equilibration times of one and five minutes with a digital hygrometer probe sealed within a rubber hemisphere at the surfaces of wood and plaster board that had acclimatised to humidity values of 66, 79, 88, and 100%, ranges normally found indoors in the United Kingdom. The free moisture content of the wood samples (WM) at each humidity could be predicted from standard theoretical sorption isotherms. We checked this by weighing the sample before and after drying at 110°C. WM as assessed by drying gave values similar to those predicted from the sorption isotherms. The RH values after one minute of equilibration were about 10% below, and the five minute values fell within the predicted RH range. To minimise survey times, a compromise two minute period of equilibration is recommended. By adding a constant 10% to this RH value all readings were within 5% of predicted. There were no significant differences in the RH values obtained from wood or plaster exposed to similar levels of humidity. We suggest that this method can be used in medical surveys to quantify dampness in homes, giving information on its severity and hence likelihood of mould growth, both of which may have an impact on health.

Prevalence of respiratory symptoms among workers in the Irish mushroom industry

D MOLONEY, J HAYES, G KELLY, O DOYLE, MX FITZGERALD *National Agricultural and Veterinary Biotechnology Centre and Departments of Medicine and Statistics, University College, Dublin, Ireland* Mushroom workers are exposed to a variety of fungi, bacteria and chemicals that may induce respiratory disease. We assessed the prevalence of respiratory symptoms in an interview administered questionnaire (modified MRC) among 254 (77%) workers in the mushroom industry from nine rural based compost yards and mushroom growing units. Of those questioned 117 (46%) were women. There were 132 (52%) current smokers and seven (3%) ex-smokers, mean age 30 (4·1) (range 15–61) years. Workers were categorised according to their job description. The overall number of persons with at least one symptom was 28%. Prevalence of symptoms that improved when away from the workplace included dry cough (16%), cough with phlegm (15%), a wheeze or whistle in breathing (8%), difficulty with breathing (8%), tightness of chest (13%), fever/general aches and pains following work (24%), and flu-like symptoms in association with work (13%). A positive response to two asthma questions (sleep disturbance and early morning symptoms) was found in 6·7% of the population. Similarly a positive response to two of three symptoms of extrinsic allergic alveolitis (difficulty breathing, flu-like symptoms and fever/general aches and pains) was found in 5·1% of the population. Using stepwise regression analysis there was a significant association of exercise induced cough among mushroom pickers and flu-like symptoms among compost workers ($p < 0.05$). There was no relation with symptoms and cigarette smoking or duration of exposure. Thermophilic actinomycetes, *Aspergillus* and *Penicillium* species were the most common microorganisms identified (Burkard spore trap analysis). This study indicates a significant level of respiratory symptoms among mushroom workers in Ireland.

Sump bay fever: a new inhalational fever associated with a *Pseudomonas* laden water aerosol

K ANDERSON, C CLARK, G MORRIS, C MCSHARRY *Departments of Respiratory Medicine and Immunology, Western Infirmary, and Environmental Health, University of Strathclyde, Glasgow* A cross sectional survey was performed in an engineering laboratory after several employees complained of feverish, flu-like symptoms which seemed to be work related. These symptoms appeared as episodes, and were attributed to the generation of aerosol spray from a covered 130 000 gallon pool (surface 15 × 4 metres) by pumps that recirculated the water flow from test rigs. All staff within the complex of buildings (n = 83) completed a screening questionnaire for symptoms, and attended for interview and clinical examination. Twenty employees had symptoms suggestive of a work related illness with pyrexia, shivering, profound tiredness, headache, muscle ache, and mild shortness of breath as the predominant symptoms. Every member of staff had passed through the suspect area of the building—known as the sump bay—on at least one occasion. On the basis of temporal exposure, 16 with symptoms worked close to the suspect area (out of 22). Four with lesser contact (out of 49) and none of those with least contact (who were mainly in the office area) had symptoms (χ^2 42·7, $p < 0.001$). Air sampling for organisms detected 8 colony forming units/m³ with the pumps off, and >10 680 cfu/m³ with the pumps on. A mixed growth of pseudomonads was present (*P putrifaciens*, *P testosteroni*). Venous blood was obtained from 76 of the employees and antibody to these organisms was present in 8/22 highly exposed, 14/42 moderately exposed, and in 2/11 of the group with least exposure. The development of symptoms was unrelated to the presence of antibody or smoking history that was confirmed by serum cotinine. Pulmonary function (FEV_1

and FVC) was normal in 77/81. Transfer factor was normal in all those with the fever symptoms. Chest examination was normal in 80/81. Chest radiology was normal in five subjects who were the highest exposed and most symptomatic including the only man who was ill enough to stop work. These findings superficially resemble humidifier fever, which also has a water based cause, but in this case the illness occurred in the absence of air conditioning, in a building designed around 750 metres of pipe of varying calibre and the sump bay that seemed to have been the cause.

Quality of self recorded peak expiratory flow

PFG GANNON, S DICKINSON, D HITCHINGS, PS BURGE ON BEHALF OF THE OCCUPATIONAL ASTHMA SYSTEM GROUP *Occupational Lung Disease Unit, Hartlands Hospital, Birmingham and Electrical and Electronic Engineering, Staffordshire University, Stafford* Little information exists on the quality of self recorded peak expiratory flows (PEF). Twelve workers with a suspected diagnosis of occupational asthma recorded PEF at and away from work with a self recording electronic PEF meter (Midland Thoracic Society). This dates and times each reading and records up to five readings per test session. A manual record was also kept including date and time of PEF to the nearest hour. On return six sets of records were technically unsuitable for analysis (for example, corrupted electronic memory). The remaining records (mean duration:19 days, mean number of readings per day: 7) were analysed. 99·2% of test sessions contained at least three PEF readings and 95·1% of sessions had a 5% reproducibility between the two highest PEF readings per session. In 92·6% of sessions the electronic memory confirmed that a reading had acutually been taken as manually recorded, 7·4% of manual readings were therefore probably falsified. The manually timed recording was out by one hour on 17·8% occasions (two hours in 2·1%). These results suggest that workers can carry out PEF readings to the recommended standard away from supervision. Occasional falsification of readings and errors of manual timing of up to two hours are unlikely to affect diagnosis of occupational asthma. More accurate timing is required for some forms of analysis such as spectral analysis. [PFG Gannon is supported by the Health and Safety Executive, UK.]

Computer assisted diagnosis of occupational asthma (OA)

PFG GANNON, DT NEWTON, J BELCHER, CFA PANTIN, PS BURGE *Occupational Lung Disease Unit, Hartlands Hospital, Birmingham and ICHRC, North Staffordshire Hospital Centre, Stoke* A computer assisted diagnostic aid, OASYS, for identifying work-related effects in serial peak expiratory flow (PEF) measurements, based on expert practice is under development. 86 PEF records from workers under investigation for possible OA were scored by an experienced observer. Each work or rest period was scored for changes consistent with OA. Scores ranged from 1–4 (1 = 0% chance of OA, 2 = 1–49%, 3 = 50 − 99%, 4 = 100%). 50 measurements of PEF change comparing each work or rest period with the surrounding periods were reduced by discriminate analysis to the most predictive measurements for the score for these periods. The analysis gave two formulae with which OASYS scored each period in a manner similar to the expert. The score for the whole PEF record was obtained by adding the period scores, with a weight for scores 1 and 4. The OASYS scores were compared with the experienced observer scores on a set of 40 new records. The results are shown in the table. The results are encouraging, the score produced by the observer being closely matched by OASYS. [PFG Gannon is supported by the Health and Safety Executive, UK.]

	OASYS overall score			
Observer	*1*	*2*	*3*	*4*
1 (n = 14)	7 (50%)	7 (50%)	—	—
2 (n = 9)	33 (33%)	5 (56%)	1 (11%)	—
3 (n = 8)	—	4 (50%)	4 (50%)	—
4 (n = 9)	—	—	6 (67%)	3 (33%)

Tuberculosis in a cohort of gold miners

RL COWIE *Department of Medicine, Ernest Oppenheimer Hospital, Welkom, South Africa* A cohort of 1153 southern African gold miners including 818 men with and 335 men without chronic simple silicosis were followed up for seven years by routine radiological surveillance and with a central tuberculosis diagnostic service and registry. Tuberculosis was diagnosed in 23 (1% per annum) of the men without silicosis and in 155 (2·7% per annum (pa)) of the men with silicosis. The relative risk for tuberculosis was 2·8 (95% CI 1·9–4·1) for the men with silicosis compared with the similar aged miners without silicosis. The risk of developing pulmonary tuberculosis increased with the extent of silicosis: 2·2% pa for category 1 nodule profusion, 2·9% pa for category 2 and 6·3% pa for category 3 (χ_2 9·8, df 2, p = 0·007). Extrapulmonary tuberculosis developed in 30 men and there was no significant difference in the proportion of extrapulmonary to pulmonary tuberculosis between the men with and those without silicosis. In a separate study which included 73 men with silicosis from the cohort, 240 miners with silicosis with category 2 or greater nodule profusion had Mantoux tests with 5 TU. The tests were positive (>9 mm induration) in 238 men: a prevalence of 99% tuberculin positivity in this population. It appears that these men with silicosis were highly susceptible to infection with *Mycobacterium tuberculosis* and had a roughly three fold increase in risk of developing pulmonary tuberculosis.

Long term efficacy of short course chemotherapy for pulmonary tuberculosis in men with silicosis

RL COWIE *Department of Medicine, Ernest Oppenheimer Hospital, Welkom, South Africa* There has been concern about the long term risk of relapse following short course chemotherapy for pulmonary tuberculosis in subjects with silicosis. In this study of gold miners, 549 consecutive cases of pulmonary tuberculosis assessed for the presence of silicosis at the time of the diagnosis of tuberculosis have been followed up since completion of treatment for tuberculosis. The men received streptomycin 1 g IM, rifampicin 600 mg, pyrazinamide 2 g and isoniazid 300 mg given daily on weekdays for 5 months. The last man included in the study completed treatment 5 years before 20 December 1992. A total of 167 of the 549 men had evidence of silicosis on their initial chest radiograph. All of the men were followed up to the time of their departure from mine service, relapse, or 20 December 1992 by the routine mine radiological surveillance for tuberculosis and by a central tuberculosis registry. A total of 29 of the 167 men with silicosis followed up for a total of 796 person-years and 43 of the 382 men without silicosis followed up for 1826 person-years suffered a relapse of their tuberculosis. The incidence density ratio for relapse of tuberculosis in men with silicosis was 1·55 (95% CI 0·97–2·48) that for the men without silicosis. There was no difference in the pattern of relapse over time between the two groups: the mean period to relapse in the men with silicosis was 2·6 (SD 1·89) years and for the men without was 3·1 (SD 2·23) years (p = 0·6). It seems that silicosis causes a small increase in the risk of relapse of tuberculosis that might justify an extension of the treatment period in such cases.

Lung function of workers seeking compensation for "welder's lung"

M MOHAN, SC STENTON, EH WALTERS, DJ HENDRICK *Regional Unit for Occupational Lung Disease, Newcastle General Hospital, University of Newcastle upon Tyne* After a recent court settlement, a large number of welders have been encouraged to seek compensation for "welder's lung" (chronic obstructive airways disease caused by exposure to welding fume, rather than siderosis). We have analysed the lung function of 82 such claimants (two women, median age 59 (range 28–78) years) referred for assessment by local solicitors. They had selected themselves because of a belief that welding fume had adversely affected their health. Their median exposure (exp) to welding fume was 25 (range 0–49) years. 55 had spent more than 30% of their time working in confined spaces. 24 were never smokers and 58 were current or ex-smokers. 64 complained of breathlessness (NYHA grade >0). Their postbronchodilator lung function expressed as median percentage of predicted (and range) is shown in the table. 55 (67%) of the claimants had normal lung function (within 1·65 SD of the mean predicted values). FEV_1, TLCO and KCO measurements were significantly lower in smokers than non-smokers (<0·01) but were not related to duration of welding fume exposure or work in confined spaces. 33 workers were thought by the assessing physician to have asthma or possible asthma. 18 had >15% reversibility of FEV_1 and 10 had reversibility in the range 10–15%. This might represent a high asthma prevalence among welders, or a selection bias making asthmatic welders more likely to

seek compensation. Together with the effects of smoking, it probably accounts for much of the airflow obstruction seen in these workers.

	Exp <25y	*Exp >25y*	*Never smoker*	*Smoker*
FEV_1	92 (35–127)	88 (31–139)	98 (51–139)	81 (31–137)
FVC	97 (51–126)	97 (53–165)	103 (65–131)	93 (51–165)
TLCO	96 (37–149)	94 (38–187)	108 (77–187)	83 (37–149)
KCO	111 (42–193)	107 (44–167)	118 (80–167)	102 (42–193)

Repeatability of provoked airway responses to occupational agents

BJ GRANEEK, JP HAYES, AJ NEWMAN TAYLOR *Department of Occupational and Environmental Medicine, National Heart and Lung Institute, London* Inhalation challenge tests with occupational agents are not generally standardised and methods employed are primarily dictated by experience. Whereas occupational asthma is a good model for study purposes, interpretation of dose response data is dependent on the repeatability of provocation test methods. With the method of Bland and Altman (*Lancet* 1986;307–10) we have investigated the repeatability of early (up to one hour) and late (one to 10 hours) phase changes in FEV_1, and changes in histamine PC_{20} at 24 hours after inhalation challenge with various occupational agents (isocyanates four patients, colophony four patients, wood dust one patient, platinum salt one patient). All 10 patients (seven male, three female) underwent two single blind challenges for diagnostic purposes to the same exposure at the same time on different days. Histamine responsiveness was measured prechallenge and 24 hours postchallenge in nine patients. Prechallenge histamine PC_{20} values were within one doubling concentration of each other. Airway responses were measured as the maximum % fall in FEV_1 from baseline during the early and late phases. For the early phase mean % fall was 22·7%, mean difference +1, SE of difference 1·85, and coefficient of repeatability 11·7. For the late phase mean % fall was 15·5%, mean difference +1·2, SE of difference 1·64, and coefficient of repeatability 10·4. For changes in PC_{20} at 24 hours expressed as doubling concentrations, mean change was −0·97, mean difference −0·12, SE of difference 0·25, and coefficient of repeatability 1·4. When considering future dose response studies, these results are more encouraging than those associated with allergen challenge, despite better standardisation of the latter methods. Variability may reflect population size.

Hospital admissions for asthma in relation to a sugar beet factory in Kidderminster

S WALTERS, J JACKSON, J AYRES, C BILLINGHAM *Institute of Public and Environmental Health, University of Birmingham Medical School, Chest Research Institute, Birmingham Heartlands Hospital, and West Midlands RHA Information Department, Birmingham* The standardised hospitalisation ratio for asthma was noted to be high in Kidderminster DHA during routine study. We investigated a reported association with a sugar beet factory. Processing takes place between the months of October and February. This was studied using Korner inpatient data for 1988–91 for the residents of Kidderminster DHA. There was a peak of asthma admissions between October and February among children <15 living in Kidderminster that was not seen in the rest of the West Midlands, nor for other diagnoses in Kidderminster residents. There were 7·9% (95% CI 3·4%–12·4%) more asthma admissions between October and February in Kidderminster than in the rest of the Region. Four groups were studied by computer mapping of postcodes: group A (n = 433), children <15 admitted to hospital for asthma; group B (n = 177), children <15 admitted to hospital for other acute respiratory conditions; group C (n = 909), random sample of acute non-respiratory hospital admissions in children <15 (hospital controls); group D (n = 461), random sample of children <15 from the FHSA register (1992) (community controls). The proportion of asthma admissions living <1 km and ⩾1 km from the factory were compared with the same proportions in each control group. The odds ratio (OR) for asthma (group A) against community controls was 1·52 (95% CI 1·02—2·25, $p < 0·05$), and for asthma against hospital controls was 1·46 (1·05–2·04, $p < 0·05$). The OR was not significantly raised for a similar analysis for other respiratory admissions (group B). When potential confounding effects of other factories to the north were removed by inclusion only of residents living within 2·5 km of the factory, the ORs were even higher, 2·36 (1·49–3·75, $p < 0·05$) and 1·71 (1·14—2·56, $p < 0·05$), respectively. The raised ORs and unusual seasonality of admissions suggest that emissions from the sugar beet factory may be affecting the health of children with asthma in this area of Kidderminster.

Effect of an air pollution episode on respiratory function of patients with asthma

S WALTERS, J MILES, JG AYRES, G ARCHER *Institute of Public and Environmental Health, University of Birmingham Medical School, and Chest Research Institute, Birmingham Heartlands Hospital* An unusual pollution episode occurred in Birmingham between 17 and 27 December 1992. Levels of sulphur dioxide (SO_2) rose to 130 parts per billion, respirable particulates (PM 10) to 231 $\mu g/m^3$ and nitrogen dioxide (NO_2) to 207 ppb. As part of their participation in other studies, 24 patients with asthma living within 5 km of the enhanced urban air quality monitoring station in Birmingham were keeping peak flow records. 10 patients were recruited from general practice with mild asthma (mild group) (median age 50, seven males and three females) and 14 patients from the West Midlands brittle asthma register (severe group) (median age 38·5, five males and nine females, mean inhaled steroid dose 2214 μg/day). The peak flow records were analysed to evaluate the effects of the pollution episode. The level of statistical significance accepted was 1%. Bivariate linear regression showed no significant association between maximum daily levels of any pollutant and mean morning or evening prebronchodilator peak flow for patients in the mild group. In the severe group some significant negative correlations were found. Maximum NO_2 showed strongest negative correlation with morning peak flow four days later ($r = -0·57$, x-coeff, −0·82, 99% CI ± 0·13). Maximum PM10 showed the strongest negative correlation with morning peak flow four days later ($r = -0·57$, x-coeff −0·14, 99% CI ± 0·10). No significant associations were noted between SO_2 and peak flow. In the mild group there was no significant difference between mean morning and evening peak flow rate in the period before and during the episode, lagged by two days to allow for the delayed effect of air pollution on respiratory function. In the severe group, the mean morning peak flow rate was 15·5 l/min less (99% CI 5·3–25·7) and the evening peak flow rate 27·3 l/min less (99% CI15·6–38·9) during the episode than before the episode, lagged by two days. Bronchodilator usage and oral prednisolone dose also increased in response to the episode in the severe group. Patients with severe asthma showed significant adverse health effects as a result of this pollution episode.

Audit of chest clinic investigations of patients referred with a suspected diagnosis of asthma

IJ WILLIAMSON, CJ CLARK *Department of Respiratory Medicine, Hairmyres Hospital, East Kilbride* The symptoms of asthma vary widely and patients at the time of first clinic presentation may have no evidence of airflow obstruction. We audited the investigations performed in this specific subgroup of patients who attended the chest clinic over a two year period, to determine which were of benefit in establishing a diagnosis of asthma. Patients in whom asthma had been previously diagnosed, or had a FEV_1/FVC ratio <70% at referral were excluded from audit. 107 patients (48 males) were included, age 33 (16) years, FEV_1 (% predicted) 98·5 (12·7)% and FEV_1/FVC 83 (6·7)% (mean (SD)). Despite normal spirometry, additional measures of lung function revealed 28 patients to have evidence of small airways obstruction or air trapping as denoted by a low $FEF_{25-75\%}$ or a raised RV/TLC ratio. 74 patients had bronchial hyperreactivity defined as a histamine PC_{20} <8 mg/ml. Exercise challenge testing was performed in a subgroup of 29 patients in whom there was a strong suspicion of exercise induced asthma. This was confirmed in only eight patients although 18 had a histamine PC_{20} <8 mg/ml. Skin prick testing was positive in 53% of patients and was found to be more sensitive than RAST IgE levels in assessing atopic state. This study suggests that a district general hospital chest clinic can obtain additional data relevant to the diagnosis of asthma if full lung function and histamine challenge testing are available for patients in whom simple dynamic spirometry is normal. The results of such investigations may offer an alternative to, or complement the information obtained from, outpatient serial peak flow monitoring and also have the benefit of being obtained at a single clinic visit.

Peak flow variability and asthma severity

JP JAMISON, RK MCKINLEY *School of Biomedical Science, Medical Biology Centre, Queen's University of Belfast, Belfast* Asthmatic subjects (n = 123), aged 10–70 years, recorded their peak expiratory flow (PEF) three times daily for 12 days. Several indices of PEF and its variability were correlated with a severity score (range 0–40), the sum of four symptoms and four limitations of lifestyle due to asthma, each graded 0–5 (*Soc Sci Med* 1987;**25**:1033–8). Significant negative linear correlations with the severity score were obtained for the minimum and maximum PEF on the day of greatest variability, the overall mean PEF for the 12 days, and the FEV_1 ($r < -0{\cdot}3$, $p < 0{\cdot}0003$). There were significant positive linear correlations with the severity score for PEF amplitude variability as a percentage of minimum, maximum, or mean PEF ($r > +0{\cdot}2$, $p < 0{\cdot}02$). Wheeze was best correlated with PEF variability and exercise limitation was best correlated with the FEV_1. Variability of PEF amplitude, if uncorrected for baseline PEF, was not linearly dependent on the severity score ($r = +0{\cdot}07$, $p = 0{\cdot}43$), increasing with severity at low scores and decreasing again at high scores (quadratic coefficient = $-0{\cdot}17$, $p = 0{\cdot}01$). Similar curvilinear dependency on the severity score was obtained for PEF amplitude variability as a percentage of predicted PEF. These data suggest that PEF variability is a suitable index of asthma severity when the PEF variability is expressed as a percentage of some measure of the subject's actual baseline PEF.

Regression coefficients (95% CI); $Y = a + b$ (severity score)

Y	*a*	*b*
FEV_1 (% predicted)	92	−1·11 (−1·69 to −0·52)
Minimum PEF (% predicted)	86	−1·14 (−1·69 to −0·59)
Maximum PEF (% predicted)	109	−1·10 (−1·66 to −0·54)
Mean PEF (% predicted)	101	−1·13 (−1·70 to −0·56)
PEF amplitude (1/min)	96	+0·47 (−0·69 to +1·63)
PEF amplitude/minimum PEF (%)	27	+1·00 (+0·25 to +1·75)
PEF amplitude/maximum PEF (%)	22	+0·38 (+0·08 to +0·68)
PEF amplitude/mean PEF (%)	24	+0·49 (+0·08 to +0·90)
PEF amplitude/predicted PEF (%)	24	+0·04 (−0·23 to +0·32)

What do general practitioners carry for the assessment and treatment of asthma?

SA EVANS, JM STONER, CC HARDY *Unit M6, Manchester Royal Infirmary, Oxford Road, Manchester and Peterloo Medical Centre, Middleton* The British Thoracic Society (BTS) guidelines on asthma management (*BMJ* 1990;**30**:651–3 and 797–800) were issued in response to the unacceptably high morbidity and mortality associated with asthma in the United Kingdom. They suggest how acute severe asthma should be assessed and treated. To determine if the equipment and drugs routinely carried by general practitioners (GPs) are appropriate for this, a brief questionnaire was sent to the 102 GPs on the medical list of the Rochdale Family Health Services Authority. 64 GPs responded. 55% carry peak expiratory flow meters (PEFM), 38% spacing devices, 23% nebulisers, and 50% either a spacing device or a nebuliser. The % of respondents carrying each drug was β agonists: metered dose inhaler (MDI) 84%, nebules 20%, and intravenous preparation (iv) 60%; anticholinergic drugs: MDI 21%, nebules 5%; steroids: oral 70%, iv 66%, 88% carrying steroids in some form; theophylline: oral 28%, iv 38%; adrenaline: 73%. 56% of respondents said they would never consider using adrenaline for the treatment of acute asthma. The BTS guidelines suggest PEF as a useful criteria for assessing asthma and making treatment decisions, but little more than half the respondents carried a PEFM. Whereas the high % of respondents carrying steroids is encouraging, the fact that half carried neither a spacer nor a nebuliser suggests probable excessive reliance on the intravenous route for the administration of bronchodilator treatment. Also there is a reluctance to consider the use of adrenaline even in life threatening asthma. It seems that the assessment and treatment of acute asthma by GPs is often suboptimal, and suggests that the BTS guidelines have made little impact on current practice in the community.

Management of acute asthma in the accident and emergency department: how practical are the guidelines?

JM MEIGHAN, VHF MAK, DJ WILLIAMS, NT BATEMAN *Departments of Thoracic Medicine and Accident and Emergency, St Thomas' Hospital, London* The British Thoracic Society (BTS) guidelines for the management of acute asthma in the accident and emergency (A and E) department involve (i) recognition of severity, (ii) use of objective measurements, and (iii) careful assessment of response to treatment. To evaluate how practical and successful these guidelines are in a busy A and E department, we carried out a study over a four month period of patients presenting to A and E with acute asthma. The A and E case notes of 67 consecutive adult patients were analysed retrospectively to determine how far the BTS guidelines were being followed. The BTS guidelines suggest using percent predicted or percent of previous best PEF values as an objective indicator of severity. In the 66 cases where PEF on arrival was recorded, there was no indication of how this value compared with predicted or best, despite tables for predicted PEF being readily available. If the patient improved after nebulised bronchodilators, none had a further repeat assessment of the PEF after one hour as recommended. Of the 54 patients who were discharged, there was no record of whether inhaler technique was checked in 45 (83%) patients. Eighteen patients (33%) were discharged without oral corticosteroids, only four of whom had an estimated percent predicted PEF of more than 75%. Two of these 18 patients did not receive any form of anti-inflammatory treatment (one of whom did not have bad asthma on arrival), three had inhaled steroid treatment introduced, three were told to take previously prescribed inhaled steroids, and four had their inhaled steroid dose increased. Twelve patients were given oral corticosteroids without addition of inhaled steroid treatment. All but one patient were given a letter for their general practitioner. In conclusion, asthmatic patients discharged from the A and E department are not assessed for maintained improvement after nebuliser treatment. Very few have their inhaler technique checked as a cause of treatment failure, and some were discharged without appropriate anti-inflammatory treatment. This could be due to the time constraints placed upon the casualty officers and nurses in a busy A and E department.

Primary care after treatment for acute asthma in the accident and emergency department: are the British Thoracic Society guidelines being followed?

JM MEIGHAN, VHF MAK, NT BATEMAN *Department of Thoracic Medicine, St Thomas' Hospital, London* If a patient attends the accident and emergency (A and E) department with acute asthma, this may imply failure of prior treatment. These patients should be identified as requiring more careful monitoring and reappraisal of their treatment. The British Thoracic Society (BTS) guidelines for the management of asthma suggest a stepping up or down of treatment according to a monitored response. To investigate whether the BTS guidelines are being followed in primary care for this at risk group, we undertook a retrospective study of patients registered to local GPs who attended our A and E department for acute asthma over a four month study period. The GP records of these patients were analysed three weeks after their A and E visit to assess if there was adequate monitoring of the patient's asthma, and if there were appropriate changes to treatment in response to the clinical state. The study was performed with the full cooperation of the GPs, and the retrospective nature meant that we did not influence the management of the patients in the study. We managed to follow up 41/54 patients who were discharged from A and E. All patients were given letters for their GP and told to visit them within one week; 32/41 of these were received. Of these 41 patients, only one reattended the A and E department within three weeks. Sixteen patients were monitoring peak flows before their A and E visit, six patients were prescribed home peak flow meters on discharge from A and E, and all of these continued to use them. Four patients were using self management plans before the A and E visit, two patients were given one on discharge, and a further two by their GPs after their A and E visit. Of nine patients whose asthma control was deteriorating, two had stopped taking inhaled corticosteroids (ICS), two were not taking any prophylactic treatment, and the other six remained on their current dose of ICS. Of 32 patients who were stable or improving, six were not taking any form of prophylactic treatment, seven actually stopped taking ICS, 13 remained on the same dose, two had an increase, and two had a reduction in their ICS dose. In conclusion, despite the existence of BTS guidelines for over two years, their recommendations are still not being acted upon, even in an at risk group.

In acute severe asthma is arterial blood gas analysis always essential or can measurement of arterial oxygen saturation be used to determine which patients require blood gas measurement?

DM CURRUTHERS, BDW HARRISON *Department of Respiratory Medicine, West Norwich Hospital, Bowthorpe Road, Norwich* We aimed to determine whether arterial oxygen saturation (Sao_2) as recorded by pulse oximeter in patients admitted with acute severe asthma was a safe and reliable method of predicting those in respiratory failure and therefore in need of more aggressive management. We aimed to define the Sao_2 below which arterial gases should be taken for safe asthma management. Arterial blood gases and Sao_2 by pulse oximeter were measured in seventy five patients admitted consecutively with acute severe asthma to our respiratory medical ward. Measurements were made either on or off oxygen at the initial assessment, along with other indices of asthma severity. Results show that 62 out of 75 patients had an $Sao_2 \geqslant 92\%$. Only two of these 62 had a $Pao_2 < 8$ kPa and one other had a $Pao_2 > 6$ kPa. None of the others had arterial blood gases indicating respiratory failure. When an $Sao_2 \geqslant 90\%$ is considered (70 out of the 75 patients) then six had blood gases indicating respiratory failure. It seems that in the initial assessment of acute asthma an $Sao_2 \geqslant 92\%$, as measured by pulse oximeter, indicates that respiratory failure is unlikely and therefore measurement of arterial blood gas is unnecessary. We recommend that blood gases should be taken in patients who have an $Sao_2 < 92\%$ and in other patients whose condition deteriorates as assessed by other standard criteria no matter what the initial Sao_2.

Effect of inhaled corticosteroids on blood spot cortisol concentrations in asthmatic children

IJM DOULL, SJ DONOVAN, PJ WOOD, ST HOLGATE *University Medicine and Regional Endocrine Laboratory, Southampton General Hospital, Southampton* Conventional dynamic testing of the hypothalamic-pituitary-adrenal axis shows little measurable effect in asthmatic patients on normal doses of inhaled steroids. We have developed a new method of measuring cortisol by fingerprick on to blotting paper. This is acceptable to children and has excellent correlation with conventional plasma cortisol assays ($r = 0{\cdot}965$). We used it to assess the effect of inhaled steroids on daytime cortisol. 20 mild to moderate asthmatic children aged 7 to 9 years were randomised to receive double blind either placebo or beclomethasone dipropionate (200 μg twice daily). Blood was taken by fingerprick immediately on waking in the morning (T1), and treatment was given. Blood was then taken at one hour after treatment (T2), at lunchtime (T3), and in the evening (T4). Area under the curve (AUC) for the four time-points was calculated as a composite index of daytime cortisol. Blood spot cortisols fell progressively during the day at each time from a mean of 226·8 nmol/l at T1 to 56·4 nmol/l at T4. Mean cortisol in the steroid treated group was lower at times T1, T2, and T3 but reached significance only at T2 (111·5 *v* 203 nmol/l, $p < 0{\cdot}04$). Mean AUC for the steroid treated group was significantly decreased (487 *v* 333, $p < 0{\cdot}03$). Thus blood cortisol is significantly decreased immediately after inhalation of steroid and, furthermore, composite daytime cortisol is significantly decreased.

Serum magnesium in elderly inpatients with acute asthma

DS RENWICK, MJ CONNOLLY *Robert Barnes Unit, Manchester Royal Infirmary* Intravenous magnesium (Mg) supplements can produce bronchodilatation in hypomagnesaemic asthmatic patients. Magnesium deficiency may be common in the elderly. We have assessed serum Mg in acute elderly asthmatic inpatients >65 years with acute asthma (suggestive history plus 15% peak flow (PEF) variability). Those with smoking history >10 pack years, renal failure, or recent change of diuretic were excluded. On admission serum electrolytes including Mg, evidence of chest infection (pyrexia, high white cell count, chest *x* ray film changes), and PEF response to nebulised bronchodilators were measured. 29 subjects were studied (21 women), mean age 78·9 (range 69–92) years. Mean serum Mg was 0·82, range 0·59–1·01 (normal 0·6–1·0) μmol/l. Mean Mg of a group of elderly controls (mean age 79·9) was 0·75 μmol/l (NS). Serum Mg was not lower in subjects on diuretics and was not related to PEF response. 20 subjects had evidence of chest infection (group A), nine subjects did not (group B). Serum Mg and potassium (K) concentrations were significantly higher in group A than group B (see table). Serum Mg was higher in group A than in controls ($p = 0{\cdot}008$). Acute asthma in the elderly is not associated with hypomagnesaemia. Patients with chest infection have higher serum Mg than non-infected patients and controls; this may reflect electrolyte changes associated with infection. Measurement of serum Mg does not contribute to the management of elderly patients with acute asthma.

	Mean Mg (SE)	*Mean K (SE)*
Group A (μmol/l)	0·86 (0·02)	4·3 (0·15)
Group B (μmol/l)	0·73 (0·03)	3·8 (0·17)
p	0·003	0·04

Group therapy in the management of chronic severe asthma

JF MILES, G GARDEN, JG AYRES *Chest Research Institute, Birmingham Heartlands Hospital, Birmingham* Psychological morbidity in severe asthma has been well documented but there have been few interventional studies undertaken in adult asthma. We studied eight patients (six women), mean age 44 (range 19–68) years, with well characterised severe asthma who attended weekly group sessions for six months in the presence of a facilitator. Each patient completed three questionnaires covering various psychological variables (GHQ60, Living with Asthma Questionnaire, Asthma Symptom Checklist) and were interviewed about their coping skills with asthma (Sibbald, *Thorax* 1989), at the beginning and the end of the six month period covering the months of May to October 1992. Eight age/sex and treatment matched patients with severe asthma who did not attend the group also completed the above assessments. Objective measures of lung function were measured at their routine outpatient visits over the study period. No significant changes in coping strategies during attacks occurred over the six month period. Patients' knowledge of what they should do during attacks differed greatly from what they actually did. At a point when oral steroids should have been started, 13 out of the 16 patients delayed, although recognising that use of steroids was appropriate. All 16 patients delayed seeking medical attention because they knew that the consequence of so doing would be admission to hospital. Reported use of oral steroids was comparable in the two groups over the six months before the intervention (mean dose per month 249 *v* 247 mg) but fell significantly to a mean of 141 mg/month in those attending the group and rose to a mean of 379 mg/month in the non-attenders. At the end of the six month period there was a significant improvement in the GHQ score in the active group (31·6 to 14·7, $p < 0{\cdot}003$) compared with the controls (19·5 to 18·2, $p = 0{\cdot}84$). No consistent difference was seen in the other two questionnaires. No changes in mean group FEV_1% could be shown (active 65·6 to 63·7, $p > 0{\cdot}87$; passive 68·4 to 64·2, $p > 0{\cdot}76$).

Choosing an alternative to the metered dose inhaler: the patient's preference

D DOCKRELL, M ROONEY, P KELLY, L CLANCY *Peamount Hospital, Newcastle, Co Dublin, Ireland* 43 patients with chronic obstructive airways disease/asthma and 20 normal controls were instructed in the use of all inhaler devices. Questionnaires were administered to determine preference in learning, inhaler technique, and overall preferred device. 63 people took part in the study and the results are shown in the table. Certain devices are obviously more preferred by patients. They are easier to learn and more acceptable to use. Patient compliance will be improved by prescribing devices that they would prefer.

Most preferred device		*Easiest device to learn to use*	
Autohaler	20	Autohaler	22
Turbohaler	15	Turbohaler	18
MDI	14	MDI	6
Rotahaler	6	Rotahaler	5
Volumatic	3	Volumatic	2
Spinhaler	2	Spinhaler	8
Dischaler	2	Dischaler	1
		Haleraid	1
Adequate inhalation technique			
Autohaler	58	Spinhaler	51
Turbohaler	57	Dischaler	57
MDI	39	Haleraid	43
Rotahaler	56	Nebuhaler	56
Volumatic	57	Spacer	50

β_2 agonist dose reduction: strategy and early results

MJ PETERS, DH YATES, KF CHUNG, PJ BARNES *Department of Thoracic Medicine, National Heart & Lung Institute, Dovehouse St, London*
The use of high doses of inhaled β_2 agonists has been associated with an increased risk of death from asthma, accelerated decline in lung function and increased asthma morbidity. The excess risk of death seen with the more potent β_2 agonist, fenoterol, in comparison with salbutamol, was greatest with nebulised treatment. The use of 50 puffs of salbutamol per week has been associated with a doubling in the risk of asthma death, yet an equivalent amount of nebulised salbutamol is used at one or two doses. By inference, reduced β agonist consumption may improve asthma control but rapid reduction from high doses arouses reasonable concern in both physician and patient. We have used a five stage outpatient strategy to evaluate, in an open study, the effects of β agonist dose reduction. Phase 1: Long acting and oral β agonists are tapered or ceased; phase 2: 5 mg salbutamol doses are changed to 2·5 mg, at most four/day; phase 3: 2·5 mg doses are sequentially replaced with four puffs from an MDI; phase 4: the number of MDI puffs per dose is halved to two; phase 5: salbutamol is used as required only. Intervals between reductions are at least three weeks. At entry, inhaled steroids are increased to at least 1500 μg BDP (subject 5 only—from 1000 μg) or else not changed. Anticholinergics and theophylline are not changed. Oral steroids may be reduced in parallel. Eight patients have been recruited of whom five have been followed up for over three months. Data at baseline and latest follow up are shown. To this time, no complication has occurred. No patient has been kept in hospital with asthma. With this protocol, reduction in β agonist use may be achieved without hospital but the frequent outpatient visits are time consuming for all involved. The rate of reduction seems to be safe and has proved acceptable to patients. In this group, it has been associated with reduction in oral steroid requirement and/or improvement in lung function but coincidental change and/or placebo effect cannot be excluded in this open study. Although not a primary aim, there is an annualised cost saving for pharmaceuticals of £1230 (410) per patient. Cautious attempted reduction in β agonist use should be further evaluated as a cheap, non-toxic alternative to methotrexate or cyclosporine.

	Baseline				Follow up			
Age/ Sex	Years on nebuliser	Salbutamol (mg/day)	Prednisone (mg/day)	FEV_1 (% pred)	Duration (months)	Salbutamol (mg/day)	Prednisone (mg\day)	FEV_1 (% pred)
58/M	7	6·6	37·5	34	16	0·4	25	34
36/F	6	31	20	39	12	0	5	34
44/F	5	28	15	29	9	3	15	59
56/F	13	15	5	48	7	7·5	5	49
58/F	6	20	25	50*	4	0·8	15	94

*Predicted PEF: this patient cannot perform spirometry.
[MJP is an Allen and Hanburys/Thoracic Society of Australia and New Zealand Travelling Fellow.]

Retrospective review of the use of budesonide nebuliser solution (Pulmicort Respules) in the treatment of chronic severe asthma

S BUTTERFIELD, G BOOTE, S MARGEL, ST ATHERTON, DR GRAHAM *Whiston Hospital, Prescot, Merseyside*
There are few published data available on the efficacy and side effects of budesonide nebuliser solution (Pulmicort Respules, Astra). This study on 37 asthmatic patients (13 males, 24 females) examined our experience with this new preparation. Patients received the drug for a mean of 18·5 (range three–46) weeks. A questionnaire was used to compare symptoms before and after treatment with budesonide. Objective measurements included FVC, FEV_1, PEF. Concurrent treatment before and after budesonide treatment was also examined. Symptom scores improved in 17 patients, 15 were unchanged, and five became worse. Mean FVC before treatment was 2·66 (0·81) l compared with 2·82 (0·8) l while on budesonide. FEV_1 improved from 1·88 (0·67) l to 2·02 (0·72) l on treatment. Peak expiratory flow rate was more variable, however, and there was an overall impression of improvement (before 266(118) and 397(97) l/min after). Thirty three patients were on oral steroids. There was a fall in the daily mean dose of prednisolone before treatment from 24·9 (13·3) mg to 13·2 (8·6) mg on nebulised budesonide ($p < 0·001$). There was a high incidence of side effects, which occurred in 26 out of the 37 patients, they reported nose bleeds, sore throat, and headache. Side effects were severe enough to stop treatment in 14 patients (two due to pregnancy). Nebulised budesonide seems to be effective, providing improved control of chronic severe asthma with decreased oral prednisolone. This effect may be due directly to inhaled steroid deposition in the lung or could be due to increased systemic absorption from the stomach. Further prospective evaluation of this expensive preparation is required before it becomes part of accepted practice in the treatment of asthma.

Trial of a "credit card" asthma self management plan in adult asthma

W D'SOUZA, C BURGESS, C CULLING, M AYSON, N PEARCE, J CRANE, R BEASLEY *Department of Medicine, Wellington School of Medicine, Wellington, New Zealand*
The aim of this study was to assess the efficacy of a credit card asthma self management plan in a high risk group of asthmatic patients. In an open prospective trial adult asthmatic patients treated and discharged for acute asthma in the emergency department of Wellington Hospital were invited to attend a series of hospital outpatient clinics at which the "credit card" asthma self management plan was introduced. The "credit card" plan uses guidelines for the self management of asthma based on patient self assessment of PEF recordings and symptoms, printed on to two sides of a plastic "credit card". Questionnaires were used to compare markers of asthma morbidity and use of medical care six months before and six months after intervention with the "credit card" plan. Of the 30 eligible patients who attended the first outpatient clinic, 26 (21 female) completed the programme. Among these 26 participants the proportion waking with asthma more than once a week decreased from 65% to 23% ($p = 0·005$), the proportion reporting a day "out of action" decreased from 58% to 19% ($p = 0·01$), and the proportion visiting the emergency department with acute asthma decreased from 58% to 15% ($p = 0·04$). Other markers of medical care utilisation also improved. Our findings suggest that the "credit card" asthma self management plan can be an effective and acceptable system for self managing asthma, when used as part of an asthma educational programme.

Assessment of peak flow monitoring on respiratory wards

MB ALLEN, C PRASAD, RL PAGE, SP PEARSON, MF MUERS *Department of Respiratory Medicine, Killingbeck Hospital, Leeds*
Peak flow (PF) measurements are important in monitoring the response to treatment in patients with airflow obstruction admitted to hospital. Such measurements are usually made by the patient under nurse supervision. We have attempted to determine the accuracy of this monitoring. Fifty eight patients performing PF measurements on three chest wards in two hospitals were assessed. The highest and mean of three previously recorded routine nurse supervised blows were compared with three doctor supervised blows by the same study doctor (CP), with the patient's own Mini Wright (MW) meter. The comparisons were made within 30 minutes of each other and always more than four hours after inhaled bronchodilators. The nurses were unaware of the study objectives. Also, three blows with the standard Wrights (SW) meter were obtained by the doctor. Mean (SD) results were calculated for the 58 patients and compared by means of the paired *t* test and Bland and Altman plots. The mean difference between the nurse and doctor supervision was 11·1 l/min for the highest blow and 15·5 l/min for the mean of three blows. These results confirm that the MW overestimates PF in the range of our subjects. "Routine" PF measurements were significantly lower than those obtained by the study doctor, although the differences for both the highest and mean values are probably too small to be of clinical significance.

PF	1 Nurse (MW)	2 Dr (MW)	3 Dr (SW)	p value (2 v 1)	(3 v 2)
Highest(l/min)	200 (104)	211 (110)	174 (101)	0·016	0·001
Mean (l/min)	183 (102)	299 (108)	168 (96)	0·003	0·001

Reference equations for spirometric indices in native Nigerian men

GE ERHABOR *Respiratory Department, Bristol Royal Infirmary, Bristol*
Presently there are few reference equations available for spirometric indices in native Nigerian men. Measurements of peak expiratory flow (PEF, l/min), forced expiratory volume in one second (FEV_1,

litres) and forced vital capacity (FVC, litres) were obtained in 241 male subjects who had a normal clinical examination, chest *x* ray film, and no history of cardiorespiratory disease. PEF was measured on a Wright meter, and FEV_1 and FVC were measured on a wedge-bellows spirometer. The age range was from 19 to 60 (mean 29·9) years and standing height from 1·54 to 1·93 (1·71) m. Dynamic lung volumes and PEF significantly decreased with increasing age and significantly increased with increasing height. Regression analysis of each index against Ht and age gave the equations:

PEF = 358Ht − 1·28Age − 33·9	RSD = 53·7 r^2 = 0·228
FEV_1 = 3·85Ht − 0·28Age − 2·50	RSD = 0·50 r^2 = 0·393
FVC = 4·62Ht − 0·24Age − 3·42	RSD = 0·56 r^2 = 0·368
FEV% = − 0·21Age +92·8	RSD = 5·39 r^2 = 0·111

where RSD is the residual standard deviation and FEV% is the FEV_1/FVC. These relations were not improved by the inclusion of body mass and various transformations and interactions of age, standard height and body mass. Comparison of these equations with the European summary equations showed that, although the decline in dynamic lung volumes with age was similar, the FEV_1 and FVC were about 20% lower in Nigerian men. For PEF, there was a smaller decrease with age in Nigerian men than in European men, with PEF values being 6% lower at age 20 and 3·5% higher at age 60. [G E Erhabor is a British Thoracic Society Overseas Fellow.]

Inspiratory muscle strength assessed by occlusion of mouth pressure twitches induced by magnetic stimulation of cervical nerve roots

PF DE BRUIN, A WATSON, NB PRIDE *Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London* Cervical magnetic stimulation (CMS) has been shown to induce maximum activation of the diaphragm (Similowski *et al. J Appl Physiol* 1989;67:1311–8). We have examined the reliability of mouth pressure twitches elicited by CMS in the assessment of inspiratory muscle strength by obtaining simultaneous measurements of transdiaphragmatic, oesophageal, and mouth pressure twitches (PdiT, PoesT, PmoT) in five normal men (mean age 32·2(SD 1·8) years). Subjects were studied on two separate days, seated, with the neck flexed 60° from the vertical and breathing through a mouthpiece. CMS was produced by a magnetic stimulator connected to a 90 mm diameter coil (Magstim 200, Magstim Comp, UK). Single supramaximal stimuli were delivered at FRC during relaxation and while performing graded voluntary isometric inspiratory efforts against a closed airway. As voluntary effort transdiaphragmatic pressure (Pdi) increased, PdiT decreased linearly (lowest $r = 0·87$). The relationship between voluntary oesophageal pressure (Poes) and PoesT was similar (lowest $r = 0·89$). PmoT during relaxation was unreliable due to poor transmission of intrathoracic pressure, but during all voluntary efforts the relation between voluntary mouth pressure (Pmo) and PmoT was also linear (lowest $r = 0·84$) and very close to Poes *v* PoesT (table). On average, our subjects voluntarily generated 99, 101, and 101% of the maximum Pdi, Poes, and Pmo estimated by extrapolating the equations above to the x axis. These studies confirm that CMS induces maximum activation of the inspiratory muscles. Twitch pressures induced by CMS can be assessed at the mouth in normal subjects, providing a simple and non-invasive technique for estimating true maximum strength of the inspiratory muscles.

	PmoT = a + b × Pmo		*PoesT = a' + b' × Poes*		*PdiT = a" + b" × Pdi*	
	(cmH_2O) *a*	*(%max)* *b*	*(cmH_2O)* *a'*	*(%max)* *b'*	*(cmH_2O)* *a"*	*(%max)* *b"*
Day 1	17(4)	−0·15(0·04)	18(3)	−0·16(0·04)	24(5)	−0·19(0·05)
Day 2	18(2)	−0·15(0·04)	18(3)	−0·15(0·04)	24(3)	−0·17(0·04)

[PF De Bruin is supported by the Cons Nac Des Cient Technológico-CNPq of Brazil.]

Effect of anterior spinal surgery via a thoractomy incision on lung volumes in idiopathic scoliosis

WJM KINNEAR, L WATSON, JK WEBB, IDA JOHNSTON *Harlow Wood Orthopaedic Hospital, Mansfield and University Hospital, Nottingham* In patients with idiopathic thoracic scoliosis, correction of the spinal curvature by posterior instrumentation leads to a small increase in vital capacity (VC). We have investigated whether this is also true when the spine is approached anteriorly through a thoracotomy incision. We studied 10 patients (nine women) median (range) age 30 (23 to 39) years and pre-op Cobb angle of 60 (38 to 110) degrees. All were over 18 years of age at the time of operation. Lung volumes were measured with a wedge spirometer (Vitalograph) for VC and helium dilution (PK Morgan) for residual volume (RV), functional residual capacity (FRC), and total lung capacity (TLC). Preoperative VC was 76 (39 to 100)% predicted. Nine patients had a Zielke procedure and one an anterior release. Four subsequently also underwent posterior instrumentation. Lung volume measurements were repeated, with the same equipment, at least one year after surgery. Compared with preoperative values, postoperative VC was −0·125 (+0·05 to −0·65) litres ($p < 0·05$) and RV was +0·135 (−0·03 to +0·28) litres ($p < 0·01$). TLC and FRC were not significantly different. Anterior spinal surgery leads to a fall in VC. This seems to be related to an increase in RV, the reasons for which are unclear, as correction of ribcage deformity should increase chest wall compliance and lead to a fall in RV.

Excursion-volume relation of the diaphragm measured by ultrasonography with a fixed transducer: normal values

E COHEN, P HEYWOOD, K MURPHY, J BOULTBEE, A GUZ *Departments of Medicine and Radiology, Charing Cross and Westminster Medical School, London* We have used a new technique to assess the relation between diaphragmatic excursion (DE) and different inspired volumes (V_T) using simultaneous M-mode ultrasonography and pneumotachography. A specially designed frame was built to hold the transducer in a fixed position. All studies were carried out in the supine position. Fifteen normal subjects were tested (ages 22 to 73 years, seven women). In 10 subjects, excursion of the right and left posterior hemidiaphragms was measured in a coronal plane with V_T varied up to 1·2 1 above functional residual capacity (FRC). At a larger V_T the diaphragmatic view was obscured. Measurements in the longitudinal plane subcostally were carried out in 10 subjects on the right side only, as the view of the left hemidiaphragm is obscured by air in the stomach. In this position V_T varied up to 3 1 above FRC. Results are summarised in the table. Measurements in the coronal plane were larger ($p < 0·05$) than in the longitudinal plane due to an angle between the M-mode line and the cephalocaudal movement of the diaphragm. Confirming the results of Houston *et al*, British Thoracic Society winter meeting, 1992, we conclude that the relation between the excursion of the hemidiaphragm and V_T is linear over the range studied. Ultrasonography of DE is a simple quantitative technique that could be applied in the clinical investigation of patients with suspected abnormalities of diaphragmatic movement.

	"r" range	*Slope Y/X cm/l (SD)*	*Intercept (Y) cm (SD)*
Right coronal	0·949–0·997	3·24 (1·26)	0·03 (0·39)
Left coronal	0·942–0·999	3·78 (1·72)	0·15 (0·64)
Right longitudinal	0·968–0·996	1·86 (0·53)	0·85 (0·34)

Y = DE (cm); X = V_T (l).

Diaphragmatic movement in hemiplegic patients measured by ultrasonography

E COHEN, P HEYWOOD, K MURPHY, J BOULTBEE, A GUZ *Departments of Medicine and Radiology, Charing Cross and Westminster Medical School, London* Automatic breathing is controlled by centres in the lower brain stem, whereas voluntary breathing is controlled by cerebral cortical centres. In hemiplegic patients due to a lesion above the brain stem, there is confusion whether excursion of the hemidiaphragm is affected on the paralysed side. We planned to compare right and left diaphragmatic excursion in both voluntary and automatic breathing. Because a normal difference exists between the sides, it was necessary to compare both types of breathing on each side separately at a range of tidal volumes. Six normal subjects (three men) average age 65 (SD 8) range 54–73, and seven hemiplegic patients (two men) average age 61(8) range 51–75, were studied. Four patients had a right hemiplegia and three had a left hemiplegia, all with a unilateral suprabrainstem lesion shown by CT. None suffered from respiratory disease. The subjects' inspired volume and diaphragmatic excursions were measured simultaneously in the supine position with pneumotachography and M-mode

ultrasonography in the coronal plane. In the normal subjects, the difference of excursion at a V_T of 600 ml between voluntary and automatic breathing was 0·04(0·08) cm and 0·17(0·21) cm for the right and left sides respectively. The diaphragmatic excursions in the stroke patients are summarised in the table. We conclude that on the paralysed side in *some* hemiplegic patients there is an impairment of diaphragmatic movement during volitional compared with automatic breathing.

Plegic side	Right diaphragm		Left diaphragm	
	Voluntary	Automatic	Voluntary	Automatic
Right	0·95 cm	1·90 cm	3·01 cm	1·45 cm
Right	1·27 cm	1·43 cm	1·24 cm	1·05 cm
Right	1·77 cm	2·80 cm	2·70 cm	1·63 cm
Right	2·00 cm	1·70 cm		
Left	1·42 cm	1·27 cm	2·30 cm	2·64 cm
Left	2·05 cm	2·15 cm	2·26 cm	2·07 cm
Left	2·22 cm	2·51 cm	1·65 cm	2·10 cm

Effect of probe tissue separation on laser Doppler measurements of nasal and forearm blood flow

SC TOYNTON, AR ROBSON, RC SCHROTER, NB PRIDE *Department of Medicine, RPMS Hammersmith Hospital and Centre for Biological and Medical Systems, Imperial College, London* Many of the problems experienced when using laser Doppler flowmetry (LDF) to assess nasal mucosal blood flow are due to technical difficulties with probe positioning. Probe mucosal separation is required as even minor physical stimulation of the inferior turbinate induces reflex congestion and rhinorrhea, especially in rhinitic patients. The effect on raw flux (FR), normalised flux (FN), and surface laser power (dc) of increasing the probe-surface distance was investigated with the inferior nasal turbinate, forearm skin, and a 0·5% (w/w) suspension of 500 nm diameter latex microspheres to simulate tissue with random, homogenous flow. Separation distances were measured with a probe holder mounted on a vernier scale. A laser Doppler flowmeter (Moor Instruments MBF2D) was used supplying a 1mW power output of 810 nm wavelength laser light with an angular spread of about 40°. Settings were: time constant = 1 s, sampling rate = 10 Hz, filter bandwidth = 14·9 kHz with probe fibre separation distance of 0·5 mm. Mean values from data collection times of one minute were used. FR values are normalised for power fluctuations at the photodetector by dividing by the square of the dc. Concentration readings become inaccurate at high flow rates and so are unreliable for nasal use. No significant changes in FN, as compared with the touching values, were found for the turbinate (FN at 3 mm $p = 0·09$; $n = 12$). No clear decrease in dc was seen until 2·5 mm ($p < 0·02$) although there was a trend towards an increase in dc at 1·5 mm. Similarly, no significant changes were seen using forearm skin (at 4 mm FN $p > 0·20$; dc $p > 0·10$) although again there was a trend towards an increase in dc at 1·5 mm. Therefore, for nasal mucosa and forearm skin, probe-mucosal separation, within normal working limits of up to 3 mm, does not significantly alter FN values. By contrast, a mean decrease in FN of 42·5% (SE 2·2%; $p < 0·03$) and an increase in dc of 119% (SE 19%; $p < 0·03$) were seen for the latex suspension, both being maximal at 1·5 mm. This study highlights the dependence of laser Doppler instruments on algorithmic assumptions and confirms the suggestion that probe-mucosal separation up to 3 mm is unimportant in the nose (Olsson, Bende and Ohlin 1985). The weighting factor used for generating the flux value is valid for nasal mucosa. The microsphere suspension, however, has different surface and deep optical properties hence the failure of the normalisation procedure to maintain linearity of the FN signal. These findings are probably relevant when making LDF measurements elsewhere in the respiratory tract.

Arterial earlobe blood gas analysis: an underused technique

AD PITKIN, CM ROBERTS, JA WEDZICHA *Department of Thoracic Medicine, London Chest Hospital, Bonner Road, London* Measurement of arterial blood gas tensions is a routine part of the assessment of patients with respiratory and other disorders producing abnormalities of gas exchange. Direct arterial puncture is routinely used in clinical practice but it must be performed by qualified medical staff, is time-consuming, and may result in significant discomfort and morbidity for the patient. Techniques for sampling of arterialised capillary blood from the finger pulp and the earlobe were first described over two decades ago and although close agreement between arterial values and earlobe samples has been shown in normal subjects (*Br J Dis Chest* 1976;**70**:263) the technique is not in common use. We tested the accuracy of earlobe blood gas sampling in 40 unselected patients attending for lung function testing with a wide range of values of PaO_2 and $PaCO_2$ by measuring blood gas in simultaneous earlobe and arterial samples. We also conducted a survey of other hospitals to find out how commonly the technique is used elsewhere, and the reasons, if any, for not adopting this method. We found a close concordance between earlobe and arterial blood gas tensions over a wide range of values of PaO_2 (95% confidence intervals −1·0 to +0·72 kPa) and $PaCO_2$ (95% confidence intervals −0·25 to +0·68 kPa). A particularly good correlation between samples was observed at PaO_2 values lower than 8 kPa. Above this level the earlobe PaO_2 tended to be slightly lower than the arterial PaO_2. Nearly all values however lie within 0·5 kPa or less and underestimation of true PaO_2 at higher levels of oxygenation is unlikely to be of clinical significance. Fifty United Kingdom hospitals with a respiratory department were surveyed by telephone. Of these, nine used the arterialised earlobe technique and two had plans to introduce it. In 32 centres the main reason for not using earlobe blood gases was that the laboratory staff were unaware of the technique. In three hospitals a blood gas analyser was not available in the laboratory. In two centres the technique was considered inaccurate and in a further two there were insufficient technical staff to carry out the procedure. Our data indicate that earlobe blood gas analysis is sufficiently accurate to be reliably substituted for arterial sampling in routine clinical practice. Despite its advantages, most centres in the United Kingdom do not use the technique. The main reason for this seems to be lack of knowledge of its existence or uncertainty over its accuracy.

Oxygen saturation during methacholine challenge in a mixed population

DS RENWICK, MJ CONNOLLY *Manchester Royal Infirmary* It is unclear whether the fall in arterial oxygen saturation during non-specific bronchial challenge relates to degree of bronchoconstriction produced or to dose of challenge agent given (Fontana *et al*, *Am Rev Respir Dis* 1991;**143**:A411; Reed, Calhoun, *Am Rev Respir Dis* 1991;**143**:A411). We recorded oxygen saturation during methacholine challenge in a large number of subjects over a wide age range. 133 subjects (80 women) aged 24 to 87 (mean 56) years underwent methacholine challenge by dosimeter (Connolly *et al*, *Am Rev Respir Dis* 1992;**146**:592). The sample included those with and without airways obstruction. Those with baseline FEV_1 < 60% predicted were excluded. Arterial oxygen saturation was monitored by finger oximetry. Bronchial responsiveness was expressed as methacholine dose causing 20% fall in FEV_1 (PD_{20}). 78 subjects achieved a PD_{20}. Mean fall in oxygen saturation ($fallSaO_2$) was 2·4% (−1 to 10%); 16 subjects had $fallSaO_2$ >5%. Multiple regression analysis showed independent positive relations between $fallSaO_2$ and baseline SaO_2 ($p = 0·007$), log of total methacholine dose ($p < 0·0001$) and %fall in FEV_1 ($p = 0·008$). $FallSaO_2$ was independently negatively related to age ($p = 0·015$) and baseline actual FEV_1 ($p = 0·0003$). Coefficient of multiple regression (r) = 0·48. Methacholine challenge can produce appreciable desaturation in those receiving large doses of methacholine, or developing marked bronchoconstriction. Desaturation is not greater in the elderly.

Within breath changes in respiratory impedance and correlations with fored spirometry during bronchochallenge in normal and asthmatic subjects

D MACLEOD, W VAN DER PUTTEN, J PRICHARD *Department of Clinical Medicine, Trinity College, St James's Hospital, Dublin, and Manitoba Cancer Treatment Research Foundation, Winnipeg, Canada* Alterations in airway calibre and the airway wall are a feature of asthma and may partially explain respiratory impedance changes in the condition. We used 10 Hz monosinusoidal forced oscillation measurements gated by computer to end-inspiration and end-expiration (Van der Putten *et al. Thorax* 1993 (in press)) during methacholine challenge tests (European Respiratory Health Survey Protocol) to determine correlations of impedance, reactance, and resistance with FEV_1 and $FEF_{25-75\%}$. Seven normal subjects (three men aged 23 (0·5), four women aged 21 (1)) and four asthmatic patients not taking oral steroids (two men aged 21·5 (0·5), two

women aged 22 (1)) were studied. One asthmatic and one normal subject smoked. Data acquisition was for 54 seconds (sampling rate 25 Hz) with respiratory cycle monitoring for gating. Gated impedance and resistance rose during challenge with significant negative correlations with FEV_1 and $FEF_{25-75\%}$ in all asthmatic patients (except one excluded from challenge by sensitivity to control nebulisation) and in normal patients showing a 10% or greater fall in FEV_1 ($r = -0{\cdot}7$ to $-0{\cdot}8$, $p < 0{\cdot}05$, df 6). Gated reactance was positively correlated with FEV_1 in asthmatic patients ($r = +0{\cdot}78$ to $+0{\cdot}88$, $p < 0{\cdot}01$, df 6), compatible with other studies. Asthmatic patients also had 0·4–2·5 Hz spikes in impedance with a phase angle maximal at the time of $PDIg_{20}FEV_1$ and reversed by inhaling 200 μg salbutamol.

Pulmonary resistance is diminished by exercise in asthmatic patients

S FREEDMAN, R LANE, P BOYLE, A GUZ *Department of Medicine, Charing Cross and Westminster Medical School, London* Despite the recognition of exercise as a common precipitant of asthma, there is a paucity of measurements of airway patency made during exercise rather than afterwards. We have measured total pulmonary resistance (R_L) in six asthmatic patients, aged 35–51 years, who all had exercise induced symptoms. R_L was calculated breath by breath from flow and oesophageal pressure with a hybrid computer (Lane *et al. Clin Sci* 1991;**82**:31). Patients abstained from all treatment for 12 hours before the test, and mean initial FEV_1 was 53% predicted (range 18%–78%), and corresponding R_L 5·25 (range 3·0–10·45) cm H_2O/l/s. Exercise was for 10 minutes on a cycle ergometer at around two thirds of predetermined maximum in an air conditioned room maintained at about 18°C. Patients achieved maximum steady state ventilations of 45–102 l/min. In five patients R_L fell within three minutes of the start of exercise by 44–58%, to reach minimum values of 1·5–5·3 cm H_2O/l/s. R_L was unchanged in the sixth patient, but in all there was a significant rise in R_L within five minutes of the end of exercise to values equal to or greater than the pre-exercise level. From our previous work on methacholine induced bronchoconstriction in normal subjects (Freedman *et al. Thorax* 1988;**43**:631–6) we believe the fall in resistance to be due to the increased tidal volumes, which cause a disproportionate increase in hysteresis of large airways compared with lung parenchyma.

Stage changes and awakenings as indicators of sleep architecture: effect of patient group and an acclimatisation night

MARTIN ALLEN, KEITH PROWSE *City General Hospital, Stoke on Trent, Staffs* The number of changes in sleep stage has been suggested as a useful measure of sleep architecture. No single laboratory has assessed the usefulness of stage changes (SCs) and awakenings (As) as an indicator of sleep architecture in either different subject groups or after an acclimatisation night. Nine normal subjects, five patients with chronic obstructive airways disease (COAD) and seven patients with obstructive sleep apnoea (OSA), underwent full polysomnography on two consecutive nights. Sleep was staged visually with 20 second epochs by one experienced scorer. The number of SCs and As were divided by the time from sleep onset to produce a comparable ratio in all three subject groups. No significant differences were found between the two consecutive nights within the same group or for all three groups together. Between subject groups the only significant differences were in the number of SCs between the OSA and COAD patients on the first ($p = 0{\cdot}03$) and second nights ($p = 0{\cdot}05$). Although SCs and As were greater in patients with OSA, the results suggest that routine calculation of SCs and As are of little clinical use in assessing sleep architecture.

	Stage changes		*Awakenings*	
	1st	*2nd*	*1st*	*2nd*
Normal	17·3 (7·1)	15·5 (3·7)	3·7 (2·7)	3·4 (2·2)
COAD	11·0 (4·1)	12·2 (4·7)	3·5 (0·9)	2·9 (0·9)
OSA	22·4 (10·1)	20·7 (8·3)	6·1 (3·5)	4·6 (2·1)

Results are means (SD).

Scoring of apnoeas during sleep

AH KENDRICK, N WILTSHIRE, JR CATTERALL *Sleep Unit and Respiratory Department, Bristol Royal Infirmary, Bristol* Apnoeas are routinely scored in the assessment of patients with breathing disorders during sleep (BDS), and may be categorised as obstructive, central, or mixed. The definitions and techniques used to score apnoeas vary, however. The purpose of this study was to examine the diversity of definitions used to score apnoeas. Eighty questionnaires were sent worldwide to sleep centres with an interest in BDS. Each was asked to give their precise definition of each type of apnoea in terms of the magnitude of desaturation, the duration of the event, and the inclusion of thoracoabdominal movement (TAm) and airflow. Scoring of hypopnoeas was asked separately. 36 questionnaires were returned. One centre did not score apnoeas in these terms, but scored only arousals; six did not score mixed, and two did not score central apnoeas. 32/35 centres used complete absence of airflow with continued TAm to define obstructive apnoeas; 25/33 centres required complete absence of TAm and airflow to define central apnoeas; and 24/29 centres defined a mixed apnoea as a central followed by an obstructive apnoea. We conclude that (1) there is not complete agreement on the definitions of scoring apnoeas, and (2) until such time as universal definitions are agreed, the precise definition of each type of apnoea should be included in epidemiological and intervention studies.

	Obstructive	*Mixed*	*Central*
Saturation:			
None given	23	18	21
2%–4%	3	2	3
>4%	9	9	9
Duration:			
None given	4	4	4
>10 s	31	25	29

Addition of sound recording to oxygen saturation in screening a snoring population for obstructive sleep apnoea

JES WHITE, AJ SMITHSON, PR CLOSE, MJ DRINNAN, AJ PRICHARD, CJ GRIFFITHS, GJ GIBSON *Departments of Respiratory Medicine, Medical Physics, and Ear, Nose, and Throat Surgery, Freeman Hospital, Newcastle upon Tyne* Recording of overnight oxygen saturation (Sa_{O_2}) is often used as a screening test for possible obstructive sleep apnoea (OSA) but is unreliable in less severe cases (Cooper *et al. Thorax* 1991;**46**:586–8). We postulated that the addition of sound recording would improve the sensitivity of the method. Thirty nine full sleep studies including sound measured by calibrated sound level meter were performed on snorers who were being investigated for possible surgical treatment. Polysomnography showed an apnoea/hypopnoea index (AHI) $\geqslant 20$ events per hour of sleep in five subjects, $\geqslant 15$ in seven, and $\geqslant 10$ in 21. Two experienced observers independently and without knowledge of the other data scored paper records of Sa_{O_2} alone and Sa_{O_2} plus sound level. Records were classified as OSA unlikely, equivocal, or definite. The addition of sound reduced the number of equivocal results from 23 to 14. The sensitivity and specificity of the screening investigations were calculated by defining a positive test as one where both observers reported OSA definite; any other classification was taken as negative. The resulting values depend on the level of AHI used to define OSA and are shown for different criteria in the table. We conclude that (1) an appreciable number of snorers referred for possible surgical treatment have unrecognised OSA, (2) the sensitivity of oximetry with or without sound recording increases as the threshold AHI used in diagnosis of OSA increases but at the expense of decreasing specificity, and (3) in the recognition of mild OSA the addition of a sound profile increases sensitivity without impairing specificity.

Definition of OSA		Sa_{O_2} *alone*	Sa_{O_2} *and sound*
AHI $\geqslant 10$	Sensitivity	0·30	0·62
	Specificity	1·00	1·00
AHI $\geqslant 15$	Sensitivity	0·71	0·86
	Specificity	0·94	0·78
AHI $\geqslant 20$	Sensitivity	1·00	1·00
	Specificity	0·94	0·76

Central versus reflex activation of genioglossus muscle in subjects after laryngectomy

JA INNES, MJ MORRELL, I KOBAYASHI, RD HAMILTON, A GUZ *Department of Medicine, Charing Cross Hospital, London* Activation of the genioglossus (GG) muscle during inspiration may help to defend upper airway (UA) patency in humans. Such activation may occur by central respiratory drive or as a reflex response to the negative pressure present in the UA or trachea during inspiration. To differentiate between these mechanisms, we studied seven subjects who have undergone laryngectomy and breathe only via a tracheal stoma. Square wave negative pressure stimuli (-15 cm H_2O for 0·5 s) were applied at functional residual capacity (a) by facemask to the isolated UA and (b) to the stoma. GG activity was recorded with intraoral bipolar surface EMG electrodes, and quantified as described previously (Horner *et al. J Physiol* 1991;**436**:15–30). As a measure of spontaneous central respiratory drive, we quantitated (by RMS integration) phasic and tonic GG activity during normal and inspiratory loaded stomal breathing. Significant activation of GG occurred with stimuli of -15 cm H_2O applied to the isolated UA (mean ratio post/pre stimulus EMG = 1·70, $p < 0·01$) but the same stimuli caused no significant activation when applied to the stoma (ratio 1·22, $p = 0·06$). In five of the subjects, larger stimuli (-25 cm H_2O) were also applied; these again caused significant activation of GG when applied to the UA, but not when applied to the stoma. During normal breathing, four of five subjects showed phasic inspiratory GG activation; with inspiratory loading all five showed increased phasic and tonic activation. We conclude that in these subjects, inspiration activates GG via central respiratory drive; negative tracheal pressure alone does not activate GG. By contrast, despite the absence of the larynx, negative pressure in the isolated UA can reflexly activate GG without airflow or respiratory effort.

Deleterious effect of nasal continuous positive airways pressure (NCPAP) on cardiac function in chronic heart failure (CHF)

R LISTON, PC DEEGAN, C MCCREERY, R COSTELLO, B MAURER, WT MCNICHOLAS *Departments of Respiratory Medicine and Cardiology and the Respiratory Sleep Laboratory, University College and St Vincent's Hospital, Dublin 4, Ireland* NCPAP has been reported to improve cardiac function acutely (over a 10 minute period) in chronic heart failure (CHF) (*Am Rev Respir Dis* 1992;**145**:377–82), and also during sleep in patients with coexisting sleep apnoea (SAS) and CHF. We assessed the effect of NCPAP on cardiac function over three hours in seven male patients aged 51–75 years with stable severe CHF (ejection fraction <30%), all of whom had atrial fibrillation. Six patients completed the protocol and all had overnight sleep studies by standard polysomnography to investigate any associated SAS. After Swan-Ganz catheter insertion, patients were commenced on NCPAP (5 cm H_2O) and standard haemodynamic variables were measured at baseline, at regular intervals during NCPAP, and one hour after stopping NCPAP. All patients had pulmonary capillary wedge pressure (PCWP) >12 mm Hg and showed a significant deterioration in cardiac function during NCPAP (table shows means) that recovered after withdrawal. Two patients had SAS (26 and 18 apnoeas and hypopnoeas/hour of sleep). We conclude that NCPAP has a detrimental effect on cardiac function during wakefulness, even in patients with SAS.

Time	CI (l/min/m²)	SI (ml/m²)	SBP	SVR	RAP	PCWP	HR
0 h	3·5	46·7	134	1229	8·2	19	82
15 min	3	41·6	142	—	—	20·5	78
2 h	2·9	36·6	151	1521	9·3	22·7	82
3 h	3	39·3	152	1473	10·8	21·5	82
Recovery	3·4	39·6	148	1353	8·8	21·7	82
p	0·005	0·02	0·007	0·02	0·07	0·27	0·9

CI—cardiac index; SI—stroke index (by thermodilution); SBP—systolic blood pressure, RAP—right atrial pressure (mm Hg); HR—heart rate; SVR—systemic vascular resistance (dynes/s/cm^{-5}).

Nasal biopsies in human rhinovirus 16 infection: an immunohistochemical study

DJ FRAENKEL, PG BARDIN, SL JOHNSTON, G SANDERSON, ST HOLGATE *University Medicine, Centre Block, Level D, Southampton General Hospital, Southampton* Rhinoviruses are a common cause of viral upper respiratory tract infection and serotype 16 (RV16) has been aetiologically linked with exacerbations of asthma. Little is known of the histology of the infection and the pathophysiology of associated increases in airflow obstruction. We have studied the inflammatory changes in the cell population of the nasal mucosa during RV16 infection in 14 normal adult volunteers. Baseline nasal biopsies were taken two weeks before innoculation. RV16 was then insufflated on days 2 and 3 of a one week hospital admission with appropriate isolation procedures. Nasal biopsies were taken on day 6, and then again after six weeks of convalescence. Biopsies were fixed in acetone and processed into glycolmethacrylate resin for semithin sectioning. Immunostaining used the streptavidin-biotin horseradish peroxidase technique with appropriate monoclonals to enumerate cell types; AA1-mast cell tryptase; EG2-eosinophil cationic protein; CD3, CD4, CD8 T-cell markers; and neutrophil elastase. All patients developed colds confirmed by symptom scores, viral culture, and serology. Thirty two biopsies were evaluable from 13 subjects. Median cell counts for baseline, infection and recovery phases respectively were (cells/mm²): mast cells 26,29,18; eosinophils 2·2, 1·0, 0·7; neutrophils 21, 31, 27; lymphocytes 3·2, 1·4, 1·1. No differences were found in cell types between the different phases (Wilcoxon paired test, $p > 0·05$). This is in keeping with previous semiquantitative studies and suggests that mediator release rather than increased cellularity may be responsible for coryzal symptoms. [This work was supported by The British Council, Schering-Plough, Australian Bicentennial Scholarship, British Lung Foundation.]

Rhinoviral infection of nasal epithelium detected by non-isotopic in situ hybridisation

PG BARDIN, SL JOHNSTON, G SANDERSON, S ROBINSON, M PICKETT, ST HOLGATE *Immunopharmacology Group, Level D, Southampton General Hospital, Southampton* Rhinoviruses (HRVs) are the predominant cause of the common cold and HRV serotype 16 (HRV 16) may increase bronchial responsiveness and late asthmatic reactions. It is not known whether HRVs infect cells other than nasal epithelium. We have examined nasal epithelium in vivo to explore localisation of HRV infection, employing non-isotopic oligonucleotide probes and in situ hybridisation (ISH). Sections (4 μm) were cut from six paired nasal biopsies obtained before and during HRV 16 colds in four volunteers and two wild type HRV colds. Oligonucleotide probes were 3'-labelled with biotin-11-dUTP and hybridisation was performed with two antisense oligonucleotides, a sense probe and control probe. Sections were washed at high stringency and the signal detected with the streptavidin-biotin-alkaline phosphatase method. Controls included RNase digestion, a control probe of similar length and G-C content, and cells infected with adeno- and influenza A virus. Specific hybridisation signals to (+) viral strand were obtained in nasal epithelium from three subjects (one HRV 16 and two wild type HRV). Intracellular HRV 16 replication could be confirmed by demonstration of hybrids of oligonucleotide and viral (−) strand in one case, but no evidence was found to suggest infection of non-epithelial cells. Use of ISH has confirmed in vivo epithelial HRV infection in the nose; this method may be explored to trace the possible spread of HRVs to the lower respiratory tract. [This work was supported by a grant from the British Lung Foundation.]

Cytokine profile of lung tissue in lung transplant recipients

JJ EGAN, S GUY, N YONAN, PS HASLETON, A WOODCOCK *North West Lung Centre, Cardiothoracic Surgery and Histopathology Departments, Wythenshawe Hospital, Manchester, and Department of Medical Genetics, St Mary's Hospital, Manchester* Bronchoalveolar lavage (BAL) fluid provides a ready source for the study of cytokines in lung transplantation. BAL is, however, subject to various factors that may influence the quality of the sample as a source for cytokine study with reverse transcription polymerase chain reaction. We have therefore examined directly the lung tissue of lung transplant recipients to build a cytokine profile of the tissue. Prospectively, lung tissue was obtained by standard transbronchial biopsy technique from six lung transplant recipients (four heart and lung, two single lung). Six biopsies were routinely taken from each patient to assess the presence of rejection or infection and one extra biopsy (average size 1 mm³) was saved for cytokine study. Lung rejection was graded by international classification. A total of 13 biopsies were examined for I11, I12, I13, I14, I16, I18, I110, TNF α, TGF β, and γ interferon. To confirm extraction of undegraded high molecular weight RNA

and satisfactory reverse transcription, all biopsies were examined with primers for glyceraldehyde 3 phosphate dehydrogenase, β-actin and c-abl. In five normal biopsies and one biopsy with CMV inclusion bodies (no pneumonitis) no cytokine signals were identified. Six biopsies had evidence of rejection, two A3a, one A3d, one A2d, and two A1a and one biopsy showed an inflammatory bronchitis. Positive signals for I13, I14, and I16 were found in the A3d biopsy. I16 and I13 signals were seen with the bronchitis and in one A1a biopsy. These results suggest that cytokine gene expression in lung tissue does not closely correlate with histopathological rejection.

Bronchoalveolar lavage (BAL) macrophage, and cytokine profiles alter before respiratory disease in patients infected with HIV

MCI LIPMAN, MA JOHNSON, DH BRAY, LW POULTER *Royal Free Hospital and School of Medicine, London* The degree to which the pulmonary immune system reflects the systemic immune failure of advancing HIV infection has not been well characterised. We therefore investigated interleukin 1β (IL-1β), tumour necrosis factor α (TNFα), and transforming growth factor β (TGFβ) in bronchoalveolar lavage (BAL) from HIV infected patients with and without pneumonitis and with different blood CD4 lymphocyte counts. Cell populations recovered at BAL were investigated for the presence of macrophage (MO) antigens identifying antigen presenting cells (RFD1+ D7−), effector cells (RFD7+ D1−), and suppressor cells (RFD1+ D7+). The collected supernatant was assayed for IL-1β, TNFα and TGFβ (Quantikine, R and D systems). Results (medians) are shown in the table. These data suggest that alterations in BAL cytokines and alveolar MO subsets precede HIV related respiratory disease. Preliminary in situ hybridisation studies reveal cytokine mRNA within these MO implying that they may be responsible for the production of these cytokines in the airway.

	CD4 (× 10⁶/l)	*MO subsets D1:D7:D1D7*	*IL-1β (pg/ml)*	*TNFα (pg/ml)*	*TGFβ (pg/ml)*
HIV with pneumonitis	10	23:60:17	12·7	27·1	68·3
HIV, CD4 <400	230	17:62:21	11·3	23·3	186·9
HIV, CD4 >400	820	29:49:22	3·8	0	75·6
Normal controls	955	27:49:24	5·6	0	81·2

Smoking related bronchial inflammation

MJ IREDALE, S WANKLYN, IP PHILLIPS, T KRAUSZ, PW IND *Departments of Medicine and Cytopathology, Hammersmith Hospital, Du Cane Road, London* Quantitative induced sputum cytology provides a simple, non-invasive assessment of bronchial inflammation. Smoking related airway diseases involve inflammation of large and small airways. We examined the effect of smoking by inducing sputum and simultaneously determining bronchial responsiveness in three groups of subjects free of infection. We studied 13 non-atopic non-smokers (mean age 32 years; N), eight smokers (one atopic, mean age 45 years, mean pack-years 34; SM), and four ex-smokers (one atopic, mean age 64 years, mean pack-years 73, who have stopped smoking for a mean 12·5 years; EX). Hypertonic (4·5%) saline (HS) was nebulised for increasing time periods (0·5–16 minutes) as a bronchial challenge. FEV_1 was measured at baseline and one minute after each inhalation period. Sputum expectorated during the procedure was collected. Differential cell counts (mean of four counts of 500 cells) were performed on direct smears stained with Chromotrope 2R. Mean baseline FEV_1 (% pred) was 107 (95% CI 101–113 for N, 97 (87–106) for SM ($p < 0·05$), and 69 (40–98) for EX ($p < 0·01$ *v* SM, $p < 0·001$ *v* N). Mean maximum fall in FEV_1 on challenge was 4·4 (2·7–6·1) % for N, 10·9 (5·3–16·4) % for SM ($p < 0·01$), and 22·8 (18·7–26·8) % for EX ($p < 0·01$ *v* SM, $p < 0·001$ *v* N). Adequate sputum samples were obtained from 11/13 N, 6/8 SM, and 4/4 EX. There were no differences in % lymphocytes, eosinophils, or epithelial cells between the three groups. Neutrophil counts (%) were 23·6 (9·0–29·4) for N, 42·3 (26·5–52·6) for SM ($p < 0·002$), and 60·2 (15·1–65·7) for EX ($p = 0·07$ *v* N). Median (range) % macrophages on differential counts were 62·3 (54·4–74·7), 46·0 (40·1–65·0), and 30·1 (26·6–51·3) for N, SM, and EX, respectively ($p < 0·02$ N *v* SM, $p < 0·005$ N *v* EX). We have found no previous work on quantification of induced sputum in smokers. We report significantly increased numbers of neutrophils, which have not been found in bronchial biopsies or bronchoalveolar lavage. Preliminary results suggest that this effect persists long after stopping smoking.

Eicosanoid metabolism in squamous cell carcinoma of the lung

MARY O'SULLIVAN, FP HOGAN, D LUKE, JS PRITCHARD *Department of Clinical Medicine, TCD Medical School, St James's Hospital, Dublin* Numerous studies have suggested an association between arachidonic acid metabolites (eicosanoids) and cancer. We have previously shown that normal bronchial epithelial cells metabolise tritiated arachidonic acid (^{3}H-AA) via the 15 lipoxygenase pathway to produce 15 hydroxyeicosatetraenoic acid (15 HETE) (O'Sullivan *et al Thorax* 1992,**47**:242P. We then compared the ^{3}H-AA profile of normal bronchial epithelial cells with that of cells from squamous cell carcinoma of the lung. Tumour tissue and macroscopically normal bronchus were collected from patients undergoing lobectomy or pneumonectomy for squamous cell carcinoma of the lung. Isolated cells were prepared by enzymatic dissociation in 0·3% collagenase for two hours at 37°C. Cell yield and viability were determined by ethidium bromide/acridine orange staining and fluorescent microscopy. The cells were characterised by immunohistochemical staining with AE1/AE3, an anticytokeratin monoclonal antibody, and with LCA, an antibody directed against leucocytes. Cell suspensions were incubated with 2 μCi of ^{3}H-AA and calcium ionophore A23187 (2 μM) for 30 minutes at 37°C. Labelled eicosanoids released by the cells were separated by reverse phase high pressure liquid chromatography and their relative abundance was determined by β scintillation counting. The peaks were identified by coelution with authentic standards. The relative amounts of 15 HETE released by the cells were calculated as a percentage of the total radioactivity in disintegrations per minute. The production of 15 HETE from ^{3}H-AA by tumour cells was significantly less than that of normal cells ($p < 0·001$). In six out of 11 patients there was no detectable 15 lipoxygenase activity in the tumour cells. The pathophysiological role of 15 HETE in vivo is not known. In vitro, 15 HETE regulates the adhesion of normal and tumour cells to the basement membrane (Buchanan *et al. Agents and Actions* 1990,**29**:16) and inhibits proliferation in a variety of normal cells (Spector *et al. Prog Lipid Res* 1988,**27**:271). Therefore, a reduction in 15 HETE synthesis by lung tumour cells may contribute to the aberrations in growth and differentiation characteristic of tumour progression. A causal relation between eicosanoid metabolism and lung cancer has yet to be established, however.

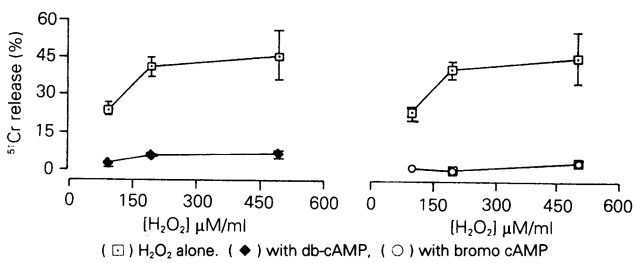
Lung interstitial albumin increases after 24 hours exposure to 100% oxygen

ENS O'GORMAN, KLI WEIR, DJ GODDEN, JAS ROSS, PW JOHNSTON *Departments of Pathology, Medicine, Environmental, and Occupational Medicine, University of Aberdeen, Scotland* Exposure of rats to high concentrations of oxygen produces pulmonary interstitial oedema visible microscopically after 48 hours (Kistler *et al. J Cell Biol* 1967;**33**:605–28), attributed to increased capillary permeability. We postulated that this increase considerably predates oedema. We studied relative albumin concentration (RAC) of lung interstitium after hyperoxia. Male Sprague Dawley rats were exposed to 100% oxygen in a low flow partial recirculation chamber for 24 hours ($n = 8$) and 60 hours ($n = 8$). Air control groups (both $n = 8$) were exposed in the chamber for equal time. Rats were killed by intraperitoneal injection of anaesthetic, lungs were fixed in situ by instillation of glutaraldehyde (1·15%, 350 mOsm, pH 7·4, 4°C), and processed to LR White acrylic resin. Sampling protocols used systematic random methods. From the eight rats in each group, two blocks from six were sectioned and stained for native albumin with a two stage immunocytochemical technique marked by 10 nm colloidal gold. After morphometric quantification, adapting the method of Johnston *et al* (*Int J Microcirc Clin Exp* 1991;**10**:395), RAC was used as an index of capillary permeability. RAC in interstitial ground substance, expressed as mean (SE) gold particles $\times 10^2$ per randomly counted point was 17·7(6·2) after 24 hours of air exposure and 31·4 (16·1) after 60 hours of air. After 24 hours 100% oxygen RAC was 98·1 (27·2) and, after 60 hours, 108·4 (18·0). These changes are related to the gas ($p < 0·001$) and not

duration of exposure. We conclude that hyperoxia induces albumin leak into the interstitium during the first 24 hours of exposure.

Oxidant induced pulmonary endothelial cell injury is protected by cAMP analogues

WJ BOURKE, TJ MCDONALD *Department of Respiratory Medicine, St Vincent's Hospital, Dublin and University College, Dublin, Ireland* The protective effect of the cyclic AMP analogue dibutyryl cyclic adenosine monophosphate (db-cAMP) on in vivo models of lung injury has previously been demonstrated. We have previously shown that db-cAMP protects endothelial cells against injury from exotoxin in vitro. The manner in which db-cAMP exerts its protective influence is unknown and its efficacy against oxidant forms of endothelial cell injury is unclear. We postulated that the protective effect of db-cAMP may be related to a specific property of db-cAMP and not to the elevation of intracellular cAMP associated with cAMP analogues. To test this hypothesis we preincubated a different cyclic AMP analogue, 8 bromo-cAMP, and db-cAMP with endothelial cells before adding hydrogen peroxide (H_2O_2) as an oxidant injury stimulus. Endothelial cell injury was studied in bovine pulmonary artery endothelial cells (BPAEC) obtained from the American Type Culture Collection (ATCC). Standard tissue culture techniques were used and the release of incorporated radiolabeled chromium (^{51}Cr) was used to assess cell injury. Both db-cAMP and 8 bromo-cAMP protected against H_2O_2 injury. There was no difference between the two agents in the protection conferred. We conclude that the protection afforded by cyclic AMP analogues is not specific to db-cAMP and requires further studies to elucidate the mechanisms involved.



(⊡) H_2O_2 alone. (◆) with db-cAMP, (○) with bromo cAMP

Six year experience in referral, assessment, and transplantation at Freeman Hospital pulmonary transplant unit

D FISHWICK, AD GASCOIGNE, N WRIGHTSON, JH DARK, PA CORRIS *Department of Cardiopulmonary Transplantation, Freeman Hospital Cardiothoracic Unit, Newcastle upon Tyne* Over a six year period, commencing June 1986, 297 patients (mean age 39 years) were referred to this unit for assessment of lung or heart lung transplantation. Six major diagnostic categories emerged (n, mean age): cystic fibrosis n = 55, 24, chronic obstructive pulmonary disease n = 74, 48, fibrotic lung disease n = 70, 48, bronchiectasis n = 29, 42, congenital heart disease n = 30, 31, and primary pulmonary hypertension n = 19, 33. A total of 92 (31%) had received a transplant up to June 1992. The mean time in days (range) from referral to assessment as a group was 81 (0–741), from referral to active listing 186 (3–1322, n = 183), and from referral to transplantation 407 (38–1027). Fifty seven patients died before transplantation while listed at a mean time of 244 days from referral, despite a mean time from referral to assessment of only 53 days reflecting recognition of the clinical urgency of the referral. The mean time from active listing to transplantation was 235 (1–860) days. This value was significantly shorter for the first 10 patients transplanted (mean 80 days, from June 87 to September 88) in comparison with the latest 10 (198, from August 92 to November 92) and peaked (mean 381 days) for the 10 patients transplanted between November 90 and May 91. The main limiting factor imposed on this form of treatment remains donor availability.

Isolated lung transplantation for cystic fibrosis

A HASAN, M HEALY, AD GASCOIGNE, JH DARK, CJ HILTON, PA CORRIS *Cardiopulmonary Transplant Unit, Freeman Hospital, Newcastle upon Tyne* Heart lung transplantation was initially the operation of choice for patients with cystic fibrosis (CF) referred for pulmonary transplantation; however bilateral sequential lung transplantation (BSLT) is now becoming the operation of choice in many centres with the perceived advantage of recipients retaining their native hearts. We report our experience with this technique. Between August 1990 and March 1993, 14 patients have undergone isolated lung transplantation for CF. Thirteen patients had BSLT and one patient had single lung transplant and contralateral pneumonectomy. Their ages ranged from 15 to 30 (mean age 22) years. There were no intraoperative deaths. There were three early and one late deaths. The early deaths were due to donor organ failure (n = 1), bronchial dehiscence (n = 1), and CMV pneumonitis (n = 1). The late death was due to bronchiolitis obliterans. Only two patients had significant airway complications, one with dehiscence of the right bronchial anastomosis, the other requiring stenting of the intermediate bronchus for ischaemic stenosis. All surviving patients have demonstrated a significant functional improvement in their pulmonary function as is shown in the table. Survival at six months was 86%. Actuarial survival at one year was 71% which is comparable with published data for heart lung transplantation. In conclusion isolated lung transplantation offers a good functional result and intermediate survival for patients with CF with acceptable early morbidity and mortality.

	FEV_1 (% predicted)	*Arterial Po_2 (kPa)*	*Six minute walk (m)*
Before operation	22 (8·7)	8·2 (1·7)	358 (164)
Three months after operation	74 (12)	10·8 (1·01)	625 (64)
	p < 0·01	p < 0·01	p < 0·01

Cytomegalovirus antigenaemia: a predictor of cytomegalovirus pneumonitis/pulmonary infection in lung transplant recipients

JJ EGAN, L BARBER, J LOMAX, A FOX, A TURNER, A WOODCOCK *North West Lung Centre, Wythenshawe Hospital, Manchester and Public Health Labortory,. Withington Hospital, Manchester* Human cytomegalovirus (HCMV) pneumonia in lung transplant recipients carries significant morbidity and mortality. HCMV antigenaemia is the demonstration of HCMV pk65, an early internal matrix protein, by immunofluorescent staining using a monoclonal antibody (Biosoft) in cytospin preparations of polymorphonuclear leucocytes (PMNL). The technique is rapid (three hours) and quantifiable, avoiding the need for tissue culture enhancement. We prospectively (June 92–February 93) studied the utility of HCMV antigenaemia in nine lung transplant recipients surviving 100 days. Seven patients received HCMV matched grafts (two HCMV seropositive recipient/donors (R+, D+), five HCMV seronegative recipient/donors (R−, D−)). Two HCMV seropositive recipients received a graft from a seronegative donor (R+, D−). One of the R+ D+ patients was HCMV antigenaemia positive (six positive cells/50 000 PMNLs) at day 60 after transplantation and at day 91 this patient had a bronchoalveolar lavage that was HCMV positive by DEAFF and culture (no HCMV pneumonitis), while remaining IgM negative. One R+ D− patient became HCMV antigenaemia positive (50 positive cells/50 000 PMNLs) on days 50 and 57 after transplantation. He developed a significant rise in IgM in parallel with the onset of HCMV pneumonitis on day 103. The remaining eight patients did not develop clinical or histological evidence of HCMV disease and they remained HCMV antigenaemia negative. HCMV antigenaemia may be a useful early indicator for the subsequent development of HCMV pulmonary disease/infection in lung transplant recipients.

Necrotic ulcerative bronchitis as the presenting feature of lymphoproliferative disease after lung transplantation

JJ EGAN, NY YONAN, PS HASLETON, KB CARROLL, A WOODCOCK *North West Lung Centre and Departments of Cardiothoracic Surgery and Histopathology, Wythenshawe Hospital, Manchester* After lung transplantation the incidence of post-transplant lymphoproliferative disease (PTLD) is in the region of 8%. At our centre, two of 25 long term survivors, women aged 49 (case 1) and 31 (case 2), have developed PTLD, each presenting as a localised necrotic ulcerative bronchitis documented at flexible bronchoscopy (FB) before progression of a more typical clinical picture of PTLD. Both had a

flexible bronchoscopy (FB) and transbronchial biopsy performed because of a 10% fall in FEV_1 at four and five months after transplantation respectively. At FB a necrotic ulcerative bronchitis was observed, photographed, and biopsied. Histology showed necrotic material with an inflammatory infiltrate and ulceration in both cases. The bronchial biopsy of case 2 also demonstrated lymphoproliferative disease. Both had a normal chest *x* ray film at the time of FB and no evidence of fungal or herpes simplex infection. Case 1 later developed lung nodules and a monoclonal high grade B cell non-Hodgkin's lymphoma was confirmed by open lung biopsy. Each case was Epstein Barr virus seropositive but neither showed evidence of reactivation using IgG capsid antigen serology. Neither case responded to reduction in immunosuppression and intravenous acyclovir. Both patients then received VAPEC-B chemotherapy. Case 1 died 6 months later from progressive lymphoma and aspergillus pneumonia. Case 2 showed regression of lymphoma and is alive on treatment two months from diagnosis. The features described should alert clinicians to PTLD as an underlying diagnosis and may suggest that the lymphatic follicles in the mucous membrane of the bronchi are the initial site for mitosis in PTLD.

Pulmonary capillary leakage/haemorrhage late after cardiac transplantation

JJ EGAN, N MARTIN, PS HASLETON, A WOODCOCK *North West Lung Centre and Department of Histopathology, Wythenshawe Hospital, Manchester* Diffusion abnormalities are recognised late after cardiac transplantation (Egan *et al*, *Chest* 1993, in press). To investigate this phenomenon prospectively, we completed flexible bronchoscopy (FB) and bronchoalveolar lavage (BAL) on 10 heart transplant recipients (HTRs). A consistent feature of the cytological examination of the BAL taken from the right middle lobe of HTR was the presence of haemosiderin laden macrophages. We compared the haemosiderin score (HS) of the BALs of the 10 HTRs with 10 heart lung transplant recipients (HLTRs). All HLTRs had previous transbronchial biopsies but none of the HTRs had. 200 macrophages stained by prussian blue were scored according to scale 0 = no colour, 1 = faint blue, 2 = medium intensity <50%, 3 = deep blue >50%, 4 = deep blue throughout the cell, and the HS was determined by counting 200 scored macrophages and dividing by two. The HTRs had a significantly higher HS than the HLTRs (HTR median = 144, range 2–260; HLTR median = 12, range 0 – 140; $p = 0{\cdot}019$, Mann–Whitney U test, $W = 136{\cdot}5$). All the HTRs had a normal right heart catheter measurement before BAL and no patient had cardiac rejection or pulmonary infection. The significantly higher HS scores in the HTRs late after transplant (mean 6·3 months) suggest an interstitial process with microvascular leakage that may contribute to abnormalities of diffusion.

Effectiveness of patient controlled analgesia after thoracic surgery

GW PARRY, CR CAMERON, OJ LAU *Cardiothoracic Unit, Brook General Hospital, London* Analgesic response after standard posterolateral thoracotomy was compared in two patient groups with a visual analogue scale. Group A (n = 28) were managed postoperatively with opioid patient controlled analgesia (PCA). Group B (n = 30) were managed postoperatively with either intermittent intramuscular opioids (n = 12) or with continuous intravenous opioid infusion (n = 18). All patients received local (intercostal) infiltration with 0·5% bupivacaine before thoracotomy closure, and all except three received regular oral diclofenac in the postoperative period to discharge. Group A patients achieved significantly lower pain scores than group B ($p < 0{\cdot}003$). Total opioid consumption (mg/24 h) was also less in group A than group B ($p < 0{\cdot}05$). No adverse effects were seen with PCA; respiratory rate, pulse, and systemic blood pressure were not affected. Patient and staff acceptability of the PCA were both high. We conclude that PCA is safe and highly effective after thoracotomy and would commend more widespread use of this method of pain control in thoracic surgical patients.

Evolving experience in thoracoscopic management of recurrent pneumothorax

MI ISTARABADI, R HUSSAIN, A O'DONNELL, D LUKE, E MCGOVERN *Cardiothoracic Department, St James's Hospital, Dublin* In the period between June 1992 and March 1993, 23 operations, 21 patients (14 male, 7 female) ages ranging between 16–67 years had thoracoscopic pleurectomy with excision of apical bullae. Indications for surgery were two or more pneumothoraces on the same side (15 cases), prolonged air leak (seven cases), and generalised bullous disease (one case). 16 patients had right pleurectomy and seven patients had left pleurectomy. Patients were positioned in the lateral thoracotomy position, three cannulae were inserted in the anterior, middle, and posterior axillary line sixth intercostal space. This was followed by apical pleurectomy with bullae resection using an Endo GIA stapler. An intercostal chest drain was inserted into the apex of the cavity at the end of the procedure. Average operating time was 45 minutes and average blood loss was 80 ml. 15 patients were discharged within 72 hours of their operation. One operation was converted to an open thoracotomy. Thoracoscopic pleurectomy is a satisfactory method of treating recurrent pneumothorax; our evolving experience has resulted in alteration of techniques to improve results.

Exploring the role of video assisted thoracic surgery

J MCCARTHY, J HURLEY, AE WOOD *Department of Cardio-Thoracic Surgery, Mater Hospital, Dublin* Video assisted thoracic surgery (VATS) spares the patient the morbidity associated with formal thoracotomy. It allows excellent visualisation of the intrathoracic structures for both diagnostic and therapeutic procedures. With advances in technology and operator familiarity, the role of VATS has continued to expand. Using video thoracoscopic techniques in 45 patients, we have been able to perform 48 procedures. We have found the applications of this procedure to be diverse, being both diagnostic (22) and therapeutic (26). The diagnostic procedures included lung biopsy (eight), intrapulmonary masses (eight), mediastinal mass (one), pleural effusions (four), pleural biopsy (one), and were associated with a high diagnostic yield and allowed accurate staging of lung cancer, in particular nodal status in N2 disease. It also allows assessment of the disease process in patients with malignant pleural effusion. The therapeutic procedures included pleurectomy and blebectomy (seven), excision of emphysematous bullae (two), trauma (three), lung resections (five), pericardial window (one), ligation of patent ductus arteriosus (two), closure of bronchopleural fistula (one), drainage of an empyaema space (two), oesophageal resection (one), paraoesophageal hernia repair (one), and evacuation of haemothorax (one). These procedures were associated with minimal morbidity and short hospital stay. There were no intraoperative complications in either group and we did not have to resort to formal thoracotomy in any case. Although we have reservations concerning the use of VATS for resection of malignant disease, our experience indicates an expanding role for video assisted thoracic surgery and we list its chief advantages—namely, reduced morbidity and shorter hospital stay together with a high diagnostic facility and an expanding therapeutic role.

A vascularised rib strut technique: an improved chest wall fixation for correction of pectus excavatum

J F KHALIL-MARZOUK *Regional Department of Thoracic Surgery, East Birmingham Hospital, Bordesley Green East, Birmingham* Reconstruction of pectus deformities involves resection of the abnormal cartilaginous and osseous structures, restoration of normal contour, and sternal fixation in the correct anatomical position. Techniques of sternal fixation include the use of wires, metal struts, pins, synthetic mesh, and plates. Infection remains a serious problem when associated with the use of synthetic material, and recurrence of chest depression after removal of the supporting strut is often encountered. The use of an autologous vascularised rib as a strut for supporting the elevated sternum should overcome these problems of infection and recurrence; due to maintenance of vascularity there is also no postoperative resorption. The chosen rib is dissected with its vascular pedicle based on the internal thoracic artery and the intercostal artery. It is then turned 180 degrees behind the sternum and fixed to rib ends bilaterally. We have used this method in eight cases, with ages ranging between seven and 22 years. The results have all been satisfactory up to 30 months. Postoperative ventilatory control was not routinely used. Two children required artificial ventilation postoperatively. None of the adolescents or adults required reintubation. This technique is currently

our method of choice for the correction of pectus deformities. We recommend elective postoperative ventilation only in children. We intend to continue using this type of repair and to observe long term follow up.

Aetiology and outcome of congenital tracheobronchial obstruction in neonates and children

J MCCARTHY, J HURLEY, M NELIGAN, AE WOOD *Our Lady's Hospital for Sick Children, Crumlin* Recognition of the aetiology of congenital tracheobronchial obstruction is essential for a logical approach to management and an assessment of likely outcome. We have reviewed all cases of congenital tracheobronchial obstruction presenting to our unit since 1984. Seventeen patients were shown to have congenital tracheobronchial obstruction. The aetiology of the airway obstruction was congenital tracheal stenosis including funnel shaped and segmental stenosis (n = 5), segmental bronchial stenosis (n = 2), vascular rings (n = 7), vascular compression (n = 3). One patient died before surgery. The surgical procedures carried out on the remaining 16 patients included tracheal resection with end to end anastomosis using absorbable monofilament suture (n = 7) and sleeve resection of the bronchus with a similar anastomotic technique (n = 2). Seven patients had vascular ring division, two of this group also required tracheal resection. There was one aortopexy and one lobectomy. The hospital mortality was 12%. The major independent predictor of mortality and morbidity was associated cardiac anomalies. In a follow up ranging from two months to nine years there has been one death at one month after operation due to inoperable cardiac anomalies. The remaining 13 patients are well. In conclusion we have found the aetiology of congenital tracheobronchial stenosis to be divided equally between extrinsic and intrinsic causes, that the majority can be managed in a single stage procedure with a low operative mortality and incidence of postoperative strictures, and that the single most important predictor of mortality is associated intracardiac anomalies.

Changes in gastric tissue oxygen tension during mobilisation for oesophageal replacement

GJ COOPER, KM SHERRY, JAC THORPE *Departments of Thoracic Surgery and Anaesthetics, Northern General Hospital, Sheffield* We have measured changes in gastric tissue oxygen tension (PtO_2, mm Hg), using a modified Clark electrode, in eight patients (median age 59 years, range 52 to 74) undergoing oesophagectomy for carcinoma. Operations were performed with a cervical anastomosis. The stomach was mobilised on the right gastric and gastroepiploic arteries. PtO_2 was measured in the gastric fundus (1) before mobilisation, (2) after mobilisation with the stomach in the abdomen, (3) with the fundus lifted to the neck, and (4) after anastomosis. There were no significant differences in blood pressure, cardiac output, or oxygen delivery at each of the readings but PtO_2 fell. Mobilising the stomach halves fundal PtO_2 but there is no further fall with transposition to the neck. These findings suggest that concern about gastric ischaemia should not influence the choice of level of anastomosis for oesophagectomy.

	Reading			
	1	*2*	*3*	*4*
Mean PtO_2	76·47	35·63	35·95	36·20
95% CI	48·5–104·5	25·2–46·0	26·2–45·7	24·3–48·1

$p < 0·001$ 1 *v* 2; $p > 0·05$ 2 *v* 3 and 3 *v* 4, paired *t* test.

Capsaicin cough sensitivity increases during naturally occurring upper respiratory infection

F O'CONNELL, VE THOMAS, JM STUDHAM, RW FULLER, TP O'NEILL, NB PRIDE *Departments of Clinical Pharmacology and Respiratory Medicine, Royal Postgraduate Medical School, Du Cane Road, London and Proctor and Gamble, Miami Valley Laboratories, Cincinnati, Ohio, USA* To assess the effects of uncomplicated upper respiratory infection (URI) on the sensitivity of respiratory responses, capsaicin induced cough and methacholine induced bronchoconstriction were studied in a prospective study in 103 normal healthy volunteers. Thirty one subjects reattended with URI over a one year period. Fourteen complained of dry cough, eight of productive cough, and nine had no cough. The log concentration of capsaicin required to elicit at least two coughs (C2) was significantly lower during infection compared with recovery ($p = 0·002$) but not baseline ($p = 0·11$) in all 31 subjects. Log C5 (concentration that caused at least five coughs) was lower during infection than baseline and recovery values ($p = 0·008$ and $0·0005$ respectively). Subjects with dry cough showed enhanced C2 and C5 responses during infection compared with both baseline (C2 $p = 0·04$, C5 $p = 0·009$) and recovery (C2 $p = 0·016$, C5 $p = 0·003$) values. Subjects with no cough showed less increase in capsaicin sensitivity during infection compared with recovery but not baseline and those with productive cough showed no change (figures are mean (SE) μM capsaicin). FEV_1 values were unchanged during infection. Only 10 subjects achieved a PC_{15} methacholine $\leqslant 64$ mg/ml on at least one visit and values were unchanged during infection compared with baseline. Changes in capsaicin sensitivity were therefore unrelated to alteration in bronchial tone or reactivity. Significant correlation was found between change in capsaicin sensitivity and severity of cough symptoms. Twenty six control subjects who reattended without URI showed no change in capsaicin sensitivity. Upper respiratory tract infection may cause cough as a result of increased sensitivity of airway sensory nerves involved in mediation of cough.

		"Baseline"	*"Illness"*	*"Recovery"*
All subjects	log C2	0·81 (0·16)	0·55 (0·11)	0·95 (0·14)
(n = 31)	log C5	1·84 (0·15)	1·47 (0·16)	1·94 (0·12)
Dry cough	log C2	0·89 (0·24)	0·48 (0·16)	0·98 (0·17)
(n = 14)	log C5	1·66 (0·22)	1·21 (0·23)	1·90 (0·17)
Wet cough	log C2	0·86 (0·31)	0·89 (0·27)	0·93 (0·30)
(n = 8)	log C5	1·68 (0·27)	1·61 (0·25)	1·72 (0·22)
No cough	log C2	0·63 (0·33)	0·36 (0·15)	0·93 (0·31)
(n = 9)	log C5	2·26 (0·29)	1·76 (0·34)	2·20 (0·27)

Relation of static lung compliance to dyspnoea and exercise capacity in chronic heart failure

SA EVANS, WJM KINNEAR, L WATSON, AJ COWLEY, IDA JOHNSTON *University Hospital, Nottingham* The pathogenesis of dyspnoea in chronic heart failure (CHF) is poorly understood. Static lung compliance (SLC) is reduced in CHF, and may be a causal factor in the dyspnoea experienced in this condition. To examine this hypothesis we have investigated the relation of SLC to exercise capacity and levels of dyspnoea in CHF. SLC was calculated from expiratory pressure-volume curves in 20 patients (three women) with CHF, (mean age 62 years). Catheter mounted pressure transducers (Gaeltec) were used to measure changes in oesophageal pressure. Changes in lung volume were determined by integrating flow at the mouth as measured by a pneumotachograph (Fleish). New York Heart Association (NYHA) class for dyspnoea was determined by a single observer. Patients underwent treadmill exercise to symptom limited maximum using staged and fixed rate protocols. Borg ratings for dyspnoea at submaximal exercise were also measured. SLC, whether expressed as % total lung capacity (TLC)/cm H_2O, or % predicted TLC/cm H_2O, was unrelated to NYHA class. Similarly, there was no significant relation between SLC and exercise capacity with either protocol, or with Borg ratings for dyspnoea at submaximal exercise, with the exception of that measured after 11 minutes of the staged protocol ($n = 7$, $r = 0·8$, $p < 0·02$). SLC is not related to treadmill exercise capacity in CHF, and its relation to measures of dyspnoea is variable. It is unlikely that lung elasticity has a role in determining the symptomatology of CHF.

Basal metabolic rate in patients with chest bellows disease

MK SRIDHAR, MEJ LEAN, SW BANHAM *Department of Respiratory Medicine, University Department of Human Nutrition, Glasgow Royal Infirmary, Glasgow* Patients with chest bellows disease (CBD)-like kyphoscoliosis (KS) and thoracoplasty (T) are characterised by an increased work of breathing. We studied 12 patients (mean age 58·8 years) with CBD (seven KS; five T) and six healthy matched controls to determine whether increased work of breathing is associated with a raised BMR as measured by an indirect calorimeter

(Deltatrac MBM-100 metabolic monitor). Vital capacity (VC) was measured by a whole body plethysmograph (PK Morgan Ltd). Height, weight, triceps skin fold thickness, and midarm circumference were also measured. VC was 20%-64% predicted in patients (mean 41%). For controls there was a close correlation between measured and predicted BMR (Harris-Benedict and Schofield equations; mean (SE) measured 5229 (381); predicted 5335 (276); 95% CI −450 to 520 kJ/24h). For patients, although there was no significant difference between measured and predicted values at the 5% level, the 95% CIs were wider (measured BMR 6048 (424); predicted 5345 (347); 95% CI −436 to 1843 kJ/24h]. The BMR was within 5% of the predicted values in all the controls; it was greater than 10% predicted in seven out of 12 patients (five KS, two T). There was no correlation between resting lung function, anthropometric measures, and BMR in the patients. We conclude that the increased work of breathing in patients with CBD is not always associated with an increase in BMR. Methodological problems relating to interpretation of anthropometric and metabolic data in patients with CBD are discussed.

Change in lung density by computed tomography: measure of microscopic emphysema with age

H MOUDGIL, D MORRISON, K SKWARSKI, S PHILLIPS, M CONNELL, JK BEST, W MACNEE *University Department of Respiratory Medicine, City Hospital, Edinburgh* Lung density by computed tomography correlates with morphometric measurements of distal airspace size as a measure of microscopic emphysema and functionally with the volume corrected diffusing capacity (KCO) (*AARD* 1988;37:380); pathological measurements of distal airspace size also correlate with age in non-smokers and most smokers. Furthermore there is the suggestion that functional correlations with CT scanning are more significant if expiratory rather than inspiratory scans are used. If CT lung density, as a non-invasive and repeatable investigation, is to provide a surrogate measure for detecting and quantifying the severity of emphysema, a reference range of normality has to be defined against increasing age. Also methods used in CT assessment need to be optimised, in particular inspiratory *v* expiratory scans. Data would enable application of CT lung density during life to study the pathogenesis and epidemiology of emphysema, and in the evaluation of newly proposed treatments. 34 subjects (surgical candidates with peripheral resectable tumours and normal subjects) were studied (mean age 54·4 (range 27–78) years and mean FEV_1 2·49 (range 1·4–5·1). There were 20 smokers (16 men, four women, mean age 61 (range 30–78) years and mean FEV_1 2·49 (range 1·4–3·85) l) and 14 non-smokers (10 men, four women, mean age 44·9 (range 24–78) years and mean FEV_1 3·48 (range 1·62–5·1) l). Two CT slices at and 5 cm above the carina were analysed in full inspiration and expiration on a 9000 CT scanner. Lung CT density was analysed on a SUN workstation with specifically designed software generating histograms and providing Hounsfield unit values for the mean and the lowest fifth percentile of the distribution density values of the full slices and lateral 2/5th of each lung. Preliminary results suggest a weak correlation ($r = 0{\cdot}48$, $p < 0{\cdot}01$) between CT density (of the lateral 2/5th of the lungs) and age for the group as a whole but only on the expiratory scan. There was no significant correlation between CT density and age when data from smokers and non-smokers were analysed separately. Significant correlations between KCO and CT lung density were shown for the group as a whole using data from the inspiratory scans ($r = -0{\cdot}43$, $p < 0{\cdot}02$) and expiratory ($r = 0{\cdot}50$, $p < 0{\cdot}01$); a weak correlation was also shown in the group of smokers for both inspiratory ($r = -0{\cdot}45$, $p < 0{\cdot}05$) and expiratory ($r = -0{\cdot}45$, $p < 0{\cdot}05$) scans, but not for non-smokers. CT density on expiratory scans separated smokers from non-smokers better than inspiratory CT lung density. We conclude that CT lung density does decrease with age and that expiratory CT scans may be the better method to quantify microscopic emphysema from CT lung density. [This work was supported by the Norman Salvesen Emphysema Research Trust.]

Use of the inspiratory effort quotient in predicting weaning outcome

P AGARWAL, K CHATHAM, K MCCONNOCHIE *Section of Respiratory Medicine, University of Wales College of Medicine, Llandough Hospital, Penarth, South Glamorgan* Inspiratory muscle fatigue may occur when the mean inspiratory pressure ($Pmus_I$) developed during a breathing movement expressed as a fraction of the maximum static inspiratory muscle pressure exceeds a critical ratio of 0·15–0·20. This ratio is known as the inspiratory effort quotient (IEQ). As a working approximation, $Pmus_I = (kV_T/Cdyn)\ (T_I/T_{TOT})$ where V_T is the tidal volume, Cdyn is the effective dynamic compliance, T_I/T_{TOT} is the inspiratory duty cycle, and k is a constant (0·75 in intensive care unit patients). From this:

$$IEQ = \frac{(kV_T/Cdyn) \times (T_I/T_{TOT})}{Pimax}$$

where Pimax is the maximum inspiratory pressure. This study aimed to evaluate the bedside use of IEQ to predict successful weaning given that this should occur when IEQ is less than 0·15. Factors for the equation were deduced from ventilator settings. Dynamic compliance was taken as the product of ventilator tidal volume and peak airway pressure deflection − positive end expiratory pressure. The duty cycle was taken as 0·3 with a V_T of 400 ml. Pimax was recorded with a commercially available pressure manometer. Twelve patients were studied. The decision to wean was made on clinical grounds only. Six weaned successfully at the first attempt. IEQ on day of extubation ranged from 0·06 to 0·18. Six failed to wean at first attempt (IEQ range 0·13–0·4). The patient who failed to wean with IEQ of 0·13 had Guillain-Barré syndrome and subsequently weaned with IEQ of 0·07. We conclude that the IEQ equation can usefully contribute to the decision to wean.

Nasal masks for positive pressure ventilation: survey of patient use and complications

DJ MEECHAM JONES, GM BRAID, JA WEDZICHA *Department of Thoracic Medicine, The London Chest Hospital, Bonner Road, London* Nasal intermittent positive pressure ventilation (NIPPV) and nasal continuous positive airway pressure (CPAP) are used in the domiciliary treatment of chronic ventilatory disorders, with ventilation administered through tightly fitting nasal silicone masks. The success of the technique depends on long term patient acceptance of the masks, which may cause complications, although the incidence of mask problems is unknown. We have carried out a survey of nasal mask use and complications in all patients using NIPPV or nasal CPAP with the Respironics nasal mask at the London Chest Hospital. 66 patients (46 men 20 women) were surveyed, median age 55 (range 21–75); 26 patients were using NIPPV (median use 13 (2–58) months), 40 CPAP (use 16 (3–60) months). The stated median daily use of ventilation was seven (3–13) hours. Complications were categorised as major: broken skin or open sores, or minor: slight skin irritation, red or painful areas of skin. 29 patients (44%) described no mask problems, 12 (18%) had major problems, and 25 (38%) had minor problems, with no difference between the NIPPV and CPAP patients. Of those with major problems, eight patients had broken skin or ulceration for less than four weeks, four had problems for longer. 16 patients (23%) (six NIPPV, 10 CPAP) experienced disruption of treatment on at least one night per week due to mask discomfort. 20 patients (12 NIPPV, eight CPAP) started using the nasal mask during an acute exacerbation; five of these developing problems (two major, three minor). Of the remaining 46 patients who used the mask solely for chronic use, four developed major problems within the first month of treatment. There was no significant difference in the rate of major mask complications between those starting treatment acutely or chronically. Patients on oral steroids however, were significantly more likely to develop complications ($p = 0{\cdot}03$). For improved mask fitting, 24 patients used foam wedges, four used cloth linings, and two used Granuflex patches for major nasal complications. For the four patients with persistent ulceration, we have developed individually moulded silastic mask pads (Otoform K2) for protection and healing. All patients with major mask complications have experienced satisfactory healing and good compliance with treatment. Although the overall incidence of nasal mask complications with home NIPPV or CPAP is high, treatment is very effective and allows continuation of ventilation. Silastic moulds are especially useful for major problems and achieve successful healing. Attention to mask complications will improve the compliance and efficacy of home ventilatory support. [This work is supported by The British Lung Foundation.]

Prediction of dangerous hypoxaemia during aircraft flight

AOC JOHNSON, RL PAGE, SB PEARSON, D SAPSFORD, JG JONES *Respiratory Unit, Killingbeck Hospital, Leeds and Department of Anaesthesia, University of Leeds* Passengers with impaired gas

exchange are at risk of developing dangerous hypoxaemia during air travel and should receive in flight oxygen if their saturation will fall below 85%. We investigated a new method for predicting altitude related desaturation. Arterial saturation (Sao_2) is measured at five different inspired oxygen pressures (Pio_2) and the data used to plot a curve relating Pio_2 and Sao_2. The curve is similar to the oxyhaemoglobin dissociation curve but is displaced downwards when there is intrapulmonary shunting and to the right when there is ventilation perfusion inequality. The curve should then allow prediction of Sao_2 at differing Pio_2 without exposing the subject to that Pio_2 (*Br J Hosp Med* 1989;42:140). We initially studied 13 subjects with chronic obstructive pulmonary disease. Each had Sao_2 measured on five different Pio_2 between 21 and 40 kPa. The data were used to construct a Pio_2/Sao_2 curve as above. Each subject also inhaled 15–17·5 kPa oxygen to simulate aircraft cabin Pio_2. This observed cabin Sao_2 was then compared with the predicted value (derived from the curve) for the same Pio_2. The results as mean (range) were (1) Sao_2 on air: 93·1 (89–95%); (2) observed cabin Sao_2: 85·4 (81–91%); (3) predicted cabin Sao_2: 73·5(51–86%); (4) difference (observed − predicted): 12·0 (5–33%). Predicted cabin Sao_2 was always lower than the observed indicating that a compensatory mechanism is being activated to protect against more severe hypoxaemia. This is currently being studied in detail. In a larger group of 23 subjects, we found a good correlation between rightward displacement (shift) of the Pio_2/Sao_2 curve and observed cabin Sao_2 ($r = -0{\cdot}83$, $p < 0{\cdot}0001$). Correlation between saturation on air and observed cabin Sao_2 was less good ($r = 0{\cdot}56$, $p = 0{\cdot}0054$). More importantly, all subjects who had a cabin saturation below 85% had a shift of greater than 9 kPa, whereas there was no particular saturation on air that could identify subjects at risk of inflight desaturation. We propose a novel method of assessing the risk of dangerous hypoxaemia in flight. It requires only the measurement of saturation on air and four different levels of Fio_2 delivered by face mask. (This obviates the need for special equipment, for example, oxygen analyser, nitrogen source as required in conventional assessment.) The data are entered into a computer and shift calculated. Patients with a shift of >9 kPa are at high risk of dangerous hypoxaemia and require in flight oxygen.

Determination of effective inspired oxygen concentration ($F_IO_2$eff) during oxygen treatment

CB COOPER, JM STRAKOVA, LS WILKINSON, JR COLTHURST *UCLA School of Medicine, Los Angeles, California, USA* During oxygen treatment inspired oxygen concentrations fluctuate because of variations in inspiratory flow rate and tidal volume. Determination of the "effective $F_IO_2$eff) is therefore difficult. We used a graphical analysis of respiratory gas exchange as described by Rahn and Fenn (*American Physiological Society* 1955) to derive a linear relation between expired concentrations of CO_2 and O_2. We extrapolated to obtain the "inspired point" and this was taken to represent $F_IO_2$eff. We studied 10 subjects (three men, seven women) with chronic hypoxemia. Breath concentrations of CO_2 and O_2 were measured from a standard mouthpiece using a mass spectrometer with a sampling frequency of 100 Hz. Four subjects had transtracheal catheters allowing direct sampling of tracheal gas. We compared a molecular sieve (SI) producing 96% O_2 with a membrane separator (SE) producing 47% O_2. We compared three types of O_2 delivery: standard nasal cannulae (NC), occluding cannulae (OC), and transtracheal catheters (TC). Mean values of $F_IO_2$eff are given in the table. The "effective F_IO_2" with oxygen treatment is lower than previously believed. Fifty nine paired determinations of $F_IO_2$eff showed agreement between tracheal and mouthpiece sampling ($r = 0{\cdot}92$). Two types of nasal cannulae gave similar values of $F_IO_2$eff, reaching 33·6% with the 97% O_2 and 28·5% with the 47% O_2 supply. Transtracheal delivery gave significantly higher values of $F_IO_2$eff, reaching 45·2% with the 97% O_2 and 32·0% with the 47% O_2 supply. Expired gas analysis is a valid means of determining $F_IO_2$eff in chronically hypoxaemic patients receiving oxygen treatment.

		O_2 supply (l/min)						
	Sample	*RA*	*SI 1*	*SI 3*	*SI 5*	*SE 4*	*SE 6*	*SE 8*
NC	Trachea	20·8	22·8	28·0	32·3	23·4	25·2	27·8
	Mouth	20·7	22·3	26·8	31·8	23·2	24·8	27·6
OC	Trachea	20·8	22·8	27·3	31·4	23·8	26·7	28·5
	Mouth	20·7	22·9	27·5	33·5	23·9	26·2	28·1
TC	Mouth	20·7	25·0*	34·9*	45·2*	26·1*	29·9*	32·0*

*p < 0·05 (ANOVA); RA = room air.

Effect of hyperoxia on renal blood flow in normal humans

M LONG, R COSTELLO, D O'DONNELL, S O'NEILL *Department of Respiratory Medicine, Beaumont Hospital, Dublin, Ireland* The effect of high inspired oxygen concentration (O_2) on renal blood flow (RBF) in humans is unknown. Studies in animals show hyperbaric O_2 to have a vasoconstrictor effect on renal, cerebral, retinal, and limb vessels. In a previous study of patients with hypoxaemic respiratory failure (a condition where RBF is known to be reduced) correction of hypoxia was associated with an improvement in RBF (Long *et al. Eur Respir J* 1992;5(suppl 15):486s). This study examines the response of the renal vasculature to high concentration of inspired O_2 in nine healthy male volunteers. RBF was assessed non-invasively with duplex Doppler ultrasound. An Acuson 128 system with a 2 MHz probe was used to scan the renal interlobar vessels via the translumbar route. Pulsatility index (PI) was calculated as a measure of renovascular resistance. PI is obtained by dividing the difference between the maximum systolic and the minimum diastolic velocity by the mean velocity. A fall in PI corresponds to a fall in distal resistance to flow. PI is measured sequentially while the subject is breathing room air/100% O_2 for 10 minutes and after discontinuation of 100% O_2. We found an immediate and significant ($p < 0{\cdot}005$) fall in PI while breathing 100% O_2. We conclude that hyperoxia is associated with renal vasodilation in normal subjects.

	Patient no.								
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
A	0·72	0·85	0·65	0·76	0·73	0·69	0·69	0·66	0·69
B	0·63	0·65	0·52	0·57	0·80	0·61	0·55	0·52	0·53

A = PI on room air; B = PI on 100% O_2.

Autonomic nerve function and cardiac arrhythmias in patients with chronic obstructive airways disease

W BIERNACKI, S SCHOLEY, G CLAPHAM, S DEAN, MD PEAKE *The Chest Unit, General Infirmary, Pontefract, West Yorkshire* A previous study has shown impairment in autonomic nerve function in some patients with chronic obstructive airways disease (COAD) (Stewart *et al. Eur Respir J* 1991;4(suppl 14);525). This included prolongation of the QTc interval. Cardiac arrhythmias are common in these patients and may be a cause of sudden death. There is no published work on the relation between autonomic function and cardiac arrhythmias in these patients or its relation to hypoxaemia. We have studied 15 patients (eight men) aged 65 (8) years with severe COAD (FEV_1 34% (9%) of predicted) and a wide range of emphysema as judged by gas transfer (K_{CO} 22–125% of predicted). All patients underwent a battery of autonomic function tests and had 24 hour ambulatory ECG monitoring. Seven out of 15 patients had impaired sympathetic postural tone, but only three had demonstrable parasympathetic nerve abnormalities. Mean QTc interval for these three patients was prolonged at 0·54 (0·03) s whereas it was normal in others. There was no obvious correlation between the degree of airflow obstruction, resting arterial Po_2 or transfer factor and the presence or absence of autonomic abnormalities. Four out of 15 had significant cardiac arrhythmias but these seemed unrelated to the abnormalities in autonomic nerve function.

Phosphodiesterase inhibitors may not have a long term therapeutic role in chronic obstructive pulmonary disease (COPD)

AY BUTT, TW HIGENBOTTAM, M TAKAO, G CREMONA *Respiratory Physiology Department, Papworth Hospital, Papworth Everard, Cambridge* Enoximone is a type III phosphodiesterase inhibitor and has been shown to reduce pulmonary hypertension and airway resistance in decompensated chronic obstructive pulmonary disease (COPD) (Leeman *et al. Chest* 1987;91:662–6). Its role as a long term treatment of COPD is, however, not known. We have prospectively studied 12 patients with severe but stable COPD (mean age (SD) 61 (5·8), six men and six women, mean FEV_1 0·56 (0·2) litres). Right heart catheterisation was performed during which vasodilatory responsiveness to intravenous prostacyclin was assessed. Patients were then randomised either to oral enoximone (100 mg three times daily) or placebo for two six week periods

intervened by a two week washout period with a placebo followed by a crossover. Pulmonary function tests and exercise tolerance during a six minute walk were measured at baseline and at 1,3,6,9,11, and 14 weeks of the study. The results (mean (SD)) are shown in the table. By comparison with placebo, enoximone did not cause any significant improvement in airway obstruction or exercise tolerance in this group of patients. Phosphodiesterase inhibitors may not have a long term therapeutic role in the management of COPD.

Tests	*Base line*	*Placebo*	*% rise (placebo)*	*Enoximone*	*% rise (enoximone)*
6 minute walk (m)	199·2 (73·1)	267·4 (96·2)	33·7 (19·4)	258·6 (97·7)	33·7 (26·2)
FEV_1 (l)	0·56 (0·2)	0·59 (0·18)	10·6 (39·4)	0·6 (0·16)	14 (34·4)

Exhaled nitric oxide is not diminished in primary pulmonary hypertension

G CREMONA, BA MIST, TW HIGENBOTTAM *Department of Respiratory Physiology, Papworth Hospital, Cambridge* Impaired endothelium dependent relaxation has been found in the conduit pulmonary arteries of patients with secondary pulmonary hypertension (Dinh Xuan *et al. Br J Pharmacol* 1990). Endogenous NO can be measured in the exhaled air in vivo (Gustafsson *et al. Acta Physiol Scand* 1992). We have measured NO in the exhaled air of eight patients with primary pulmonary hypertension (PPH) and six healthy volunteers by chemiluminescence (Model 42, Thermoelectron, Warrington, UK). The subjects breathed NO free air (NO concentration <0·5 parts per billion) for 15 minutes through a non-rebreathing valve into a metabolic gas analyser (Model 2900z, Sensormedics, Rugby, UK) that allowed measurement of V_{O_2}. NO was measured directly from the mixing box. The NO signal was stable after five minutes of steady breathing and the measurements taken during the past five minutes were used to calculate NO production. Single breath T_{LCO} was also measured. The mean rate of NO production was 4·02 (1·15) *v* 2·84 (1·97) nmol l^{-1} min^{-1} (p = 0·59) in the control and PPH group respectively. Predicted K_{CO} was lower in patients with PPH (89 (8) *v* 63 (20)%; p = 0·01) probably reflecting the decrease in pulmonary capillary blood volume.

Effect of n^{Ω}-nitro-L-arginine (LNA) on the adaptation of the pulmonary capillary bed to increased flow in perfused pig lungs

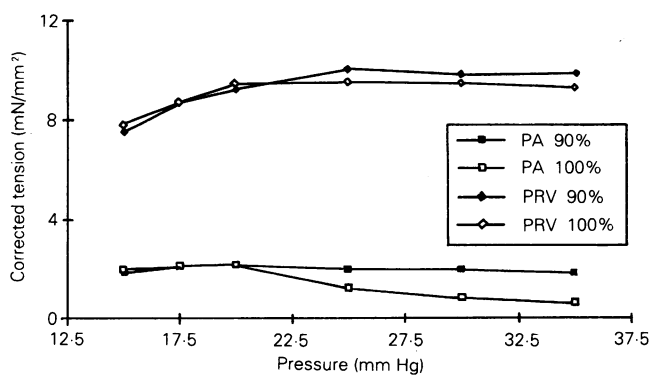
G CREMONA, M TAKAO, TW HIGENBOTTAM *Department of Respiratory Physiology, Papworth Hospital, Cambridge* The arterial and venous occlusion techniques divide the total resistance across the pulmonary vasculature into three components—namely, arterial (Ra), venous (Rv), and middle (Rm) (Hakim *et al. J Appl Physiol* 1982). We have used arterial and venous occlusion in isolated pig lungs to investigate the changes in the various segments with increased flow before and after treatment with N^{Ω}-nitro-L-arginine (LNA), an inhibitor of NO production. The perfusate consisted of 1·5 to 2 litres of autologous blood and 1 to 1·5 litres of Krebs with 3·5% dextran. Perfusate packed cell volume was 20–25%. The lungs were ventilated with a gas mixture containing 30% O_2 and 5% CO_2 in N_2. Perfusion was instituted at 1 l min^{-1} and after an equilibration period of one hour, arterial and venous occlusions were performed. This was repeated at varying flow rates (50, 75, and 100 ml min^{-1} kg^{-1}) before and after giving LNA (10^{-4}M). With increasing flow there was an increase in the resistance of the arterial segment. After addition of LNA the slope of the Q-Ra relation increased. By contrast the resistance of the middle segment decreased with increasing flow both at baseline and after LNA. LNA increased the Rm but the Q-Rm relation remained constant. Rv increased with flow but did not change after LNA. The results indicate that LNA increases the ohmic resistance of the arterial segment and the critical pressure of the middle segment.

Magnitude of acute hypoxic pulmonary vasoconstriction (AHPV) during lobar hypoxia in man

NW MORRELL, KS NIJRAN, T BIGGS, WA SEED *Departments of Medicine and Nuclear Medicine, Charing Cross and Westminster Medical School, London* AHPV plays an important role in the maintenance of ventilation-perfusion balance in many species. Despite this, few studies have investigated the magnitude and time course of the response in man. Using fibreoptic bronchoscopy we have produced localised regions of alveolar hypoxia by placing balloon tipped catheters to occlude lobar bronchi in six young normal volunteers. The P_AO_2 and P_ACO_2 inside the occluded lobe were monitored continuously by a mass spectrometer connected to the proximal end of the catheter. During the occlusion 2–3 mCi ^{99m}Tc–labelled macroaggregated albumin (MAA) were injected into a peripheral vein with the subject lying supine. The occluding balloon was then deflated and the bronchoscope removed. The resulting defect in perfusion was imaged with a gamma camera. Multiple view lung scans were performed collecting 300 000 counts per view. A control perfusion scan was performed one week after the experiment to allow calculation of percentage reduction in blood flow to the occluded lobe as measured by the distribution of ^{99m}Tc activity. During lobar occlusion the mean (SE) P_AO_2 and P_ACO_2 rapidly approached mixed venous levels of 42·9 (2·5) mm Hg and 39·8 (1·2) mm Hg, respectively. The calculated mean reduction in blood flow for the six subjects was 42% (5%) (range 27% to 58%). The mean time from occlusion to injection of ^{99m}Tc-MAA was 147 seconds (range 80 to 300 seconds). Blood flow was redistributed to the unoccluded lobes, with the largest increases in flow observed in the ipsilateral unoccluded lobes. This study demonstrates that AHPV at the lobar level is a strong reflex in normal subjects and that the response is greater than that previously reported in studies of unilateral hypoxia in an entire lung.

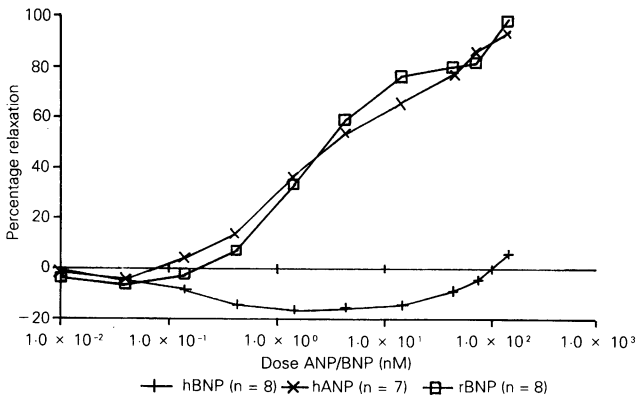
In vitro tension–reactivity relationship in isolated rat pulmonary artery

F ZHANG, JS THOMPSON, AH MORICE *Department of Medicine, University of Sheffield, Royal Hallamshire Hospital, Sheffield* Mean pulmonary artery (PA) pressure ranges from approximately 15 mm Hg in normal animals to 35 mm Hg in hypoxic pulmonary hypertensives. What tension should be used in vitro to simulate these physiological conditions? Using a small vessel myograph it is possible to investigate the vasoactive properties of isolated blood vessels under various conditions. In this study we have investigated the tension-reactivity relationship of isolated pulmonary resistance vessels (PRV) and PA. PRV (<300 μm) and PA (>800 μm) were dissected and mounted on an automated myograph (Cambustion, Cambridge). Vessels were maintained in oxygenated physiological saline solution (5 ml) at 37°C. Resting tensions equivalent to intramural pressures of 15, 17·5, 20, 25, 30, and 35 mm Hg were set. It has been suggested (Mulvaney and Halpern, *Circ Res* 1977;**41**: 19–26) that in systemic vessels vasoactivity is greater when vessel tension is reduced by an amount corresponding to 90% of the internal diameter. We therefore tested the vasoreactivity of each pulmonary vessel at 90% and 100% of the diameter at each preset pressure. KCl (100 mM) was added to the bath and tension (mN/mm) recorded when the contractile response was stable. Results were shown as active tension divided by vessel diameter (mN/mm^2). Analysis of active/passive tension (signal to noise ratio) suggests that the lowest pressure should be used as both PA and PRV had the greatest active/passive tensions at 15 mm Hg. The analysis of vascular responses requires a consistent tension-reactivity relationship. This occurred over the range of physiological passive tensions, provided that results were expressed as mN/mm^2.



Are the effects of atrial peptide on pulmonary artery species specific?

W SHEEDY, AH MORICE *Department of Medicine and Pharmacology, University of Sheffield, Royal Hallamshire Hospital, Sheffield* Brain natriuretic peptide (BNP) is a hormone which is closely related in its structure and some physiological actions to atrial natriuretic peptide (ANP). We have previously shown that both human and rat ANP are vasodilators of prostaglandin (PGF) F_{2a} contracted rat pulmonary arteries (PA). Here we report the effects of human and rat BNP compared with human ANP on rat pulmonary arteries contracted in response to PGF_{2a}. Vessels were dissected and mounted as ring preparations in the organ bath of an automated small vessel myograph (Cambustion, Cambridge). A concentration of 100 μM PGF_{2a} was used to obtain maximum contraction. When the contraction had stabilised dose-response curves were obtained using up to a maximum of 165 nM peptide. These results suggest that, unlike ANP, BNP is species specific in its actions.



National tuberculosis survey (1991): preliminary analysis for the Republic of Ireland

D MCKEOWN, P KELLY, L CLANCY *Peamount Hospital, Newcastle, Co. Dublin, Republic of Ireland* All public health specialists, hospital clinical consultants, and heads of diagnostic laboratories were surveyed by postal questionnaire to determine a profile of tuberculosis in 1991 and the results compared with our previous survey for 1986 (*Proc SEP, Freiburg*, 1988). Preliminary analysis showed that the incidence of tuberculosis has decreased from 21·4 to 16·7 per 100 000 with no significant change in age distribution; some 30% are $\leqslant$35 years; proven bacteriologically/histologically (50%). There is still no uniformity in terms of tuberculin testing, both the Heaf and Mantoux technique being used. Analysis of the incidence of tuberculosis in those aged $\leqslant$15 years showed that there is a significantly lower incidence ($p = 0{\cdot}0000019$) in this age group in areas that have a policy of neonatal BCG vaccination. HIV associated tuberculosis now comprises 3% of all reported cases with drug resistant tuberculosis and atypical mycobacterial infection (other than in HIV positive patients) comprising less than 1% each. Despite a slight increase in reported incidence of tuberculosis in the late 1980s, overall the trend in incidence of tuberculosis in the Republic of Ireland is downward. Approximately 30% are younger than 35 years. Neonatal BCG vaccination appears to offer significant protective benefit against tuberculosis in the younger age group in the Republic of Ireland.

Consumption and underconsumption: a minority problem?

DPS SPENCE, J HOTCHKISS, CSD WILLIAMS, PDO DAVIES *Aintree Chest Centre, Tuberculosis Research Centre and Public Health Observatories, Liverpool* We have previously shown a link between indices of poverty and the rate of notification of tuberculosis within the city of Liverpool. It has been suggested that this may be due to increased rates of tuberculosis among ethnic minorities from Asia, the Indian subcontinent and Africa who also suffer the highest levels of deprivation. We have re-examined by electoral ward all notifications of tuberculosis over the period 1985–90 and identified cases from ethnic minorities. Data on the ethnic mix of each electoral ward is available from 1991 census returns. Rates of tuberculosis among the white population were correlated with several indices of deprivation, free school meals (FSM), council housing (CH), Townsend overall deprivation index (ODI) and Jarman index (JI) using Spearman rank correlations. The population of Liverpool during the period studied was 452 486 of whom only 3·78% were non-white: 24% described their ethnic origin as Asian, 9% from the Indian subcontinent, and 14% from Africa. During the period studied there were 344 cases of tuberculosis of whom 49 were among ethnic minorities. Rates of tuberculosis among the white population correlated with all indices of poverty (FSM, $r = 0{\cdot}49$; CH, $r = 0{\cdot}42$; ODI, $r = 0{\cdot}58$; JI, $r = 0{\cdot}65$). We conclude that increased rates of tuberculosis among the poorest in our city are not explained by high incidences of the disease in socially deprived ethnic minorities.

Changing trends of presentation of pulmonary tuberculosis in one Liverpool hospital

FC LESLIE, MJ WALSHAW, CC EVANS, CRK HIND *The Cardiothoracic Centre and Broadgreen Hospital, Liverpool* There has been an increase in the number of reported cases of pulmonary tuberculosis both in the UK (OPCS data 1991) and in the USA (*Am Rev Respir Dis* 1989;**140**:1788). It is our impression that both the proportion of atypical presentations and cases due to non-tuberculous mycobacteria are also rising. To study this further we have analysed all 68 cases of pulmonary tuberculosis seen at this hospital over 84 months up to June 1992 (43 men, mean age 51·2 years, range 16–83; 65 white). Whilst the majority presented with classical symptoms and chest radiographic changes of pulmonary tuberculosis, seven presented with lower zone shadowing only. A further nine were initially thought to have bronchial carcinoma and the diagnosis of tuberculosis was only made after thoracotomy. We divided the study period into two halves: more cases presented in the latter half (43, 63%). There were also significantly more atypical presentations in the latter half (14/43 *v* 2/25; $z = 2{\cdot}75$, $p < 0{\cdot}01$) and more atypical mycobacterial infections (9/43 *v* 3/25); seven *M kansasii*, three *M malmoense*, one *M chelonei*, one *M avium intracellulare*. A history of previous tuberculosis was found in 13 (19%) patients and of tuberculosis contact in eight (12%). None of the patients was in a high risk group for HIV infection, and none was shown to be HIV positive. These results confirm our impression of an increasing incidence of pulmonary tuberculosis locally. They also demonstrate increasing numbers of not only atypical mycobacterial infection but also atypical presentations in a predominantly white population not thought to be at a high risk of HIV infection.

Comparison of human and bovine *Mycobaceterium bovis* infection in south west Ireland 1983–90

TP COTTER, S SHEEHAN, B CRYAN, HN CUMMINS, CP BREDIN *Departments of Respiratory Medicine and Microbiology, Regional Hospital and University College, Cork and District Veterinary Office, Cork, Republic of Ireland* A comparison of *Mycobacterium bovis* infection in humans with *M bovis* infection in cattle in south west Ireland in 1983–90 inclusive was made. Pasteurised milk was introduced in this region in the 1950s. Human *M bovis* infection was identified by culture of sputum or other body fluids at the Regional Microbiology Laboratory. Cattle *M bovis* infection cases were identified using standard tuberculin testing methods. Results show a gradual decline in positive bovine tuberculin tests over the period: 472 per 100 000 animals in 1983 compared with 126 per 100 000 animals in 1990. This compares with 0·56 cases per 100 000 human *M bovis* infections in both 1983 and 1990. Human *M bovis* infection occurred in an elderly/middle aged group of patients (mean age 57·1), probably as reactivation disease of primary infection acquired by ingestion of unpasteurised milk 40 or more years previously. The low incidence plateau of human *M bovis* infection together with the declining incidence of animal infection suggests a cutoff in the animal to human chain of infection at two points: the animal source and the ingested (now pasteurised) milk. Accordingly the virtual elimination of active human *M bovis* disease in south west Ireland in the next 10–15 years may occur.

Association of neonatal BCG vaccination with tuberculosis in the paediatric population in Ireland

D MCKEOWN, P KELLY, L CLANCY *Peamount Hospital, Newcastle, Co. Dublin, Republic of Ireland* Analysis of the 1991 National Tuberculosis Survey indicates that a policy of neonatal BCG is associated with significantly fewer cases of tuberculosis in people $\leqslant 15$ years ($p < 0{\cdot}0000019$). We estimate that 900–1100 children need vaccination to prevent one case of paediatric tuberculosis and that in 1991 neonatal BCG was associated with preventing 60–70 cases of tuberculosis in the paediatric population (<15 years). The incidence of tuberculosis in the survey was 16·3 per 100 000 (<600 cases of tuberculosis reported) for the entire country. Previous studies have shown benefit associated with neonatal BCG vaccination (*Eur Respir J* 1991;4:778–82, *Am Rev Respir Dis* 1990;141:A894, *Eastern Health Board BCG Committee Report*, Dublin, *Proc Irish Thoracic Soc*, November 1992). We conclude that neonatal BCG vaccination is associated with significant protection against tuberculosis in the paediatric age group in Ireland. With a declining overall incidence of tuberculosis the benefits of neonatal BCG will probably be outweighed by the disadvantages towards the end of this decade.

Use of sputum induction for establishing a diagnosis in patients with suspected pulmonary tuberculosis in Malawi

CM PARRY, O KAMOTO, AD HARRIES, JJ WIRIMA, CM NYIRENDA, DS NYANGULU, CA HART *Department of Medicine, Queen Elizabeth Central Hospital, Blantyre, Malawi, Malawi National Tuberculosis Control Programme, Llongwe, Malawi and Tropical Medical Microbiology Centre, Liverpool University, Liverpool* Adults with suspected pulmonary tuberculosis in whom the expectorated sputum smear is acid fast bacilli negative or who are unproductive of sputum are increasingly seen in Malawi. Limited diagnostic facilities mean the potential for misdiagnosis in this group is high, particularly if there is coinfection with HIV. We have investigated 82 Malawian adults with suspected pulmonary tuberculosis using the technique of sputum induction. Sputum was successfully induced in 73 patients. The induced sputum was smear and culture positive for *Mycobacterium tuberculosis* in 18. In a further 38, in whom the clinical and radiological features suggested pulmonary tuberculosis, 12 were smear negative but culture positive. Of the 56 patients commenced on antituberculous chemotherapy, tuberculosis was confirmed in 45 (80%), by positive bacteriology in 30 (54%) and satisfactory response to treatment in 15 (27%). Other significant pathogens were detected in only two patients (one *Pneumocystis carinii* and one *Stronglyloides stercoralis*). Sputum induction is a useful technique in Malawian adults with suspected pulmonary tuberculosis. Significant pathogens other than *Mycobacterium tuberculosis* are uncommon. [This work was supported by the Overseas Development Administration and the Scadding-Morriston Davies Fellowship].

Tuberculin conversion in medical students after elective periods in the developing world

TP COTTER, G GIBSON, EA ABERNETHY, L PLANT, CP BREDIN *Department of Respiratory Medicine, Regional Hospital and University College, Cork, Republic of Ireland* In a prospective study from 1988 to 1992 inclusive we studied the tuberculin status of 80 fourth year medical students before and after summer elective periods in Africa. As part of the medical student health service 75 of the students had Heaf tests two years before enrolment in the study; 36 were Heaf grade 0 and 32 were Heaf +1. For purposes of the study we regarded Heaf grade 0 and Heaf +1 as negative. All 80 students were Mantoux tested (10 tuberculin units) and read at 48–72 hours. Preelectively 51 students were Mantoux negative (64%). Those with negative pre-elective Mantoux tests were given non-directional advice as to the benefit of BCG vaccination. No student opted for BCG. All students except one had a pre-elective chest radiograph and those who converted had a repeat examination. No significant radiographic abnormalities were detected. After the elective period 18 (35%) had converted. Comparing the Heaf to first Mantoux test interval (two years) and the first to second Mantoux test interval (six months maximum) the rate of conversion was significantly higher in the period of time which included the elective period (z test; $p < 0{\cdot}005$). All those who were Mantoux positive and those who converted remain free of active disease to date. This study demonstrates that there is a significant incidence of tuberculin conversion associated with medical student electives in the developing world.

Influence of cigarette smoking on Heaf grade

DPS SPENCE, CSD WILLIAMS, E MAZOUK, M NISAR, PDO DAVIES *Aintree Chest Centre and Tuberculosis Research Centre, Liverpool* Tobacco smoke increases the risk of carcinoma of the bronchus and COPD but little is known of its effect on *Mycobacterium tuberculosis* infection. To examine the relationship between smoking habit and *Mycobacterium tuberculosis* infection we have studied 146 consecutive patients attending our tuberculosis screening clinic. Tuberculin sensitivity was measured by Heaf testing. Current smoking habit, previous tobacco consumption and years since BCG vaccination were also recorded. Mean (SD) or median (range) summary data are given in the table. Heaf grades are expressed as percentages. Heaf grade was significantly correlated with age ($r = 0{\cdot}18$, $p < 0{\cdot}05$), and cigarette consumption ($r = 0{\cdot}37$, $p < 0{\cdot}001$). In those who had received BCG Heaf grade correlated with years since vaccination ($r = 0{\cdot}24$, $p < 0{\cdot}05$). We conclude that inhalation of tobacco smoke may increase the risk of *Mycobacterium tuberculosis* infection through its effect on both mucociliary clearance and local lung immunological defence mechanisms. Continued subclinical infection with *Mycobacterium tuberculosis* will result in continued stimulation of cell mediated immunity and can be measured by tuberculin sensitivity. This may be important in interpreting Heaf test results.

	Heaf grade								
	0	*1*	*2*	*3*	*4*	*Pack years*	*Age*	*% BCG*	*Years BCG*
Non-smokers (n = 55)	49	16	22	11	2	0	32 (13)	58	15 (8)
Ex-smokers (n = 16)	38	0	19	19	25	12 (1–100)	50 (16)	44	26 (7)
Now smokers (n = 75)	27	12	25	12	24	13 (1–60)	37 (11)	67	24 (10)

Tuberculin reactivity in sarcoidosis: relationship to Kveim test and chest radiograph staging

TP COTTER, CP BREDIN *Department of Respiratory Medicine, Cork Regional Hospital and University College, Cork, Republic of Ireland* We conducted a retrospective case study of patients with positive Kveim biopsies and a recorded Mantoux test. From 1982–91 inclusive 38 patients fulfilled these criteria. The initial chest radiograph in each case was staged using the Siltzbach method. We identified the number of patients with positive Mantoux tests (10 tuberculin units) and compared their radiological staging with those who were Mantoux negative (see table). Ten patients (29%) had a positive Mantoux test (10 mm or more induration). No patient had any other disease known to cause false positive Kveim tests or affect Mantoux status. No patient had evidence of active tuberculosis or has developed it since. The chest radiograph stage was not correlated with Mantoux status. Scadding calculated that only 14% of his patients with sarcoidosis reacted to 10 tuberculin units (Scadding JG, Mitchell DM. *Sarcoidosis*, 2nd ed, London: Chapman & Hall, 1985). The high proportion of patients in our series with a positive Mantoux test is likely to be related to the relatively high incidence of microbiogically proved tuberculosis in south west Ireland, although the incidence has fallen from 15·3 per 100 000 in 1983 to 9·0 per 100 000 in 1992. We would expect the proportion of Kveim test positive patients with positive Mantoux tests to fall in the next decade as a result of the gradual decline in the tuberculosis incidence in the region.

Chest radiograph stage	*Mantoux positive cases*	*Mantoux negative cases*
0	2	3
1	6	19
2	1	3
3	2	3

Is the Tine test useful in HIV disease?

C DIMIAN, SP HIGGINS, CS BRADBEER, NT BATEMAN *Departments of Genitourinary Medicine and Thoracic Medicine, St Thomas' Hospital, London* It is assumed that the loss of skin reactivity to purified protein derivative (PPD) occurs with deteriorating cellular immunity, casting doubt on the reliability of tuberculin testing in HIV positive patients (*BMJ* 1992;**304**:1231–3). In a study of 167 HIV positive patients who were tine tested PPD reactivity was maintained despite a CD4 count of 200/mm³ or less (Higgins *et al. Thorax* 1992; 47:877). As part of this longitudinal study 62 patients were retested either because their CD4 count dropped by more than 100/mm³ or it was a year since they were last tested. Skin reactions were graded as nil, low (grade 1–2), or high (grade 3–4). The results are shown in the table. Five of those becoming PPD reactive had CD4 count <200/mm³. Three of the eight patients with initial CD4 <200/mm³ maintained their reactivity though their counts continued to be <200/mm³. Three of the six patients who were PPD reactive whose CD4 counts were initially >200/mm³ maintained their reactivity though their count dropped below 200/mm³. Of the 12 patients becoming PPD negative seven had CD4 counts >200/mm³ but their counts had dropped by more than 100/mm³. Tine test is useful in HIV positive patients as it can be maintained in patients with CD4 counts <200/mm³. It can be lost in some patients with CD4 counts >200/mm³, particularly when it is falling rapidly.

Grade	*CD4 <200/m³*	*CD4 >200/mm³*
Initial testing		
Nil	17	18
Low	8	17
High	0	2
Retest		
Nil	25	15
Low	11	9
High	0	2

Interleukin 2 receptor expression is increased on peripheral blood lymphocytes in patients with moderate to severe symptomatic asthma

SP MATUSIEWICZ, WAH WALLACE, D COSSAR, SEM HOWIE, AP GREENING *Respiratory Unit, Western General Hospital and University Department of Pathology, Edinburgh* Lymphocyte activation may play an important part in regulating the inflammation of bronchial asthma. Markers of activation such as CD25 (IL-2 receptor) on blood lymphocytes have been shown to be elevated in acute severe asthma and to decline with treatment. We examined peripheral blood lymphocytes and monocytes for evidence of activation in 60 asthmatic patients with persistent symptoms despite treatment with >800 μg inhaled steroid per day (including 20 also receiving long term systemic steroids), eight mild asthmatics taking prn β_2 agonists only and 30 healthy volunteers were studied as controls. All subjects were non-smokers. Mononuclear leucocytes were separated by density centrifugation. Using flow cytometry, lymphocytes were tested against a panel of 17 monoclonal antibodies (including positive and negative controls) to assess cell surface markers of activation and results given as % positive cells. CD25 expression was increased in asthmatics on inhaled (median % positive; 8·6%) or systemic steroids (10·8%) compared with normals (3·4%) ($p = 0·003$; $p < 0·001$ Mann-Whitney U test). CD25 expression was not increased in relatively mild asthmatics (2·1%). Expression of HLA-DR and DQ class II histocompatibility antigens was reduced in chronic asthmatics taking inhaled or systemic steroids. Despite high dose inhaled or systemic steroids patients with chronic symptomatic asthma show some continued evidence of T cell activation.

Neutrophil influx and increased bronchial reactivity associated with inhaled tumour necrosis factor α

DH YATES, PJ BARNES, PS THOMAS *National Heart and Lung Institute, Dovehouse Street, London* Allergen-induced mast cell activation releases tumour necrosis factor α (TNFα), a potent pro-inflammatory cytokine known to be stored within the mast cell granule. TNFα upregulates leucocyte adhesion molecules and may therefore mediate allergen associated inflammatory cell influx. We hypothesised that exogenous TNFα may cause an inflammatory infiltrate and thus induce bronchial hyperreactivity. The effect of inhaled recombinant TNFα in normal subjects was studied by serial evaluation of inflammatory cell influx in induced sputum and measurements of bronchial reactivity. Six subjects (four men, mean age 36·8) were studied in a single blind crossover manner; two were atopic. All subjects had a non-asthmatic methacholine PC_{20}. Baseline spirometry and methacholine dose-response curves (4–128 mg/ml) were performed, sputum was induced by the inhalation of 3·5% saline. Nebulised recombinant TNFα (60 ng) or saline control was inhaled and spirometry, methacholine and sputum induction repeated 1·5, 24, and 48 hours later. Sputum cell differential counts showed an influx of neutrophils starting at 1·5 hours and persisting up to 48 hours after inhalation (mean (SD) saline control at 24 hours 19·4% (8·1%), recombinant TNFα at 24 hours 50·9% (29·7%), $p < 0·05$). At baseline a PC_{20} was measurable in one of the subjects but was detectable in four subjects at 24 hours after recombinant TNFα. There was a significant shift to the left in the mean dose-response curves ($p < 0·05$) 24 hours after recombinant TNFα. We conclude that TNFα is capable of causing an inflammatory cell influx and increasing bronchial reactivity.

Bronchoalveolar lavage differential cell counts in patients with severe chronic asthma

SP MATUSIEWICZ, PH BROWN, E RAMAGE, SEM HOWIE, AP GREENING *Respiratory Unit, Western General Hospital and University Department of Pathology, Edinburgh* Bronchoscopic procedures have increased our understanding of asthma immunopathology. While bronchoscopy, bronchoalveolar lavage (BAL), and mucosal biopsy have been shown to be safe, most have studied relatively mild asthmatics. Such studies have tended to show a relative increase in the proportion of lymphocytes and eosinophils. We have examined BAL cell profiles in patients with severe chronic asthma receiving therapy. Bronchoscopic examinations with BAL were performed on a group of non-smoking, clinically stable, severe asthmatics with chronic daily symptoms despite using high dose inhaled (800–3200 μg/day) with or without systemic steroids (mean: age 49 years; histamine PC_{20} <2 mg/ml; FEV_1 64% pred). Asthmatics were defined as relatively corticosteroid resistant (CR) by a failure of FEV_1 or mean PEF to improve by >15% following two weeks of prednisolone despite >15% response to β_2 agonists (*Am Rev Respir Dis* 1991; 144:1016) or corticosteroid sensitive (CS). Normal non-smoking volunteers were used as controls. A standardised BAL was performed. Cytospin preparations were coded, Giemsa stained and cells counted (without knowledge of clinical details). The results are expressed as mean (SD) % BAL cells (table). Statistical analyses refer to Mann-Whitney tests comparing asthmatics with controls. Asthmatics with chronic symptoms despite high dose inhaled (± systemic) corticosteroids have more lymphocytes and eosinophils in BAL than normal controls. There was a trend ($p = 0·1$) for a greater proportion of lymphocytes in BAL in corticosteroid resistant than corticosteroid sensitive asthma.

Cell	*Control*	*CS asthma*	*CR asthma*
n	7	12	7
Macrocytes	95 (3)	81 (12)*	73 (18)*
Lymphocytes	4 (3)	11 (10)*	20 (17)*
Neutrophils	0·1 (0·1)	1·0 (1·0)	0·2 (0·2)
Eosinophils	0·8 (0·8)	6·0 (9·7)*	5·8 (9·3)

*$p < 0·02$.

Relationship between cytokines IL-1β and TGFβ and macrophage subsets in the bronchoalveolar lavage fluid in asthma

S SREENAN, P DEBENHAM, CM BURKE, LW POULTER *Department of Respiratory Medicine, James Connolly Memorial Hospital, Dublin and Department of Clinical Immunology, Royal Free Hospital, London* Previous work has shown alterations in the proportions of macrophage subsets in the bronchi of asthmatic subjects. This pilot study was designed to test whether or not such alterations are reflected in changes in the profile of macrophages in bronchoalveolar lavage (BAL) fluid and related levels of cytokines in BAL supernatants. BAL was performed on asthmatic and control subjects. Lavage supernatants were tested with ELISA for levels of IL-1β and TGFβ. Double immunofluorescence staining with myoclonal antibodies RFD1 and RFD7 was used to document the proportions of

antigen presenting cells (D1+), effector cells (D7+), and suppressor macrophages (D1+, D7+). Results showed lower TGFβ and IL-1β levels in asthmatics than in control subjects. There was an increase in the proportion of D1+ and an associated reduction in D7+ macrophages in asthmatic subjects (table). These data suggest that alterations in the populations of macrophage subsets in airways of asthmatic subjects may be reflected in alterations in the cytokines of BAL fluid.

	TGFβ (pg/ml/10⁶ macrophages)	*IL-1β (pg/ml/10⁶ macrophages)*	*RFD1+ (%)*	*RFD7+ (%)*	*RFD1+, D7+ (%)*
Control (n = 9)	810·18	50·6	27	49	24
Asthma (n = 5)	250·92	10·7	45	19	36

Cytokine production by bronchoalveolar lavage cells from atopic asthmatics and normal subjects

LJ RESTRICK, AP SAMPSON, PJ PIPER, JF COSTELLO *Department of Thoracic Medicine, King's College School of Medicine and Department of Pharmacology, Royal College of Surgeons, London* We have previously shown a reduction in the capacity of bronchoalveolar lavage (BAL) cells, the majority of which are alveolar macrophages, from mild atopic asthmatics to generate LTB_4 compared with cells from normal subjects (abstract in press, *Thorax*, 1993). This may be due to altered exposure of alveolar macrophages to cytokines such as GM-CSF, IL-3 or IFN-γ, which may regulate macrophage mediator release. To test this hypothesis we assessed spontaneous and stimulated cytokine production by mixed BAL cells in vitro in 12 mild atopic asthmatics using β_2 agonists only [7F;5M; mean age 23 (range 20–29) years], with mean (SD) methacholine PC_{20} 1·40 (1·29) mg/ml and mean (SD) FEV_1 3·7 (0·8) l and in nine non-smoker controls [6F;3M; age 24 (20–32) years; FEV_1 3·5 (0·9) l]. Washed BAL cell aliquots (approximately 80% alveolar macrophages; no significant differences in % alveolar macrophages or lymphocytes between atopic asthmatics and normal subjects) were incubated in RPMI 1640 at $1·0 \times 10^6$ cells/ml for 24 hours, with or without 5 μg/ml lipopolysaccharide, and GM-CSF, IL-3 and IFN-γ were measured in the supernatants by enzyme immunoassay. LTB_4 from cell aliquots stimulated with 4 μM A23187 over 0–30 minutes was measured by radioimmunoassay. Mixed BAL cells from atopic asthmatics produced less GM-CSF than normal controls, both spontaneously [atopic asthmatics GM-CSF median (range) 2·5 (0·0–148·4) pg/million cells/24 hours, normal subjects 39·7 (0·0–371·9); p = 0·071] and when stimulated [atopic asthmatics 7·5 (0·0–226·7), normal subjects 43·7 (0·0–467·5); p = 0·06]. There were no significant differences in IL-3 (n = 12) or IFN-γ (n = 6) production between atopic asthmatics or normal subjects. There was no relationship between GM-CSF, IL-3 or IFN-γ production and LTB_4 generation, although significantly less LTB_4 was generated by cells from atopic asthmatics than from normal subjects (p = 0·03). In conclusion, there was a trend to reduced GM-CSF production by BAL cells from atopic asthmatics, but no change in IL-3 or IFN-γ production, and no relationship between cytokine levels and LTB_4 generation. The reduced capacity to generate LTB_4 and GM-CSF probably reflects generalised downregulation of alveolar macrophage function in asthma.

Interleukin 8 protein (IL-8) in bronchoalveolar lavage (BAL) fluid in human asthma

IK TAYLOR, J SHUTE, J DOUGLAS, DM MITCHELL, RJ SHAW *Department of Respiratory Medicine, St Mary's Hospital Medical School, London and Medicine 1, Southampton General Hospital, Southampton* There is increasing evidence that cytokines are important in the development of airway inflammation in asthma. IL-8 is a recently described polypeptide released from various cells including monocyte/macrophages, T lymphocytes, neutrophils, and bronchial endothelium. In vitro IL-8 is principally recognised as a neutrophil chemoattractant and functional activator and has been shown to induce neutrophil adherence and transendothelial migration. By contrast, in vivo, whilst IL-8 has been implicated in the pathogenesis of idiopathic pulmonary fibrosis and the adult respiratory distress syndrome (Donnelly *et al. Lancet* 1993;**341**:643–7) little is known regarding a role in asthma. In this study we have evaluated IL-8 protein in supernatants of bronchoalveolar lavage. Three patient groups underwent bronchoscopy delineated by their inhalational therapy: (A) steroid-dependent asthmatics (AST_{ster}), n = 20, 8M, age 19–59, FEV_1 60–119% predicted, daily inhaled steroid dose 200–2000 μg [median 1000 μg], duration of steroid usage 13 <24 months, 7 $\geqslant$24 months; (B) steroid-independent asthmatics (AST_{bron}) using bronchodilator therapy only (n = 15, 13M, age 22–44, FEV_1 70–117% predicted); (C) normal non-asthmatic controls (n = 20, 10M, age 18–41, FEV_1 95–142% predicted). IL-8 in BAL supernatants was quantified using a double sandwich ELISA technique and mean (SE) results expressed as both ng/ml and ng/mg protein are shown in the table. There were no significant differences in IL-8 concentrations, either between groups or between all asthmatics (AST_{all}) and controls. Thus, in contrast to other pulmonary pathologies in which IL-8 has been implicated in the pathogenesis, we have found no evidence that this is the case in vivo in bronchial asthma. Further, these data support the view that chronic administration of therapeutic doses of inhaled glucocorticosteroids does not modulate IL-8 in BAL in vivo in asthma.

	AST_{ster}	*AST_{bron}*	*AST_{all}*	*Controls*
IL-8 (ng/ml)	0·034 (0·007)	0·026(0·005)	0·030 (0·005)	0·024 (0·003)
IL-8 (ng/ml protein)	0·895 (0·213)	0·883 (0·208)	0·890 (0·151)	0·774 (0·175)

Bronchial epithelial cytokine production in asthmatics and non-asthmatics

AE REDINGTON, P BRADDING, JA DOUGLASS, LM TERAN, JA ROBERTS, ST HOLGATE, PH HOWARTH *Immunopharmacology Group, University of Southampton, Southampton* Although the bronchial epithelium has traditionally been viewed as a target for the inflammatory process of asthma, it is now apparent that it has the potential itself to contribute to inflammatory events as it is a metabolically active cell population. To investigate the cytokine expression within the epithelium in vivo we have undertaken immunohistochemical staining of endobronchial biopsy samples with monoclonal antibodies directed against IL-1β, IL-6, IL-8 and TNFα, all cytokines described in relationship to cultured bronchial epithelial cells in vitro. Endobronchial biopsies were obtained at fibreoptic bronchoscopy from mild asthmatics treated with inhaled bronchodilators only (n = 9) and from normal control subjects (n = 7). The biopsies were processed into glycol methacrylate resin and immunostaining of 2 μm sections was performed using an avidin biotin peroxidase technique. The intensity of staining was assessed semiquantitatively using a grading system. Immunoreactivity for interleukin (IL)-8 was detected in the epithelium of both asthmatics and non-asthmatics with the intensity being significantly greater in the former ($p < 0·05$, χ^2 test). IL-1β immunoreactivity was also localised to airway epithelium but, in contrast to IL-8 immunoreactivity, there was no significant difference between asthmatics and non-asthmatics. Immunoreactivity for IL-6 and TNFα was not localised to the bronchial epithelium. These findings confirm the potential importance of cytokine production by the bronchial epithelium in the inflammatory processes of asthma.

Increased expression of CD44 and LFA-1 in bronchial biopsies from mild asthmatic patients and normal controls and correlation with leucocyte influx

DG PERONI, R DJUKANOVIC, CP BRADDING, IH FEATHER, PH HOWARTH, DB JONES, ST HOLGATE *Departments of Medicine and Pathologyy, University of Southampton, Southampton* We have investigated by immunohistochemistry in bronchial biopsies from 10 mild atopic asthmatics and eight normal subjects, the expression of leucocyte endothelial cell adhesion molecules (LECAMs) such as ICAM-1, CD11a (LFA-1), CD44 (a tissue selective adhesion molecule), CD49d (VLA-4), CD49f (VLA-6), and the expression of cell surface markers CD3, CD4, CD8 for T lymphocytes subsets and their activation (CD25), AA1 for mast cells and EG2 for activated eosinophils. Analyses showed a significant increase in the number of eosinophils (p = 0·02) in the asthmatic submucosa. The staining for endothelial ICAM-1 was constitutively expressed and the

monoclonal antibodies for VLA-4 and VLA-6 stained the basement membrane of the bronchial epithelium in both groups. In the epithelium there were more CD44+ ($p < 0.02$) and LFA-1+ ($p = 0.06$) leucocytes in asthmatics than in the normals. The CD44 staining was present in the bronchial epithelial cells in both the groups, but when the staining was expressed as the percentage of the total basement membrane a significant increase was observed in the asthmatic subjects ($p = 0.003$). In asthmatic patients a positive correlation ($p < 0.03$, $r_s = 0.69$) was found between LFA-1+ and CD4+ cells both in the epithelium and submucosa and between LFA-1+ and eosinophils EG2+ in the submucosa ($p < 0.005$, $r_s = 0.80$). These results suggest that LECAM expression may play a significant role in the influx of leucocytes into the bronchial asthmatic tissue.

Relationship of T lymphocyte activation to lung function in glucocorticoid dependent asthma

SH LOCK, NC BARNES, C CORRIGAN, AB KAY *National Heart and Lung Institute, London, and The London Chest Hospital, London* In acute severe asthma elevated numbers of peripheral blood T lymphocytes express activation markers and their reduction following therapy could be correlated with improvement in lung function (Corrigan *et al. Am Rev Respir Dis* 1990;**141**:970–7). To investigate the possible role of T lymphocytes in glucocorticoid dependent asthma we studied 35 glucocorticoid dependent asthmatics (mean age 51 years, range 26–67 yrs, FEV_1 66% (33–112%) of the predicted value) and six normal control subjects. Patients' lung function was kept stable for four weeks on their lowest maintenance dose of prednisolone (12 mg/day, 2–22·5 mg/day). Peripheral blood mononuclear cells were then separated from the asthmatics and controls. The expression of activation markers CD25 (IL-2 receptor), HLA-DR, VLA1, CD45RA (naive T lymphocytes) and CD45RO (memory T lymphocytes) were measured on CD4 and CD8 T lymphocytes using flow cytometry. The percentages of CD25 expressed on CD4 T lymphocytes in asthmatics (median 11·0%, range 2–25·7%) was significantly higher than in controls (8·0%, 5·4–9·8%, $p = 0.02$). The percentages of total CD4 and CD8 T lymphocytes and expression of other activation markers on CD4 and CD8 T lymphocytes were not significantly different in the two groups. The percentages of CD4 T lymphocytes expressing CD25 in asthmatics correlated with their spirometry (% predicted FEV_1 $r = 0.40$, $p < 0.05$). Thus glucocorticoid dependent asthmatics show evidence of ongoing CD4 T lymphocyte activation which can be correlated to lung function and CD25 expression may be a useful marker of disease severity.

Clinical response to cyclosporin A therapy in chronic severe asthma is associated with a decrease in serum soluble interleukin 2 receptor (IL-2R)

AG ALEXANDER, CJ CORRIGAN, P JARDIEU, NC BARNES, AB KAY *National Heart and Lung Institute, Royal Brompton and London Chest Hospitals, London, UK and Genentech Inc, San Francisco, USA* In a randomised placebo controlled double blind crossover trial of oral cyclosporin A in steroid dependent chronic severe asthmatics, cyclosporin A therapy for 12 weeks resulted in a mean increase above placebo of 12·0% in PEF and 17·6% in FEV_1 (Alexander *et al. Lancet* 1992;**339**:324–8). To investigate the mechanism of action of cyclosporin A in asthma, peripheral blood samples were obtained from 29 patients at the mid points of both the cyclosporin A and placebo treatment periods and serum stored at −80°C pending measurement of soluble IL-2R concentration by enzyme linked immunosorbent assay. Soluble IL-2R was detected in all samples with a range of 177–2296 U/ml, considerably above the 50 U/ml lower limit of sensitivity of the assay. Mean concentrations of soluble IL-2R were significantly lower ($p = 0.017$) on cyclosporin A (519·6 U/ml) compared with placebo (616·4). This decrease in soluble IL-2R concentration with cyclosporin A therapy correlated with the % increase in morning PEF ($r = 0.375$, $p < 0.05$). These data suggest that in patients with chronic severe asthma clinical response to cyclosporin A is associated with a decrease in serum soluble IL-2R concentration. This is compatible with the hypothesis that cyclosporin A may act in vivo, at least in part, by inhibition of T cell activation.

Nutrition and lung function in the elderly

L DOW, MTA VILLAR, ST HOLGATE *Department of Care of the Elderly, Frenchay Hospital, Bristol, and University Medicine, Southampton General Hospital, Southampton* The relationship between nutrition and lung function was examined in a sample of elderly men and women in a longitudinal study of airways disease. Spirometry was measured in 1986–7 and 1990–1. Nutritional information was only collected at the second examination and consisted of: food frequency data from a questionnaire, weight, body mass index, triceps skinfold thickness, and upper midarm muscle circumference. The mean (SD) age of this sample at the second examination was 76·3(5·2) years. From 1990–1 data 36 subjects had an $FEV_1/FVC \leqslant 60\%$ and 155 had $FEV_1/FVC > 60\%$. Obstructed subjects had marginally higher energy intake (kcal) through higher intakes of protein, fat and carbohydrate, but were lower in weight (kg) and body mass index (table). Triceps skinfold thickness and upper midarm muscle circumference were lower for obstructed than non-obstructed subjects. Change in FEV_1 between the two examinations was calculated as average yearly change in FEV_1 and categorised as: gain 0–150 ml (n = 31), loss 0–49 ml (n = 62), 50–99 ml (n = 66), 100–149 ml (n = 25), >150 ml (n = 14). Nutritional status and food intake did not show any consistent pattern across these different groups. We conclude that an association exists between nutrition and lung function cross sectionally, but is not detectable in this study with longitudinal measurements of lung function.

	$FEV_1/FVC \leqslant 60\%$	*$FEV_1/FVC > 60\%$*
Energy intake (kcal)		
Men	2145 (555)	2047 (684)
Women	1917 (573)	1648 (515)
Weight (kg)		
Men	67·8 (13·9)	76·7 (12·1)
Women	62·3 (11·1)	68·3 (12·9)

Relation of selenium and glutathione peroxidase with atopy and bronchial hyperreactivity in adults and children

B BEGISHVILI, IJM DOULL, R BEASLEY, ST HOLGATE *University Medicine, Centre Block, Southampton General Hospital, Southampton* Selenium is an essential component of the antioxidant glutathione peroxidase. Non-atopic asthma is associated with decreased whole blood selenium and in some studies with decreased glutathione peroxidase activity. We have investigated the relationship of bronchial hyperreactivity and atopy to selenium and glutathione peroxidase in 29 families (58 adults, 84 children) randomly selected without reference to atopy or asthma, who attended our department for bronchial challenge to histamine and skin prick testing to 12 allergens. To prevent the loss of censored data, bronchial hyperreactivity was expressed as area under the curve (AUC). Total IgE, serum selenium and glutathione peroxidase activity were measured by standard assays. There was no difference in mean selenium or glutathione peroxidase between atopics and non-atopics. Glutathione peroxidase was negatively correlated with IgE ($r = 0.226$, $p = 0.011$) in the families as a whole and in patients separately ($r = 0.338$, $p = 0.015$), but there was no relation between selenium and IgE. In atopics there was no relation between selenium or glutathione peroxidase and AUC; however, in non-atopics both selenium ($r = 0.378$, $p = 0.012$) and glutathione peroxidase ($r = 0.433$, $p = 0.008$) correlated with AUC. When the children were analysed separately there was no relationship between selenium, glutathione peroxidase, and AUC or IgE.

Effects of atopy, cigarette smoking and dietary vitamin C intake on lung function in the general population

J BRITTON, I PAVORD, K RICHARDS, A KNOX, A WISNIEWSKI, S LEWIS, A TATTERSFIELD, S WEISS *Respiratory Medicine Unit, City Hospital, Nottingham, and Harvard Medical School, Boston, USA* Cigarette smoke and other inhaled pollutants cause lung damage by oxidation, both as a direct effect and by recruitment of host defence systems. Individual susceptibility to oxidant damage may therefore be influenced by dietary intake of antioxidants, including vitamins C and E. We have estimated the potential importance of differences in

dietary intake of these vitamins, relative to the effects of cigarette smoking and atopy, as determinants of lung function in a cross sectional survey of a random sample of 2633 adults aged 18–70 from a district of Nottingham. Dietary intakes of vitamins C and E were measured by a semiquantitative food frequency questionnaire, lifetime smoking in pack-years from self-reported smoking histories, atopy as the mean skin weal response to *D pteronyssinus*, grass pollen and cat fur allergens by standard skin prick testing, and lung function as the FEV_1 analysed as a standardised residual after adjustment for age, sex and height within the study population. We found that FEV_1 was significantly and independently related to pack-years smoked (mean fall in FEV_1 per pack year = 5·5 ml, 95% confidence interval 4·4 to 6·6 ml), allergen skin weal diameter (mean fall per mm = 15·4, 95% confidence interval 5·8 to 25·1 ml), and to average dietary intake of vitamin C (mean increase in FEV_1 per standard deviation increase in vitamin C intake = 25·0 ml, 95% confidence interval 5·2 to 44·8 ml). There was no significant interaction between the effects of dietary vitamin C and smoking or atopy, and no additional independent effect from dietary vitamin E intake. These data demonstrate that, in cross sectional analysis of this population, vitamin C intake is an independent determinant of lung function of a magnitude such that a standard deviation decrease in vitamin C intake is associated with a change in FEV_1 approximately equivalent to five pack-years smoking.

Is screening of schoolchildren for asthma a worthwhile procedure?

RG DENT, M HUMBLE, P MCINTYRE, E ATTFIELD *East Hertfordshire NHS Trust, Hertford* Previous studies have outlined a significant number of school children with undiagnosed asthma in primary schools (Speight *BMJ* 1978;**2**:331; Hill *et al. Arch Dis Child* 1989;**64**:246). These studies have been in urban areas and the implication has been that identification of such children and subsequent intervention would lead to an improvement in morbidity from asthma. We have studied 1003 children in eight primary schools in rural Hertfordshire using a questionnaire and an exercise peak flow test. Eighty seven of the children were already known to have asthma or were receiving treatment for asthma (8·7%). A further 89 (8·9%) had a positive questionnaire or exercise test but, after a further questionnaire completed by the child's parents, only 19 (1·9%) children had clear evidence of undetected asthma sufficient to warrant further investigation. Parents of these 19 children were encouraged to seek advice about their child from their GP who was informed of the results of the screening study. Eight of the 19 visited their doctor of whom only four were subsequently commenced on treatment. Sixty of the 87 children with known asthma were considered to be "inadequately" controlled on the basis of their symptoms and exercise test results. It is concluded that screening schoolchildren for asthma in rural Hertfordshire is not a profitable use of resource, but that children with known asthma should be identified and an attempt made to improve their control. The results support the much larger urban study of Hill in Nottingham in 1991 (*BMJ* 1991;**303**:1169).

Case note review as a means of identifying potential asthma in 10 500 children

RA CLARK, RG NEVILLE, F BRYCE, J PHILLIPS *Departments of General Practice and Respiratory Medicine, University of Dundee, Dundee* The case notes of 10 685 children aged 1–5 from 12 rural, country town, or urban general practices in Tayside were reviewed by a nurse facilitator who identified 3373 children with symptom complexes suggestive of past or present asthma. The GPs were given the names of the 1585 intervention patients and asked to assess and follow them up according to standardised asthma protocols. Follow up of the 1563 children in the control group was as per standard practice, their names remaining secret. Intervention and control groups were closely matched for age, sex, previous asthma diagnosis and current asthma treatment. The records of both groups were reviewed after one year. A total of 943 intervention children had been assessed (292 asthma, 258 probable asthma, 393 not asthma); 351 had had no recent symptoms and were not assessed and 291 had not yet been seen. The same number of children in the intervention and control groups continued on bronchodilators, Intal, and inhaled steroids throughout both years but there was a significant increase in use of bronchodilator, Intal, spacer device, and PEF meter and the diagnosis of asthma in the intervention but not the control arm during the second year. Persistent cough with one or more episodes of bronchospasm were most consistently associated with the diagnosis of asthma although less than 30% of persistent coughers had proven asthma.

High prevalence of asthma-like symptoms in East Anglia

D JARVIS, E LAI, C LUCZYNSKA, R HALL, BDW HARRISON, J STARK, S CHINN, P BURNEY *Department of Public Health Medicine, UMDS, St Thomas' Campus, London, Department of Respiratory Medicine, Addenbrooke's Hospital, Cambridge, Department of Respiratory Medicine, Ipswich Hospital, Ipswich, Department of Respiratory Medicine, West Norwich Hospital, Norwich* As part of the British arm of the European Commission Respiratory Health Survey (ECRHS) 15 000 people aged between 20 and 44 years, living in Cambridge, Ipswich and Norwich, were sent the ECRHS questionnaire, a seven item self-administered questionnaire asking about respiratory symptoms over the preceding year. The response after three mailings was lowest in Cambridge (50·9%) and highest in Ipswich (66·8%), with Norwich at 60·8%, but increased to 65·0%, 74·7%, and 70·2% respectively when people known to have moved, died, or to be the wrong age were excluded. Response was greater in women and increased with age. The prevalence (%) of a positive response to the following questions (1) wheeze or whistling in your chest at any time (whz), (2) waking with an attack of breathlessness (wake SOB), (3) attack of asthma (att ast), and (4) currently taking medication for asthma (ast med) is given in the table. The range of prevalence obtained in a similar study of young men of the same age using the same questions conducted in 20 local authority areas in 1986 (Burney *et al. Thorax* 1991;**46**:574–9) is also shown. The prevalence of asthma-like symptoms in Cambridge, Ipswich and Norwich is higher than has previously been reported elsewhere. [This work was supported by the National Asthma Campaign]

	Cambridge	*Ipswich*	*Norwich*	*1986 study*
whz	24·8	25·3	25·3	8·8–13·3
wake SOB	8·3	8·0	8·0	2·8–4·8
att ast	5·7	4·9	4·9	2·3–4·4
ast med	6·9	6·6	6·3	

Quality of life in asthma

A WRIGHT, J PORTLOCK, E NEVILLE, AP ROBERTS *School of Pharmacy and Biomedical Sciences, University of Portsmouth and St Mary's Hospital, Portsmouth* An asthma specific questionnaire was developed to investigate the quality of life that asthmatics experienced. The questionnaire was administered by one interviewer and consisted of 71 items, of which 15 were positive and 55 negative. A variety of modes of response were used including binary, multi-category, descriptive, and visual analogue scales. Fifty patients aged 15–78 were interviewed, of whom 20 were judged to have mild, 14 moderate, and 16 severe asthma. There were no significant correlations with age. Men were twice as likely as women to become annoyed with their asthma and to feel anxious, but were more confident that they coped with their medicines. Women had problems *getting* to sleep, but found family members more supportive. A highly significant correlation was found between increasing duration of asthma and embarrassment, using three separate modes of assessment. Severity of asthma did not correlate with social activities or emotions, but correlated well with clinically related questions and family life and energy. Deteriorating spirometry correlated with breathlessness while talking, but not with the degree of distress caused by talking. The major causes of distress were ranked as follows: inability to do my job, inability to sleep well, inability to perform everyday tasks, not feeling in control, inability to have the social life I would like, inability to participate in activities, having to avoid certain places, embarrassment, attitudes of other people, becoming short of breath when talking and having to use inhalers; i.e. broadly speaking, functional problems were rated as causing more distress than psychological ones. Quality of life is a subjective measurement of how well a person functions in everyday life, incorporating subjective wellbeing, health and objective welfare. This questionnaire has been found to satisfactorily integrate these three areas.

Audit of acute asthma in the North West region

R FEINMANN, P ORMEROD, G COOK, P PHILLIPS *Stepping Hill Hospital, Stockport, Cheshire, Blackburn Royal Infirmary, Bolton Road, Blackburn, and North Western Regional Health Authority, Gateway House, Piccadilly South, Manchester* The North West region has completed an audit of acute admissions with asthma to all district hospitals in the region. Twenty per cent of all asthma admissions in the age range 16–46 years who were admitted over a 12 month period were audited. Using the BTS guidelines it was decided what information should be collected from the hospital notes to indicate good management. In total 343 records were audited, 23% of whom had been seen by their GP or in the Accident and Emergency department within two weeks of being subsequently admitted. Peak flow recording was disappointing in that only half had initial recordings and, although 90% had daily measurements, only 15% had QDS before and after bronchodilator measurements. Discharge peak flows were recorded in only one quarter and in 25% of patients nebulisers were not stopped 24 hours prior to discharge. One quarter of all were not followed up after discharge. Despite well publicised national guidelines and many local protocols and audits, acute asthma management remains inadequate. This audit also compared the management of chest physicians with general physicians and, despite being slightly better, the results were still disappointing.

Darlington prospective study of childhood asthma: pulmonary function and treatment

AA GATNASH, CK CONNOLLY, SM ALCOCK *Darlington Memorial Hospital and University of Newcastle upon Tyne* All children with asthma referred to one author (CKC) between 1972 and 1983 and likely to remain in the district were entered into a prospective study of the outcome. One hundred and eighty six subjects aged 5–14 (128 boys, 58 girls) were reviewed at the age of 21. Any visit after 18 years was accepted for those not attending, the remainder being traced through their last known address or general practitioner. Data were obtained for 149 (80%), of whom 109 (73%) were seen and two (1·3%) died. A boy (14 years) died from progressively severe steroid resistant asthma, and a girl (16 years) in remission from a catastrophic attack on exposure to exceptional pollen levels. Of those known to be alive, 20 (14%) were on no treatment, 65 (44%) were prescribed bronchodilators only, and 62 (42%) were on preventative treatment (oral corticosteroids 0, inhaled steroids 43 (29%), cromoglycate 19 (13%)). Peak expiratory flow (PEF) was available in 125 (82 boys, 43 girls) and forced expiratory volume in one second (FEV_1) in 114 (74 boys, 40 girls). The mean peak flow was 501 l/min (84·6% predicted) in boys and 429 l/min (86·8%) in girls. Mean FEV_1 was 3·57 l (83·5% predicted) in boys and 2·88 l (86·7%) in girls. PEF was >80% in 86 (69%) and FEV_1 in 70 (61%). PEF was 83% predicted (range 71–116%) in those on no treatment, 87% (62–120%) on bronchodilator only, 85% (66–101%) on cromoglycate, and 81% (51–106%) on inhaled corticosteroids. Of the 127 receiving treatment, 111 (87%) claimed little or no disruption to their lives, while 16 (13%) had at least moderate disruption. This was less than would be expected from published population surveys and may reflect good initial training in coping with asthma. On the other hand, the range of pulmonary function was large within the treatment groups and the differences between them small, suggesting that there might still be under-recognition of asthma, particularly in those on no treatment at all.

Airway a_2 adrenoreceptors inhibit sensory neurotransmission in guinea pigs but not humans

F O'CONNELL, VE THOMAS, RW FULLER, NB PRIDE, JA KARLSSON *Departments of Clinical Pharmacology and Respiratory Medicine, Royal Postgraduate Medical School, London and Rhone-Poulenc-Rorer Ltd, Dagenham, Essex* Previous studies in our departments have shown that oral clonidine, in a dose which causes increased drowsiness and a fall in blood pressure, has no effect on cough and reflex bronchoconstriction in guinea pigs or humans. We have now examined the effects of inhaled clonidine, a specific a_2 receptor agonist, on citric acid and capsaicin induced respiratory reflexes in guinea pigs and healthy humans. In groups (n = 8) of conscious guinea pigs exposed to citric acid aerosol (0·4 M), pretreatment with inhaled clonidine caused a concentration-dependent suppression of cough and prolongation of the time to onset of bronchoconstriction (table 1). Ten healthy human volunteers had capsaicin-induced cough and reflex rise in respiratory resistance measured before and 5 and 25 minutes after inhalation of clonidine 150 μg or placebo (saline). In contrast to the effects in guinea pigs, clonidine had no effect compared with placebo on the log concentrations of capsaicin required to elicit two (C2) and five (C5) or more coughs or the rise in respiratory resistance (cm H_2O/l/s) after inhalation of a subtussive concentration of capsaicin (table 2) These data suggest that airway a_2 receptors exert an inhibitory effect on sensory neurotransmission in the guinea pig but not in humans indicating an important difference between the two species. [This study was supported by The National Asthma Campaign.]

Table 1

		Clonidine		
	Vehicle	*10 μM*	*100 μM*	*1000 μM*
No of coughs	6·5 (0·9)	9·9 (3·7)	4·5 (1·7)*	1·7(1)*
TTB (s)	191 (24)	204 (43)	221 (43)	311 (33)*

TTB—time to onset of bronchoconstriction. Figures are mean (95% CI); *p < 0·05.

Table 2

	Baseline		*25 minutes*	
	Placebo	*Clonidine*	*Placebo*	*Clonidine*
Log C2 (μM)	0·8 (0·31)	0·8 (0·41)	1·1 (0·37)	1·1 (0·47)
Log C5 (μM)	1·8 (0·29)	1·9 (0·67)	2·0 (0·51)	1·9 (0·63)
Rrs before capsaicin	2·2 (0·6)	2·3 (0·5)	2·5 (0·8)	2·2 (0·6)
Rrs after capsaicin	2·7 (0·7)	2·5 (0·7)	2·8 (1·0)	2·5 (0·8)

C2, C5—concentrations of capsaicin required to elicit two or five or more coughs; Rrs—rise in respiratory resistance. Figures are mean (95% CI).

Effect of dopaminergic and cholinergic agonists and antagonists on capsaicin induced cough and reflex bronchoconstriction

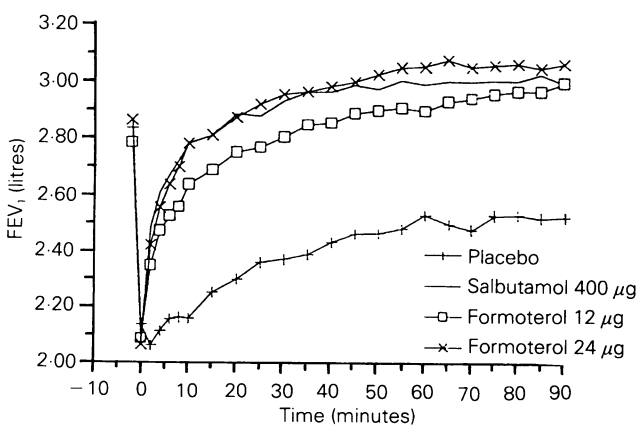
F O'CONNELL, VE THOMAS, RW FULLER, NB PRIDE *Departments of Clinical Pharmacology and Respiratory Medicine, Royal Postgraduate Medical School, London* Little is known about the central neurotransmitters involved in mediation of respiratory reflexes in humans. Previous studies have shown that systemic opiates suppress capsaicin induced cough without affecting respiratory resistance, while inhaled opiates suppress capsaicin induced rise in respiratory resistance without affecting cough, suggesting that the antitussive effect of opiates is a central effect. A further study has shown that clonidine, a centrally acting a_2 agonist, has no effect on these reflexes in humans. We have now examined the effects of central acting agonists and antagonists of cholinergic and dopaminergic receptors on capsaicin induced cough and reflex rise in respiratory resistance in healthy human volunteers. In eight subjects baseline measurements of heart rate, blood pressure, capsaicin induced cough and respiratory resistance before (pre-C) and after (post-C) inhalation of capsaicin were made. These measurements were repeated five and 30 minutes after a single intravenous dose of atropine 0·6 mg, physostigmine 0·5 mg, or saline. Atropine caused a significant increase in heart rate (HR) at five and 30 minutes compared with saline and physostigmine (mean (SD) ΔHR at five minutes: atropine 28 (5), physostigmine 5 (4), saline −4 (3); at 30 minutes: atropine 21 (4), physostigmine −2 (3), saline −5 (3)). Atropine also caused a fall in pre-C respiratory resistance of 21 (4%) at five minutes and 19 (4%) at 30 minutes compared with baseline and abolished the post-C rise in respiratory resistance. Physostigmine and saline had no significant effects on pre or post-C respiratory resistance and capsaicin induced cough was unaffected by any treatment. In a second study in 12 subjects, baseline measurements of heart rate, blood pressure, capsaicin induced cough and pre-C and post-C respiratory resistance were made and repeated one, two, and four hours after a single oral dose of levodopa 100 mg, bromocriptine 1 mg, haloperidol 1·5 mg, or matched placebo. None of the parameters measured was affected by any of the treatments. The changes in respiratory resistance after administration of atropine are most probably explained by an effect at postganglionic cholinergic nerve endings in bronchial smooth muscle. It is unlikely that central cholinergic or dopaminergic receptors are involved in mediation of capsaicin induced respiratory reflexes in humans. [This study was supported by The National Asthma Campaign.]

Comparison of the effects of inhaled frusemide and ethacrynic acid on sodium metabisulphite induced bronchoconstriction in subjects with mild asthma

S PYE, I PAVORD, P WILDING, J BENNETT, A KNOX, A TATTERSFIELD *Respiratory Medicine Unit, City Hospital, Nottingham* Inhaled frusemide prevents bronchoconstriction induced by a number of challenges in asthma. One approach to determine the mechanism of this protection has been to examine the effects of related diuretics. We have compared the effects of frusemide on sodium metabisulphite induced bronchoconstriction with those of ethacrynic acid, a loop diuretic which, unlike frusemide, does not interact with the membrane Na/K/Cl cotransporter protein or inhibit carbonic anhydrase. Eight subjects with mild asthma were studied on five occasions, receiving nebulised frusemide (20 and 40 mg), ethacrynic acid (25 and 50 mg), or placebo (normal saline) in random order and double blind 10 minutes before a cumulative dose challenge with inhaled sodium metabisulphite. The response to sodium metabisulphite was described as the provocative dose causing a 20% fall in FEV_1 (PD_{20}) and differences in PD_{20} were expressed as doubling doses. The geometric mean sodium metabisulphite PD_{20} was 7·9 μmol after placebo. Frusemide 20 mg increased the PD_{20} by 1·1 doubling doses to 17·1 μmol ($p > 0·05$) and frusemide 40 mg by 1·6 doubling doses to 24·7 μmol ($p < 0·02$). Ethacrynic acid was irritant to inhale, but also inhibited bronchoconstriction induced by sodium metabisulphite. The geometric mean PD_{20} was increased by 0·9 doubling doses to 14·5 μmol ($p > 0·05$) after 25 mg and by 1·5 doubling doses to 22·4 μmol ($p < 0·05$) after 50 mg. Thus equivalent diuretic doses of frusemide and ethacrynic acid have a similar effect on sodium metabisulphite induced bronchoconstriction in asthma. This suggests that interaction with the Na/K/Cl cotransporter protein or carbonic anhydrase inhibition is not relevant to the effects of frusemide in asthma.

Comparison between formoterol and salbutamol in reversing methacholine induced bronchoconstriction

JR BEACH, CL YOUNG, EH WALTERS, DJ KENDRICK *Chest Unit, Newcastle General Hospital, University of Newcastle upon Tyne* Formoterol is one of a new class of long acting β agonists intended for regular use in the treatment of asthma. β agonists are also used as rescue medication for episodes of acute bronchospasm, and in this role a long duration of action is not so important as a rapid onset of action. This study was undertaken to detect any difference in speed of action between placebo, two doses of formoterol, and salbutamol in reversing methacholine induced bronchoconstriction. Sixteen asthmatic subjects were recruited from a chest clinic. Each underwent four methacholine tests a minimum of two and a maximum of 10 days apart, on each occasion a >20% decrement in FEV_1 being attained. Following each test they received one of four treatments from a dry powder inhaler: placebo; formoterol 12 μg; formoterol 24 μg; salbutamol 400 μg. Following each treatment FEV_1 was recorded every two minutes for 10 minutes, and every five minutes for 80 minutes thereafter. All three active drugs produced a greater FEV_1 than placebo at each time point during recovery. Analysis of variance showed salbutamol produced a statistically significant greater FEV_1 two and eight minutes after inhalation than formoterol 12 μg; and formoterol 24 μg a greater FEV_1 at 10, 25, and 30 minutes than formoterol 12 μg, but there were no significant differences between the three active medications at other time points. Although significant, these differences in FEV_1 were small. We conclude that formoterol 24 μg and salbutamol 400 μg act equally rapidly in reversing methacholine induced bronchoconstriction, but that formoterol 12 μg is marginally less effective.



Airway responsiveness to nebulised salbutamol under different conditions of sustained methacholine exposure

AS JUBBER, NAGM HASSAN, RW FOSTER *Smooth Muscle Research Group, Department of Physiological Sciences, Manchester University, Manchester* We have previously suggested (Jubber *et al, Thorax* 1992;47:152, 253) that, when inhaled salbutamol causes bronchodilatation by functional antagonism of methacholine, the airway responsiveness to salbutamol is composed of independent sensitivity and reactivity parameters, each linked to the corresponding methacholine parameter. It is less the amount of constriction produced and more the amount of methacholine producing it that determines both the sensitivity and reactivity to salbutamol. We have now explored the correlations between the indices of sensitivity and reactivity to nebulised salbutamol under different conditions of methacholine exposure. Fourteen normal subjects each underwent three methacholine dosage individualisations (Foster *et al, Br J Clin Pharmacol* 1991;31:445) and three cumulative log dose-response curves to salbutamol from an Emin (the smallest sGaw caused by repeated methacholine inhalation) of 62·5% reduction from baseline sGaw. In order to challenge our suggestion 10 of the subjects were used to estimate in triplicate the responsiveness to salbutamol from an unconstricted baseline and six of these also underwent three cumulative log dose-response curves to salbutamol from an Emin of 35% bronchoconstriction. Interpolation in the salbutamol log dose-response curve at the mean E_{50}, half way between the mean Emin and the mean largest effect recorded (Epeak), allowed derivation of the mean log ED_{50}. There were no significant differences over the three bronchodilator protocols between the baseline states ($p = 0·76$). Naturally there were significant differences between the Emin states ($p < 0·001$ to 0·005). In unconstricted airways the salbutamol ED_{50} state (the Ed_{50} used was that *v* methacholine $PD_{62·5}$) was significantly larger ($p = 0·006$) than the E_{50} state. Also, the log ED_{50} *v* methacholine PD_{35} was significantly smaller ($p = 0·048$) than that *v* methacholine $PD_{62·5}$. The Epeak state *v* methacholine $PD_{62·5}$ was significantly smaller ($p = 0·045$) than that *v* the unconstricted airways but did not differ significantly ($p = 0·35$) from that *v* methacholine PD_{35}. These results largely sustain the above suggestion, relating sensitivity and reactivity to salbutamol to the amount of methacholine producing constriction.

Comparison of airway responsiveness to nebulised salbutamol and ipratropium in methacholine bronchoconstricted normal subjects

AS JUBBER, NAGM HASSAN, RW FOSTER *Smooth Muscle Research Group, Department of Physiological Sciences, Manchester University, Manchester* We have previously confirmed (Jubber *et al, Thorax* 1992;47:152, 253) that airway responsiveness to inhaled salbutamol is composed of independent sensitivity and reactivity parameters. In this study the component parameters of airway responsiveness to the functional antagonist salbutamol and those of the antagonist at muscarinic cholinoceptors ipratropium bromide have been compared in a model of bronchospastic asthma created by methacholine inhalation in normal subjects. The index of sensitivity was represented by log ED_{50} (half maximally effective dose), while the index of reactivity was represented by Epeak (maximal effect). Six subjects each underwent three dosage individualisation experiments (log dose-response curve and offset time-effect curve, Foster *et al, Br J Clin Pharmacol* 1991;31:445), three cumulative log dose-response curves of salbutamol and three cumulative log dose-response curves of ipratropium. A loading dose (D_0) and a sequence of maintenance doses (D_m) of methacholine were inhaled over two minutes at 10 minute intervals, aiming to cause a sustained 60–65% reduction from baseline sGaw. After the first D_m, salbutamol was inhaled over two minutes and at 20 minute intervals in cumulative doses of 7, 44, 278, and 1760 μg and ipratropium was inhaled over two minutes and at 30 minute intervals in cumulative doses of 5, 10, 20, and 80 μg. Both mean log ED_{50} salbutamol and ipratropium were determined from the corresponding mean log dose-response curves

by interpolation half way between the Emin (the smallest sGaw caused by D_m) and Epeak. Indices were compared by paired parametric methods in their logarithmic forms. There were no significant differences over the two protocols between the baseline state ($p = 0.23$) or Emin ($p = 0.67$) suggesting that an unbiased comparison can be made between them from these data. There were also no significant differences over the two protocols between Epeak state ($p = 0.39$) or Epeak amplitude ($p = 0.91$) suggesting the similarity of reactivity, but the slopes of the log dose-response curves were very different ($p < 0.001$). However, there were significant differences between the log ED_{50} values ($p < 0.01$) indicating the difference in potency of and sensitivity to the two agents.

Effect of cessation of short term treatment with ipratropium bromide on lung function in asthma

PJ WILDING, MM CLARK, ID PAVORD, D PARKER, J BENNETT, AE TATTERSFIELD *Respiratory Medicine Unit, City Hospital, Nottingham* Vagotomy and atropine upregulate muscarinic receptors and enhance the response to muscarinic stimuli in animals. Antimuscarinic drugs may therefore cause increased responsiveness to endogenous acetylcholine released from the vagus and hence deterioration in asthma when their bronchodilator effect has worn off. We have investigated this in 13 subjects with mild stable asthma who inhaled ipratropium bromide 80 μg four times daily or placebo for 14 days in a crossover fashion with a one week run-in period before each treatment period. FEV_1 and histamine PD_{20} were measured on day -1 and 24 hours after the last dose of ipratropium/placebo on day 15 of each treatment period, followed one hour later by methacholine PD_{20} and 6–8 hours later by sodium metabisulphite PD_{20}. Methacholine was included as a cholinergic stimulus, histamine as a non-specific stimulus, and sodium metabisulphite as a neural stimulus. Subjects used the short acting rimiterol hydrobromide as rescue bronchodilator throughout and recorded twice daily symptom scores and rimiterol use and PEF four hourly for three days after the last dose of placebo/ipratropium. Four subjects were withdrawn from the study, two following upper respiratory tract infection (one placebo, one ipratropium) and two for personal reasons. Following ipratropium there was a fall in FEV_1 maximal at 30 hours and lasting less than seven days. The mean changes in FEV_1 at 30 hours were -250 v -30 ml with ipratropium and placebo respectively (mean difference -220; 95% CI -82 to -358 ml; $p < 0.02$). Histamine, methacholine and sodium metabisulphite PD_{20} did not differ significantly after ipratropium or placebo. There were no significant changes in symptom scores or rimiterol use but a non-significant trend towards a lower PEF after ipratropium. Thus cessation of regular treatment with inhaled ipratropium bromide 80 μg four times daily is associated with a transient deterioration in lung function. The mechanism remains unexplained since there was no change in cholinergic or non-cholinergic airway responsiveness. The fall in FEV_1 in our study after two weeks is similar to that seen in some long term studies (Van Schayck *et al. BMJ* 1991;**303**:1426–31) and is reversible.

Comparison of ouabain binding sites in airway smooth muscle and airway epithelium

D PECKHAM, F DELAMERE, E HOLLAND, AJ KNOX *Respiratory Medicine Unit, City Hospital, Nottingham* Na/K ATPase has important roles in fluid transport across airway epithelium and in determining the contractile state of airway smooth muscle. The number of Na/K ATPase pumps and binding characteristics of ouabain in bovine airway epithelium and airway smooth muscle has not been previously characterised. We therefore characterised ouabain binding in both tissues. Studies were performed on fresh specimens of bovine trachea obtained from the abattoir. Membrane particulates were prepared from both airway epithelium and airway smooth muscle by homogenising the tissue and then using a differential centrifugation technique. Saturation isotherms to ouabain were then performed with ^{3}H-ouabain. Non-specific binding was measured as binding in the presence of 10^{-6} M cold ouabain. Kd and Bmax values were estimated using a non-linear curve fitting programme. In both epithelium and airway smooth muscle ouabain binding was to a single homogeneous population of receptors. In airway epithelium mean (SE) Kd was 8·6 (2·3) nM with a Bmax value of 44·9 (5·2) pmol/mg of protein. In airway smooth muscle mean (SE) Kd value was 4·9 (1·2) nM with a Bmax value of 4·1 (0·9) pmol/mg of protein. There was no significant difference in the Kd values between airway epithelium and airway smooth muscle, but an 11 fold difference in Bmax values ($p < 0.001$). The large number of Na/K ATPase pumps in airway epithelium relative to airway smooth muscle is likely to reflect the importance of the basolateral Na/K ATPase in sodium resorptive processes in airway epithelium.

Bradykinin increases release of PGE_2 from cultured bovine airway smooth muscle cells

F DELAMERE, E HOLLAND, I PAVORD, A KNOX *Respiratory Medicine Unit, City Hospital, Nottingham* PGE_2 has been shown to have negative modulatory effects on inflammatory processes in vitro and inhalation of PGE_2 inhibits allergen induced bronchoconstriction in vivo. We have studied the regulation of PGE_2 production by cultured bovine airway smooth muscle cells. Cultures were prepared by enzymatic digestion of whole tissue, and experiments were performed while cells were at confluence on their first passage. Cells were growth arrested by incubating in serum free medium for 24 hours before studying PGE_2 production over a six hour period. PGE_2 was measured by radioimmunoassay. Mean (SE) PGE_2 production was increased to 148 (17)% of control values after the addition of arachidonic acid 10^{-5} M ($p < 0.05$). Bradykinin (10^{-6} M) increased PGE_2 production by 230 (80)% ($p < 0.01$). To determine whether the effects of bradykinin were mediated via protein kinase C (PKC) we studied the effects of 4-β phorbol 12, 13 dibutyrate, an activator of PKC, and its 4-α isomer (which does not activate PKC). 10^{-6} M 4-β phorbol dibutyrate increased PGE_2 production to 175 (17)% of control values ($p < 0.05$); 4-α phorbol dibutyrate was without effect. In conclusion, bradykinin stimulated PGE_2 production from airway smooth muscle cells. The effects of 4-β phorbol dibutyrate suggested that bradykinin induced PGE_2 production was mediated through protein kinase C. Production of PGE_2 by airway smooth muscle after exposure to spasmogens may be a mechanism whereby airway smooth muscle cells are able to feed back and inhibit the inflammatory process.

Lack of bronchial responsiveness to bradykinin in mildly asthmatic children

IJM DOULL, D SANDALL, NJ FREEZER, ST HOLGATE *University Medicine, Centre Block, Southampton General Hospital, Southampton* As part of a large scale study in 104 children to assess the effects of inhaled steroids on viral induced wheezing episodes, we investigated underlying mechanisms of bronchial hyperreactivity in children by comparing inhalation of methacholine and bradykinin. Thirty three children aged 7 to 9 years with mild episodic wheezing took part in this part of the study. Following baseline challenges to both agents, the children received treatment or placebo for three months during which they had monthly challenges to both agents, with at least a week between each challenge. Both methacholine and bradykinin were given by hand held nebuliser as described by Yan *et al.* Methacholine was given in increasing concentrations from 2 mg/ml to 64 mg/ml (cumulative concentration 512 mg/ml) and bradykinin in concentrations from 0·03 mg/ml to 32 mg/ml (cumulative concentration 58·655 mg/ml). Cumulative PC_{20} was calculated by interpolation and extrapolation up to one doubling dilution above the maximum concentration given. Thirteen children had measurable PC_{20} to methacholine at baseline, and on each subsequent challenge a mean of 12 children had a measurable PC_{20}. In contrast only four children had a measurable PC_{20} to bradykinin either at baseline (two had a PC_{20} to both) or subsequently, and there was no relationship between hyperresponsiveness to methacholine and bradykinin. Because of the number of children responding to bradykinin no conclusions were made on the action of inhaled steroids. Even though our children were only mildly asthmatic, the discrepancy in response to the two agents suggests that the underlying mechanisms of bronchial hyperresponsiveness differ between children and adults.

Increased urinary leucotriene E_4 (LTE_4) excretion following inhalation of leucotriene C_4 (LTC_4) and leucotriene E_4 (LTE_4) in asthmatic subjects

PE CHRISTIE, P TAGAR, AW FORD-HUTCHINSON, C BLACK, A MARK-ENDORF, M SCHMITZ-SCHUMANN, TH LEE *Swiss Institute for Allergy and Asthma Research, Davos, Switzerland, Hochgebirgsklinik, Wolfgang-Davos, Switzerland, Department of Allergy and Allied Respiratory Diseases, UMDS, Guys' Hospital, London, UK, Merck-Frosst, Quebec, Canada* Urinary LTE_4 concentration was measured

before and 1·5 and 3·5 hours after inhalation of bronchoconstrictive doses of LTC_4 or LTE_4 in eight asthmatic subjects. Airway response to inhaled LTC_4 or LTE_4 was measured using specific airway conductance (sGaw) in a total body plethysmograph and increasing doses of agonist inhaled until a 35% fall in sGaw was achieved. There was no significant difference between the 52 (3)% fall in sGaw following inhalation of 61·6 ng LTC_4 (GM, range 5·5–508 ng) and the 43 (4)% fall in sGaw following inhalation of 724 ng LTE_4 (GM, range 88–3569 ng). The LTE_4 excretion rate increased significantly from 2·9 ng/h (GM, range 0·6–17·5 ng/h) to 4·7 ng/h (GM, range 0·8–20 ng/h) at 1·5 hours after LTC_4 inhalation ($p < 0·05$) and from 1·7 ng/h (GM, range 0·07–6·7 ng/h) to 6·9 ng/h (GM, range 2·9–27·3 ng/h) at 1·5 hours after LTE_4 inhalation ($p < 0·05$) and had returned to baseline by 3·5 hours. There was a correlation between the dose of LTC_4 and LTE_4 inhaled and LTE_4 excreted in the urine ($p < 0·05$, $r = 0·8$ and $p < 0·05$, $r = 0·7$ respectively). The % recovery of LTE_4 in the urine of the total dose of inhaled LTC_4 or LTE_4 administered was 7·3 (4·3)% and 1·0(0·6)% respectively. Thus inhalation of bronchoconstricting doses of LTC_4 or LTE_4 alters urinary LTE_4 excretion in a dose dependent fashion. Changes in urinary LTE_4 excretion may reflect pulmonary levels of eicosanoid mediators in asthma.

Comparison of airway responsiveness to histamine leucotriene C_4 (LTC_4) and leucotriene E_4 (LTE_4) in aspirin sensitive asthmatic subjects with that of aspirin tolerant subjects

PE CHRISTIE, M SCHMITZ-SCHUMANN, B SPUR, TH LEE *Swiss Institute for Allergy and Asthma Research, Davos, Switzerland, Hochgebirgsklinik, Wolfgang-Davos, Switzerland, Department of Allergy and Allied Respiratory Diseases, UMDS, Guys' Hospital, London, UK* Airway responsiveness to histamine, leucotriene C_4 (LTC_4) and leucotriene E_4 (LTE_4) was determined in seven aspirin sensitive and 13 control asthmatic subjects who were tolerant of aspirin. The dose of agonist which produced a 35% fall in specific airways conductance (PD_{35} sGaw) was determined by linear interpolation from the log dose-response curve. There was no difference in airway responses to histamine and LTC_4 between the groups of asthmatic subjects. Aspirin sensitive asthmatic subjects were significantly more responsive to LTE_4 ($p = 0·02$) than control asthmatic subjects. The relative responsiveness of LTE_4 to histamine (PD_{35} histamine/PD_{35} LTE_4) was significantly greater in aspirin sensitive asthmatic subjects than in control asthmatic subjects ($p = 0·05$) There was no difference in relative responsiveness of LTC_4 to histamine between each group of asthmatic subjects. Thus the airways of aspirin sensitive asthmatic subjects but not aspirin tolerant asthmatic subjects demonstrate a selective hyperresponsiveness to LTE_4 which is not observed for LTC_4.

Single high dose budesonide does not affect AMP challenge

DH YATES, S AIKMAN, B O'CONNOR, PJ BARNES *National Heart and Lung Institute, Dovehouse Street, London* Glucocorticosteroids when inhaled regularly suppress airway inflammation and bronchial hyperresponsiveness in a dose and time dependent manner. We have previously demonstrated a decrease in airway responsiveness to AMP after regular treatment with budesonide (1·2 doubling dilutions after one week, 2·9 doubling dilutions after two weeks), and glucocorticosteroid effects may be seen as early as six hours. To investigate the acute effect of glucocorticosteroids on mast cell function we conducted a randomised double blind placebo controlled trial in 18 mild atopic non-smoking asthmatic subjects (nine men, nine women) using single high dose budesonide and AMP challenge. All subjects were treated with inhaled beta agonists only, which were withdrawn for at least two weeks before entering the trial. The study consisted of two single treatments, budesonide 4 mg administered in a single dose via turbohaler, and identical placebo, separated by a washout period of two weeks. Each subject inhaled five breaths of doubling doses of AMP from 0·78 to 800 mg/ml via a Mefar dosimeter until a PC_{20} was reached. Despite a small overall rise in mean log PC_{20} (log PC_{20} (SE) placebo 1·0 (0·19), 1·12 (0·16) active treatment), there was no statistically significant change ($p = 0·83$). While in five of the 18 subjects PC_{20} increased by over 1·5 doubling dilutions, PC_{20} decreased in two (>1·5 doubling dilutions). There was no correlation between baseline AMP PC_{20} or FEV_1 and degree of response. We conclude that, despite the marked effect of regular inhaled budesonide on mast cell function, a single high dose has no demonstrable effect in vivo.

Contrasting effects of inhaled and oral WEB 2086, a specific platelet activating factor antagonist (PAF) receptor antagonist on airway and systemic responses to inhaled PAF in man

BJ O'CONNOR, YM CHEN-WORSDELL, RA STONE, PJ BARNES, KF CHUNG *Royal Brompton National Heart and Lung Institute, London* WEB 2086 is a specific PAF receptor antagonist with therapeutic potential in allergic and inflammatory diseases. In two double blind placebo controlled studies we compared the ability of four different doses of inhaled WEB 2086 with the known ability of oral WEB 2086 to inhibit PAF induced bronchoconstriction. In study 1, 12 healthy non-atopic men attended on four separate occasions, each at least a week apart, to inhale three doses of WEB 2086, 0·25, 0·5 and 1 mg, or placebo from an MDI 30 minutes before PAF inhalation challenge. Airway responses to PAF (24 μg) were measured as changes in sGaw from baseline at serial intervals for up to 60 minutes. At 30 minutes we measured ex vivo PAF induced platelet aggregation. In study 2, 12 healthy non-atopic men attended on three separate occasions, each at least a week apart, to inhale from an MDI 10 mg or take a 40 mg oral dose of WEB 2086 30 and 90 minutes respectively before PAF inhalation challenge using a double dummy design. PAF induced neutropenia at five minutes and rebound neutrophilia at 30 minutes were measured. In study 1, none of the three inhaled doses of WEB 2086 inhibited PAF induced bronchoconstriction and platelet aggregation. In study 2, PAF induced bronchoconstriction was almost completely abolished by 40 mg orally, but was only partially attenuated by 10 mg inhaled WEB 2086 (NS). PAF induced neutropenia and rebound neutrophilia was similarly affected; mean (SD) % change from baseline at five and 30 minutes after PAF were respectively: −55·4 (8·8) and 132 (40) after placebo; −35·5 (6·8) and 23·9 (8·2) after 10 mg inhaled (NS); −4·5 (2·3) and 8·6 (2·8) after 40 mg oral ($p < 0·001$) (see table). Thus inhaled WEB 2086 has no effect on airway and systemic responses to PAF inhalation challenge. These data suggest that an oral formulation is required for further evaluation of the therapeutic potential of this compound in airway inflammation.

Maximum % fall in sGaw after PAF challenge

Study 1		*Study 2*	
Placebo	47·5 (4·9)	Placebo	36·9 (6·5)
0·25 mg	41·6 (6·9)	10 mg (inhaled)	23·3 (4·9)
0·5 mg	37·4 (6·9)	40 mg (oral)	4·6 (2·3)
1 mg	47·4 (6·2)		

Are oral antibiotics as effective as intravenous in treating chest infections?

R CHAN, L HEMERYCK, J STINSON, L CLANCY, J FEELY *Medicines Evaluation Unit, Department of Therapeutics and Respiratory Medicine, Trinity Medical School, St James's Hospital, Dublin* We studied the effectiveness of oral antibiotics alone *v* a combination of intravenous and oral antibiotics in the treatment of mild to moderate community acquired lower respiratory tract infections by randomly allocating 540 consecutive non-immunocompromised patients requiring hospitalisation into one of three treatment groups: (1) amoxycillin and clavulanic acid, 375 mg orally three times a day for seven days; (2) amoxycillin and clavulanic acid 1·2 g intravenously for three days followed by 375 mg orally three times a day for four days; or (3) cefotaxime 1 g intravenously three times a day for three days followed by cefuroxime axetil 500 mg orally twice daily for four days. Patients were assessed every alternate day until discharge or death. The outcome for each patient on discharge was classified as cure, partial cure, antibiotic extended, antibiotic changed, or death. Each group had 180 patients and all were comparable. The final outcome and mean duration of stay in hospital are shown in the table. There was a non-significant trend for a higher cure rate in the oral group which had a significantly reduced duration of hospitalisation. The continued "routine" use of the intravenous route to administer these antibiotics in patients with mild to moderate lower respiratory infections is no longer supported by our data. [Supported by The Health Research Board.]

	Cure (%)	Partial cure (%)	Antibiotic extended (%)	Antibiotic changed (%)	Death (%)	Duration of stay (days)
Group 1	43·0	38·0	7·3	6·7	5·0	7·6*
Group 2	35·0	38·6	10·0	9·4	7·0	9·17
Group 3	38·6	31·0	14·0	10·0	6·4	9·49

*$p < 0.01$, ANOVA.

Airborne transmission of *Pseudomonas cepacia* in cystic fibrosis

DG PECKHAM, H HUMPHREYS, AJ KNOX *Respiratory Medicine Unit, City Hospital and Department of Microbiology, University Hospital, Nottingham* Increased prevalence of *Pseudomonas cepacia* among specialist cystic fibrosis centres in the UK has led to inpatient segregation according to sputum cultures. We are presently investigating how patient to patient transmission of *P cepacia* may occur. Room air was sampled using an SAS sampler before, during, and after the occupancy of a room by six *P cepacia* positive patients with cystic fibrosis. Samples were obtained during coughing, immediately afterwards, and 18 hours after the patient had left the room. Contact and settle plates were also used. A total of nine experiments on six patients (mean FVC 53%, FEV_1 36%) have so far been conducted. All patients had been colonised by *P cepacia* for longer than six months. All sputum samples obtained during testing were positive for *P cepacia*. In four subjects *P cepacia* was isolated from air after vacating the room and in one patient it persisted for 45 minutes. Settle plates were negative in most instances. During coughing the mean count was 40 cfu/m³ compared with 15 cfu/m³ when the patients were not coughing. During outpatient clinic similar experiments were undertaken with air sampling during and after spirometry of *P cepacia* positive patients and all results proved to be negative. Our results suggest that *P cepacia* positive patients should be separated from *P cepacia* negative patients to minimise cross infection.

Rate of decline of lung function in patients with cystic fibrosis colonised by *Pseudomonas cepacia*

KM MUHDI, S O'HICKEY, G SMITH, DE STABLEFORTH *Adult Cystic Fibrosis Unit, East Birmingham Hospital* Between 1989 and 1992, 18 of 140 adult patients with cystic fibrosis attending our unit have developed sputum colonisation with *Pseudomonas cepacia*; five of these have died, three have received transplantation, and two subjects with insufficient data are not reported further. We compared the rate of decline of FVC and FEV_1 of patients with *P cepacia* with 18 age, sex and severity matched control patients colonised with *Pseudomonas aeruginosa*. Body weight, treatment days in hospital, and number of outpatient visits per six months were also studied. These patients were studied for 24 months before known colonisation with *P cepacia* and for as long as possible afterwards. The mean (SD) rate of decline in FVC for the group with *P cepacia* was −5·5 (28·7) ml/month before and −41·4 (66·1) ml/month after *P cepacia* colonisation ($p < 0.05$) in comparison to −3·6 (24·6) ml/month in the control group. The mean rate of decline in FEV_1 for the *P cepacia* group was −6·8 (20·1) ml/month before and −29·2 (55·5) ml/month after *P cepacia* colonisation ($p > 0.05$) compared with −9 (16·1) ml/month for the control group. Days of hospitalisation for treatment of acute infective exacerbation and number of outpatient visits per six months were significantly increased for the *P cepacia* group ($p < 0.05$), the mean (SD) being 9·7 (10) days/six months, 3·2 (1·5) visits/six months before and 36·3 (16·9) days/six months, 4·7 (1·8) visits/six months after colonisation respectively compared with 11·7 (19·6) days/six months, 2–9 (1·25) visits/six months in the control group. The changes in body weight per six months did not show any significant difference between the two groups. The acquisition of *P cepacia* is associated with a significant decline in lung function, increased days of hospital treatment, and number of outpatient visits.

Five year survival on home nebuliser treatment

BR O'DRISCOLL, K WORTHY, S JOHNSTONE, A BERNSTEIN *Hope Hospital, Salford* It has been suggested that home nebuliser treatment of asthma and chronic airflow obstruction may be dangerous either because of the potential hazards of high dose sympathomimetic treatment or because of over-reliance on self-administered treatment. We assessed 50 patients (16 asthma, 34 COPD) for home nebuliser treatment in 1986–7 and now report the five year mortality data of 49 of these patients (one left the area and cannot be traced). Thirty two patients (mean FEV_1 0·87 l) requested long term home nebuliser treatment and 17 patients (mean FEV_1 0·89 l) chose conventional metered dose inhaler treatment (MDI) with or without a large volume spacer. Five year survival was 53% for MDI users and 56% for nebuliser users, the two survival curves being parallel throughout the five year period. Most deaths were due to respiratory failure (14), lung cancer (four), or myocardial infarction (three cases, one MDI, two nebuliser users). The risk of death was mainly determined by initial FEV_1 (27 survivors FEV_1 = 1·11 l, 22 deaths FEV_1 = 0·59 l; $p < 0.001$). We conclude that home nebuliser treatment and metered dose inhaler treatment are associated with similar mortality rates in patients matched for the severity of their asthma and COPD. Mortality was related to severity of airflow obstruction in both groups. These data would support the view that the increased mortality amongst nebuliser users in other studies may reflect disease severity rather than a treatment effect.

Domiciliary oxygen cylinders: a survey of indications and usage

AA OKUBADEJO, EA PAUL, JA WEDZICHA *Department of Thoracic Medicine, London Chest Hospital, Bonner Road, London* In 1989, 935 831 oxygen cylinders were supplied in England and Wales at an average cost of £140 000 to each FHSA (*Health Trends* 1991;**23**:166), although concentrators have been available since 1985. Uses of oxygen cylinders include short burst treatment for breathlessness, refilling of portable oxygen cylinders, and as back-up for concentrators. We identified from FHSA records 116 patients in Tower Hamlets district (population 165 000) who had a home oxygen cylinder. Information on each patient was collected from postal questionnaires to patients and GPs, and hospital notes where appropriate. Two groups of patients were identified: those with an oxygen concentrator and home cylinder, and those who solely used cylinders. There were 60 (37 men, 23 women) concentrator users of median age 69 (range 20–94) years: 12% used the cylinder to refill a portable cylinder, 87% used the cylinder only as a back-up for the concentrator, but 74% stated that they had never actually used the cylinder. In the second group there were 56 patients (32 men, 24 women) of median age 71 (range 29–96) years: 43 (77%) had a diagnosis of COPD, four had asthma, three had cardiac failure, two had carcinoma, and in four patients the indication was not known, with 41% under regular chest clinic review. Of this group, 44 (79%) replied to the questionnaire on usage: 26 (59%) used oxygen every day, a further 12 (27%) used it at least once a week, but only six (14%) used it less. Thirty eight (86%) patients used it for acute attacks of breathlessness and exacerbations of COPD, six (14%) patients used oxygen before a period of exertion. Only two patients had portable oxygen cylinders. Arterial blood gas results for the previous five years were available in 15 patients: only two had a Pao_2 <7·3 kPa; 20% of patients continued to smoke, with 39% stating that they were house bound. From patient usage data an average of 29·2 cylinders per patient year were delivered. We found that oxygen cylinders in the community are used mainly for regular short term relief of breathlessness, though benefits are controversial. In view of cost implications we suggest that the long term prescription of oxygen cylinders should be limited to patients refilling portable cylinders, to those using a cylinder as back-up to concentrators, and to where the benefit of short burst treatment has been clearly established and reviewed.

Oxygen therapy and the medical wards: drug or harmless panacea?

C BELL, CC HARDY *Manchester Royal Infirmary, Oxford Road, Manchester* Oxygen therapy administered in inappropriate concentrations is at best of no benefit, and at worst potentially dangerous. The current plethora of oxygen masks on the market brings potential confusion to both house officers and nursing staff. Forty eight patients receiving oxygen therapy on medical wards were identified and their treatment sheets and case notes scrutinised with particular reference to its prescription, whether "prn" or continuous, indication of an FIO_2, mask type and flow rate. Whether oxygen was prescribed in an appropriate concentration was not addressed. Oxygen had not been prescribed to 25% of patients receiving it. Of the 75%

with a prescription, 94% specified an FIO_2. However, 36% of patients were not receiving the concentration prescribed, either because of an incorrect mask (77%) or an inappropriate flow rate (23%). Oxygen was prescribed "prn" in 66% of cases, continuously in 25%, and unknown in the remainder. Of the patients prescribed continuous oxygen 78% were not receiving it at the time the ward was visited. Arterial blood gases or oxygen saturation (oximetry) were recorded in 65% of patients, with an FIO_2 recorded in 52%. Twenty five house officers were interviewed about their understanding of oxygen therapy and its prescription; 24% felt it sufficient to make a verbal request to nurses. Only 4% could name a mask suitable for asthmatic patients, and only 20% knew the principle of delivering controlled oxygen therapy. This study shows that both nursing and medical staff require more training on safe, appropriate, beneficial oxygen therapy. By limiting the number of masks available on our wards we hope to circumvent some of the current problems.

Prevalence and symptoms of air travel amongst patients with respiratory disease

AOC JOHNSON, J CONGLETON, RL PAGE *Respiratory Unit, Killingbeck Hospital, Leeds* The inspired oxygen pressure in a commercial airline cabin at maximum cruising altitude is only 15 kPa. While this is sufficient to maintain oxygenation in normal subjects, those with impaired gas exchange may become profoundly hypoxaemic. The prevalence of, and difficulties experienced by, passengers with respiratory disease has been examined in the USA but not, to our knowledge, in the UK. We surveyed outpatients attending our respiratory unit by means of an administered questionnaire. All patients over 40 years with COPD, chronic asthma (CA), bronchiectasis (B), or interstitial lung disease (ILD) were included. A total of 97 patients were surveyed; 35 (36%) said that their chest disease alters their travel plans, 34 (35%) had flown on 63 occasions in the preceding two years (table 1). Of the 34 subjects who flew 15 (44%) developed respiratory symptoms; nine (26%) during the flight, and 10 (29%) while abroad. Only nine (26%) sought medical advice before flying (five GP and four hospital doctor). This included five of the subjects who developed symptoms. No special arrangements or further assessments were made and no patient was advised not to fly. There was no significant difference in FEV_1, FVC or FEV_1/FVC between flyers and non-flyers, nor between those with and without symptoms (table 2). All subjects were asked if the oxygen level in the aircraft was lower than, higher than, or the same as on the ground. Only 15% answered correctly. These findings, in agreement with Dillard *et al* (*Arch Intern Med* 1991;**151**:1793–5), suggest that patients with chronic respiratory disease fly frequently and often experience symptoms. Patients and doctors should be more aware of the potential problems of flying, and the advantages of preflight assessment.

Table 1 Data on patients in study

	n	*COPD*	*CA*	*B*	*ILD*	*Age (mean)*	*FEV_1%pred (mean)*	*FVC% (mean)*
Flyers	34	16	13	5	0	59·3	52·8	73·9
Non-flyers	63	36	21	1	5	61·4	49·1	67·9
Total	97	52	34	6	5	60·7		

Table 2 Number of patients experiencing symptoms during flight

	n	*Age (mean)*	*FEV_1% (mean)*	*FVC% (mean)*	*FEV_1/FVC (mean)*
Symptoms	9	63·1	43·7	68·1	49·5
No symptoms	25	57·9	56·1	75·9	57·0

Association of smoking with depression in the elderly

BH GREEN, JRM COPELAND, ME DEWEY, V SHARMA, PA SAUNDERS, IA DAVIDSON, C SULLIVAN, C MCWILLIAM, PDO DAVIES *Department of Psychiatry, Institute of Human Ageing, University of Liverpool and South Liverpool Chest Clinic* As part of a prospective survey to identify risk factors for depression in the elderly, subjects were asked about their smoking habit. A total of 1070 individuals were interviewed and assessed using the Geriatric Mental State package. Smoking data were available for 628 subjects, of whom 183 (29%) were never smokers and 218 (35%) current smokers. Three years later the same individuals were interviewed and 44 incident cases of depression were diagnosed. The control group was taken from the remaining non-depressed individuals. Of 31 risk factors assessed in the interview feelings of loneliness, satisfaction with life, and smoking were the only factors to attain a level of productive significance after univariate analysis. Smoking at the year of initial interview, but not necessarily a past history of smoking, appeared to predict depression ($\chi^2 = 5{\cdot}45$, $p < 0{\cdot}02$). Previous studies have shown an association between smoking behaviour and depression and an inverse relationship between quit ratio (former smokers or non-smokers) and depression scale scores. Suggestion of a causal link between current smoking and the onset of late life depression remains intriguing but speculative.

New portable information system for research and clinical use in a sarcoidosis clinic

C QUIGLEY, R MOFIDI, G LIU, C O'CONNOR, MX FITZGERALD *Medical Professorial Unit, University College, Dublin and St Vincent's Hospital, Dublin, Republic of Ireland* The accumulation of clinical, physiological, radiological and other details over many years of regular follow up will provide greater information about the natural history and long term management of chronic lung diseases. Relational databases organise data in a logical framework of two-dimensional tables which allow easy retrieval of complex interrelated information. We have developed a relational database specifically designed for rapid retrieval of complex clinical and basic research details facilitating continued clinical care and research in patients with chronic lung conditions. Sarcoidosis was used as a model for our database because of the many different types of data required in the full assessment and management of over 600 consecutive biopsy confirmed patients attending our special sarcoidosis clinic. We used a powerful relational database software package, 4th Dimension, held on a Macintosh Powerbook 170. The new system allows access to all previous computer held data and data are entered once only to a single format using electronic transfer where possible. The system takes advantage of the "Mac" user interface which is easy to use, requiring minimal computing skills acquired within 2–3 hours, and is portable for use in clinic, on ward rounds, and at a research laboratory. All data on patients with sarcoidosis are entered into a structure designed for use during consultation. Separate files are used for clinical, biochemical, lung function, bronchoalveolar lavage, and radiological data. Individual patient information is reviewed at a glance and updated during the consultation. Laboratory data can be transferred electronically at intervals. Patient confidentiality is preserved by strict password protection. The database is currently used to support comprehensive analysis of two year and five year follow up data and response to treatment over time in different patient subsets. This new sarcoidosis relational database provides efficient access to complex clinical data and enhances the effective long term management of sarcoidosis. Similar specifically designed databases may be of value in the management of asthma, cystic fibrosis, and other chronic lung conditions, and will allow comparison of epidemiological and other information.

Review of requests for respiratory consultation

NC MUNRO, D FISHWICK, PA CORRIS, GJ GIBSON, RAL BREWIS *Royal Victoria Infirmary (RVI) and Freeman Hospital (FH), Newcastle upon Tyne* Details were collected prospectively on 508 requests for a consultation with a respiratory physician (RVI, 378 over 33 months; FH, 130 over four months). Both hospitals include general and specialist medical and surgical services, intensive care, and renal units. Consultations were performed by a consultant (56%) or respiratory registrar or senior registrar (44%). There were no significant differences between the pattern of referrals at the two hospitals studied. The largest single source of referrals (35%) was the general medical wards, followed by medical subspecialties (25%) and general surgery (14·5%). Renal medicine provided 6% of referrals and intensive care 2·5%. The most common reasons for referral were tumour (27%), COPD (16%), and asthma (10%). The respiratory consultation resulted in the diagnosis of the patient's condition being made or altered in 39% of cases, the majority of the remaining consultations being advisory. Bronchoscopy was required following 29% of consultations; 77% of consultations were seen within 24 hours of the request being received and 33% required more than one visit. The time spent undertaking the consultation was up to 30

minutes in 47% of cases, 31–60 minutes in 37%, and over an hour in 11%. In 15% of cases care of the patient was taken over by the respiratory team. Problems encountered were unavailable radiographs in 9%, no appropriate lung function tests performed in 8%, and delay in seeking a respiratory opinion in 6%. Pulmonary disease is commonly present in patients admitted under all specialties and frequently requires specialist respiratory opinion for optimal diagnosis and management.

Antiglomerular basement membrane disease: the long term pulmonary outcome

P CONLON, G O'NEILL, M LONG, M CARMODY, B KEOGH, J DONOHOE, J WALSHE, S O'NEILL *Department of Respiratory Medicine, Beaumont Hospital, Dublin, Republic of Ireland* Evidence of pulmonary involvement occurs in up to 65% of patients with antiglomerular basement membrane disease (anti-GBM) at presentation. The long term functional sequelae of this involvement are unclear. We studied the pulmonary function of 14 patients (seven men, seven women) with biopsy proven anti-GBM disease of a mean of 7·8 (1–17) years after initial presentation. All patients were anti-GBM antibody negative and lacked radiographic evidence of lung disease at the time of study. Patients had measurements of forced vital capacity, forced expiratory volume in one minute, vital capacity, total lung capacity, residual volume, and single breath carbon monoxide transfer factor corrected for alveolar volume (KCO). All patients also participated in a modified Bruce protocol using a respiratory exercise system measuring maximal O_2 uptake, CO_2 output, expired minute volume, and O_2 saturation. As a control group 14 patients attending the renal clinic were chosen. These patients were matched for age, sex, smoking history, level of renal function, method of renal replacement, and duration of renal replacement. The KCO was significantly lower in the anti-GBM patients (53% (15%) compared with the control group (69% (15%), p = 0·02). The anti-GBM patients without pulmonary haemorrhage (n = 6; KCO 60·8% (13%)) did not differ significantly from the control group in contrast to patients with pulmonary haemorrhage (n = 8; KCO 46% (10%), p = 0·006). We conclude that patients with anti-GBM disease and pulmonary haemorrhage have evidence of a persistent reduction in KCO when compared with patients matched for levels of renal dysfunction.

Sclerosing mediastinitis: Royal Brompton experience

T MOLLI, MN SHEPPARD *Department of Surgery and Lung Pathology, Royal Brompton Hospital, Sydney Street, London* Sclerosing mediastinitis is a rare condition involving dense fibrosis of the mediastinum. We have collected 18 cases from 1970 to 1993. The sex ratio was M:F 2:1, age range 9–64 years. Twelve were British (66%), two patients were Spanish, one Turkish, one Asian and two Greeks. Twelve had shortness of breath, eight developed superior vena caval obstruction, six had haemoptysis, three had hoarseness, four had pleuritic chest pain, two had pleural effusion, three general weakness, and one patient had no symptoms. Twelve (66%) patients had previous disease. Two had autoimmune disease. Three had malignancy and were treated with chemotherapy and radiotherapy. Seven patients (43%) had a history of previous pulmonary tuberculosis with positive Mantoux test. Serological tests showed one positive reaction to histoplasma and this patient had lived for five years in the USA. Erythrocyte sedimentation rate was raised in nine patients. In seven patients (43%) liver function tests were abnormal. Immunoglobulins were raised in six cases. Diagnosis was usually based upon thoracotomy with biopsy. No positive culture results were obtained in any case. All cases showed fibrosis and chronic inflammation with no granulomas of the soft tissue of the mediastinum. Ten cases are alive up to 15 years later while six are lost to follow up. Six cases had superior vena cava bypass graft and are doing well. Only two deaths occurred and this was in cases treated for malignancy with chemotherapy and radiation.

Histological diagnosis of cryptogenic organising pneumonia: value of transbronchial biopsies

R DINA, MN SHEPPARD *Department of Histopathology, Royal Brompton Hospital, London and Institute of Pathology, Belaria Hospital, Bologna, Italy* Eleven cases of clinically diagnosed cryptogenic organising pneumonia were examined in order to establish the histological features found at transbronchial biopsy and to correlate this with the results of open lung biopsy which followed in five cases. The essential pathological feature was the presence of buds of granulation tissue (Masson bodies) indicating organising of a persistent exudate by fibroblasts and capillaries within alveoli with preservation of the alveolar architecture. In addition, both acute and chronic inflammatory cells were present in the interstitium. These features, combined with the clinical history, were sufficient to come to a diagnosis in seven of the 11 cases by transbronchial biopsy. However, four biopsies lacked these features and proceeded to open lung biopsy in addition to the two cases with histological features of cryptogenic organising pneumonia on transbronchial biopsy where the clinician wanted to eliminate other diseases in rapidly deteriorating patients. Five of the six cases undergoing open lung biopsy confirmed cryptogenic organising pneumonia with Masson bodies within alveoli, but changes were focal in three cases with few Masson bodies in one case. In addition, one case which had the features on transbronchial biopsy lacked them in the open lung biopsy which is explained by the evolution of the disease and time delay. The possibility of sampling error is also considered. In summary, transbronchial biopsy can yield diagnostic material in the majority of patients with cryptogenic organising pneumonia while open lung biopsy, which is considered the gold standard, may yield negative results because of the rapid evolution and changing pattern of the disease.

Midazolam sedation for fibreoptic bronchoscopy?

MQF HATTON, MB ALLEN, NJ COOKE *Department of Respiratory Medicine, General Infirmary at Leeds, Great George Street, Leeds* Sedation is often given before fibreoptic bronchoscopy, most regimens using an opiate or benzodiazepine. In a previous study comparing an opiate/sedative combination with placebo we found the active drugs conferred no advantage over placebo and patients were significantly less willing to have the investigation repeated (*Thorax* 1991;**46**:765). To formally evaluate the benefit of benzodiazepine sedation we compared, in a double blind randomised study, midazolam 70 μg/kg (35 μg/kg for those >70 years) given immediately before fibreoptic bronchoscopy with matched placebo; all received atropine. Eighty one patients undergoing routine fibreoptic bronchoscopy but not transbronchial biopsy were studied. The assisting nurse (N), bronchoscopist (B) and patient (PT) completed a 100 mm visual analogue scale (VAS) relating to comfort, ease of procedure, and willingness to have the test repeated. Higher scores represent a less favourable view. Fifty one patients received sedation, 30 placebo. The results, expressed as medians and compared with the Mann-Whitney U test, are shown in the table. The bronchoscopist felt the investigation was easier to perform on those patients given active drug, but none of the participants thought midazolam made fibreoptic bronchoscopy more comfortable for the patient. Active sedation made no difference to the willingness to have the procedure repeated. Sedation for fibreoptic bronchoscopy has recognised risks and the benefit of the active drug in this study may not be sufficient to justify its use.

	Active (VAS)	*Placebo(VAS)*	*p*
Patient comfort (N)	20	36	0·2
Patient comfort (B)	11	14	0·3
Test ease (B)	19	14	0·016
Comfort (PT)	30	36	0·17
Repeat? (PT)	16	8	0·9

Research bronchoscopy in HIV positive patients with no respiratory disease: does it adverely affect future health care decisions?

MCI LIPMAN, D STOBBS, R MILLER, MA JOHNSON *Royal Free Hospital and School of Medicine, London* Patients are often asked to take part in research projects. We studied the response of HIV positive patients with no respiratory disease to a request to have a research bronchoscopy. A structured interview and questionnaire were completed at first approach, subsequent bronchoscopy, and follow up. Sixty subjects were approached (50 men, 10 women); 44 (73%) agreed to bronchoscopy. The commonest reason for this was "to help others" (76%). Comparison of those agreeing and not agreeing revealed generally higher CD4 counts (median 505 *v* 415 × 10^6/l), lower β_2 microglobulin (median 2·8 *v* 3·1 mg/ml), and a shorter

duration of known HIV positivity (14·5 *v* 18 months) in the former group. To date 30 patients have undergone bronchoscopy. None found it worse than expected, although 82% had symptoms after the procedure (commonly sore throat); 86% would have a repeat research bronchoscopy, those declining having symptoms lasting >4 days after the procedure. All would have one for diagnostic purposes if unwell. We found a high positive response rate to an invasive research procedure which, although associated with short term after effects, is well tolerated and does not appear to compromise future health care decisions.

Audit of transbronchial lung biopsy in one Liverpool hospital

MJ WALSHAW, CC EVANS, CRK HIND *The Cardiothoracic Centre, Liverpool* It has been suggested that transbronchial lung biopsy is of limited value in the diagnosis of diffuse lung disease and has significant complications (*Am Rev Respir Dis* 1974;**109**:67) and some patients are now referred directly for lung biopsy at microthoracotomy (*Thorax* 1992;47:490–3). As part of an ongoing audit of lung biopsy techniques in our unit we have analysed all transbronchial biopsies carried out during fibreoptic bronchoscopy under local anaesthesia since June 1990. Fifty two such biopsies have been performed (4% of all fibreoptic bronchoscopies) by seven operators, the majority (44, 85%) by two operators. The mean age was 57 years (range 21–79), mean FEV_1 72% predicted (28–115) and mean FVC 78% predicted (24–125). Ten patients (19%) had serious other diseases which would have made them poor risks for general anaesthesia, and 37 had diffuse shadowing on chest radiography. Uniplanar fluoroscopic positioning of the biopsy forceps was used in 49 cases (94%), the remainder were carried out "blind". Most cases (45, 86%) had biopsies taken from the lower lobes. On average, four biopsies were taken (range 1–6). There were no cases of post biopsy pneumothorax, although seven cases (13%) had some haemoptysis. Alveolar tissue was obtained in 46 cases (88%): all were cases performed with fluoroscopy. The samples were considered adequate for diagnosis by the histopathologist in 42 cases (81%); 11 malignancy, seven fibrosing alveolitis, five sarcoidosis, six pulmonary fibrosis, three extrinsic allergic alveolitis, two amiodarone lung, one tuberculosis, one pulmonary eosinophilia, six normal lung. Of the remaining cases, three went on to surgical lung biopsy (one malignancy, one fibrosing alveolitis, one honeycomb lung). Our results reiterate that transbronchial lung biopsy using uniplanar screening can provide a diagnosis in over 80% of cases and has a low morbidity. It should be considered before patients are referred for more invasive diagnostic procedures.

Bronchoscopic diagnosis of malignancy in patients whose chest radiograph showed only a pulmonary infiltrate

VL SCOTT, E NEVILLE, R BUCHANAN *Chest Clinic, St Mary's Hospital, Portsmouth* A total of 2453 bronchoscopies were performed at St Mary's Hospital between January 1983 and January 1993. Of these, 163 (6·6%) had radiological evidence of diffuse interstitial disease. Of the 163 cases 18 had histological diagnoses of malignancy, one showed squamous metaplasia, and two atypical or dysplastic cells. One of these patients went on to have an open lung biopsy which showed metastatic breast carcinoma. Eight of the 18 with definite malignancy had additional radiological features suggestive of carcinoma. In 10 patients where there was chest radiographic evidence of pulmonary infiltrate without visible tumour there were three female and seven male patients, with ages ranging from 43 to 81 years (mean 61·9 years). Three of these 10 were known to have other forms of malignant disease, namely non-Hodgkin's lymphoma, carcinoma of the prostate, and gastric carcinoma. On spirometry a restrictive defect was seen in seven out of eight patients. At bronchoscopy three patients had visible tumour, all of which proved to be squamous cell carcinoma. The remaining patients had normal bronchoscopic appearances. The patient with lymphoma had this confirmed on biopsy and the patients with prostatic and gastric carcinoma had histological evidence of metastatic disease. Of the four remaining patients two had squamous cell carcinoma and two adenocarcinoma. One of the latter went on to have a mammogram which confirmed a primary breast lesion. The distribution of the pulmonary infiltrate gave no clue to the underlying diagnosis of malignancy. Histological diagnoses of malignancy were reported in 10 of 163 (6·1%) of those bronchoscoped with interstitial lung disease, but no radiological evidence of cancer. This corresponds to 0·4% of all patients undergoing bronchoscopy in a 10 year period.

Evaluation of computed tomography and sputum cytology in the diagnosis of bronchial carcinoma

GA GOULD, A TROUGHTON, PR GODDARD, JR CATTERALL *Departments of Respiratory Medicine and Radiodiagnosis, Bristol Royal Infirmary, Bristol* Investigation of suspected bronchial carcinoma usually includes bronchoscopy for histological confirmation followed by computed tomography (CT) to stage disease. We prospectively studied 55 consecutive patients in whom a diagnosis of bronchial carcinoma was considered to determine the roles of CT, bronchoscopy, and sputum cytology. Adequate sputum specimens were not obtained in seven patients, and in a further four bronchoscopy was not performed for clinical reasons. The remaining 44 patients had all three investigations and were classified by CT appearance into three groups: group 1: carcinoma highly probable, with pulmonary mass/collapse and hilar, mediastinal or local invasion (n = 17); group 2: equivocal, with pulmonary mass/collapse/consolidation or hilar enlargement (n = 17); group 3: carcinoma unlikely, with an alternative diagnosis (tuberculosis four, aortic aneurysm two, fibrosing alveolitis one, emphysema one, McCloud's syndrome and cardiac fatpad one, bronchiectasis and consolidation one) (n = 10). Bronchoscopy confirmed the diagnosis of carcinoma in all patients in group 1, five patients in group 2, and none in group 3. However, sputum cytology also confirmed malignancy in nine patients in group 1, all of whom were considered inoperable due to local invasion. These results indicate that in nine of 44 patients inoperable bronchial carcinoma was confirmed by a combination of CT and sputum cytology. When bronchial carcinoma is clinically suspected and CT is negative or equivocal, bronchoscopy is mandatory, irrespective of sputum cytology results if active treatment is being considered. However, when CT confirms inoperable malignancy and sputum cytology is positive, bronchoscopy may not be necessary. Expert CT interpretation and sputum examination may avoid inappropriate bronchoscopy in a significant minority of patients, thereby reducing patient discomfort and costs.

Cervical cordotomy for the relief of pain in pleural mesothelioma

AW MATTHEWS, A PROSSER, E NEVILLE, D POUNDER *Queen Alexandra Hospital, Cosham, Portsmouth* Severe chest pain is common in pleural mesothelioma. In a survey of 200 patients pain was a presenting symptom in 58% and most were taking large doses of opiates by the time of their death (Matthews, *Thorax* 1992;47:851–2). Percutaneous cervical cordotomy interrupts the spinothalamic tract at C1–2 by means of a radiofrequency burn and produces contralateral loss of pain and temperature sensation below the level of the lesion (Rosomoff, *J Neurosurg* 1965;**23**:639–44). Twenty one patients have been treated by this technique. All were suffering from severe chest pain and taking large doses of opiates. Good pain relief was achieved in 18 and partial relief in three. The interval between onset of pain and cordotomy ranged from two to 16 months (mean 7·4), and between cordotomy and death from eight days to 11 months (mean 3·6 months). The mean daily dose of opiate was reduced from 170 mg before the procedure to 32 mg, and in 11 patients opiates were withdrawn. There were no major complications. One patient developed mild ipsilateral weakness and one experienced dysaesthesia. Recurrence of pain requiring opiates occurred in 11 patients, usually due to spread to the mediastinum or abdomen.

Relation between age and treatment of lung cancer

JS BROWN, A DAVISON, D ERAUT *Department of Cardiothoracic Medicine, Southend Hospital, Essex* We have previously shown a high incidence of lung cancer in elderly patients (43% ⩾75 years of age). How the treatment of the elderly differs from the younger patients has important implications for the provision of care. The *initial* treatment given to patients including those not cared for by a respiratory physician over a 30 month period from 1 January 1990 was analysed. A total of 563 new patients were diagnosed, 240 (42·6%) aged 75 or over, 190 (33·7%) between 65 and 74 years, and 133 (23·6%) under 65. For proven non-small cell cancer (n = 308) the relation between age and type of treatment was significant ($p < 0·001$). For small cell cancer (n = 109) the relation between age and type of treatment was also significant ($p < 0·01$). The

performance status (ECOG values) at presentation of those aged 75 and over was worse than those aged under 75 ($p < 0.001$). Three month survival of those aged 75 and over was 37% and for those under 65 years of age was 50% ($p < 0.001$). The main differences in treatment are that surgery and chemotherapy are more frequently performed in the younger patients, whilst more in the 65–74 age group receive radiotherapy, and more older patients receive symptomatic care only (table).

	Under 65 years	*65–74 years*	*75 years and over*
Surgery	16·3	10·2	1·7
Radiotherapy	38·4	44·4	33·9
Chemotherapy	18·6	6·5	0
Symptomatic	26·7	38·9	64·3

Values are percentages.

Outcome in lung cancer: a comparison between those seen by chest physicians and by other doctors

JS BROWN, A DAVISON, D ERAUT *Department of Cardiothoracic Medicine, Southend Hospital, Essex*

Few studies of lung cancer include patients who have not been under the care of chest physicians or surgeons. It is therefore important to characterise these patients and see how they differ from other patients with lung cancer. All new patients with lung cancer in the Southend district for a 30 month period from 1 January 1990 were analysed by all available methods to obtain every case, including laboratory reports and death certificates. A subgroup was formed from patients who were not under the care of a chest physician. There were 563 patients (mean age 71) with a subgroup of 102 patients (18%) who were not under the care of a chest physician. Sixteen patients only diagnosed at necropsy were excluded, leaving 86 patients (15%) with a mean age of 76 years (mean age of those seen by a chest physician 70), 63% men and 37% women. Care was provided by a physician in 13%, a geriatrician in 57%, and an oncologist in 23%. Histology showed non-small cell cancer in 35%, small cell cancer in 13%, with no histology obtained in 52% compared with 22% in the patients seen by a chest physician. One patient underwent surgical treatment, four had chemotherapy, and 13 were given radiotherapy. The six month survival was 6% in patients not seen by a chest physician and 32% for patients seen by a chest physician. In this preliminary study patients with lung cancer not seen by a chest physician are more elderly, less likely to have "active" treatment, and have a poorer prognosis. This survey poses a number of questions regarding the care of elderly patients with lung cancer.