Case report

Idiopathic azygos vein aneurysm: a rare cause of mediastinal mass

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Abstract

Venous aneurysm of the azygos arch is a very rare cause of mediastinal mass and is usually an incidental finding on chest radiography. Nowadays the diagnosis is made by non-invasive tests such as thoracic CT scanning and/or magnetic resonance imaging. The case is described of an asymptomatic woman in whom a mediastinal mass due to an azygos vein aneurysm was diagnosed by non-invasive procedures, the aetiology of which, in all probability, was idiopathic.

(*Thorax* 1999;**54**:653–655)

Keywords: mediastinal mass; azygos vein; aneurysm

Enlargement of the azygos arch vein can be due to an increase in central venous pressure, portal vein hypertension, azygos continuation of the inferior vena cava (IVC), a tumour, or local thrombosis located in the inferior vena cava.[1 2]

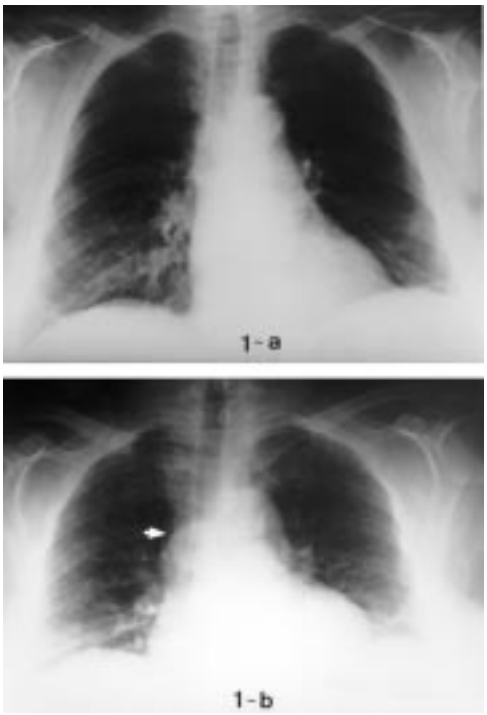

Figure 1 (a) Full inspiration. Normal appearance of the mediastinum. (b) The lesions become larger with full expiration, providing that the mass is not solid in character (arrow).

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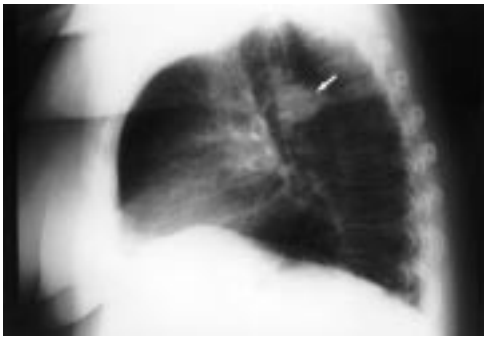

Figure 2 Lateral view showing a mass localised in the retrotracheal area (arrow).

High central venous pressure is by far the most common cause and mainly results from cardiac decompensation.[3] True aneurysmal dilatation is a highly uncommon entity which has been reported on very few occasions.[1 2 4–9]

We report a case of azygos vein aneurysm diagnosed by computed tomographic (CT) scanning and magnetic resonance imaging (MRI).

Case report

A non-smoking 64 year old woman was referred to our hospital with coughing, wheezing, and scanty expectoration. Except for mild hypertension, her past medical history was unremarkable. No significant trauma was recorded. Physical examination was normal except for the presence of bilateral wheezing; no signs of cardiac failure were detected. Blood

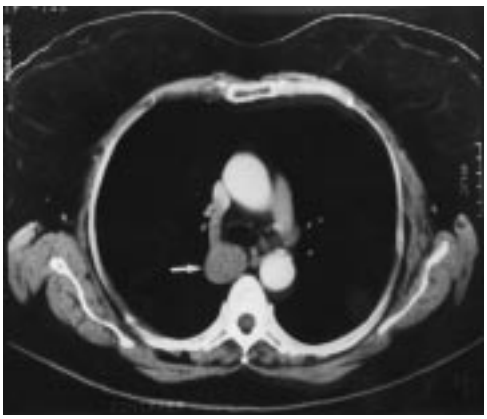

Figure 3 CT section at the level of the azygos arch confirming the presence of a mass located in the azygos path (arrow). No anomalies were seen in higher and lower slices.

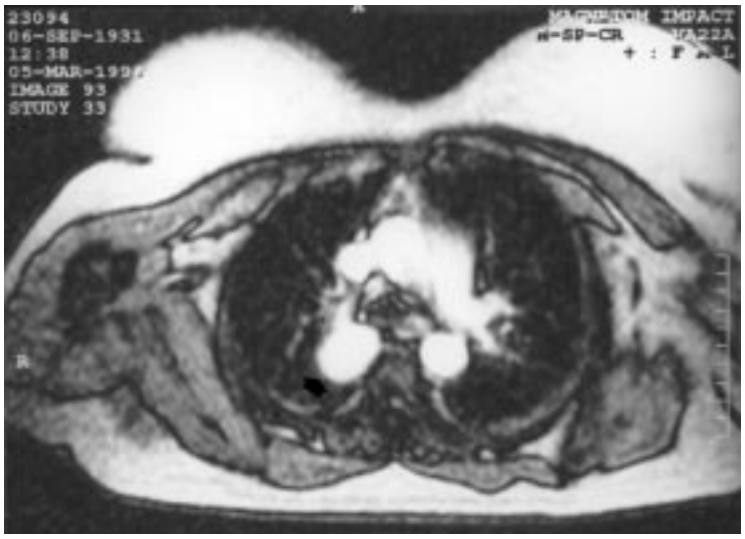

Figure 4 T1 scan after injection of gadolinium showing the mass with similar enhancement to the aorta.

analysis (including a haemogram, differential cell count, hepatic and renal function, ionogram, and proteinogram) and arterial blood gas tensions in room air were normal.

The posteroanterior chest radiograph was normal (fig 1a) but the lateral view showed a possible retrotracheal mediastinal mass (fig 2). A second chest radiograph on expiration showed a mediastinal mass (fig 1b). A CT scan before and after intravenous contrast enhancement confirmed the presence of a slowly enhancing mass in the pathway of the azygos arch measuring 3.5 cm (fig 3). Axial T1 weighted and T2 weighted magnetic resonance imaging showed a heterogeneous mass and, after injection of gadolinium-DTPA, the lesion became homogeneously hyperintense and isointense with respect to the rest of the vascular structures (aorta, vena cava). However, contrast uptake occurred later due to upward venous flow in the azygos vein (fig 4). The findings were compatible with an aneurysm of the azygos vein.

Discussion

Most patients with venous aneurysms are asymptomatic and the lesion is detected as an incidental finding on the chest radiograph (table 1). The aetiology of the azygos aneurysm was unknown, but since no history of high pressure in the azygos system or recent trauma were recorded despite extensive anamnesis, clinical and radiographic examination, it was assumed to be congenital.

During the third and fourth weeks of gestation the cardinal vein system develops. This system consists of paired anterior and posterior cardinal veins which unite to form a short common cardinal vein. The anterior cardinal vein gives rise to the subclavian, the internal jugular, the brachiocephalic vein, and the superior vena cava. The posterior cardinal veins are replaced by two additional pairs of veins, the subcardinal and the supracardinal veins (which gives rise to a portion of the inferior vena cava and the azygos system). A segment of the right supracardinal vein anastomoses with a part of the superior vena cava (derived from the anterior cardinal vein) so that the azygos drains into the right atrium via the superior vena cava.[10 11] It has been postulated that an aplasia or hypoplasia of the superior vena cava could affect azygos drainage,[6] but in our case no cava affection was observed. Moreover, the aneurysm was localised at the junction of the supracardinal and the anterior cardinal veins which, anatomically, is a weak point. This lends support to the idea of a congenital aetiology in our case.

Veins are composed of three layers: the intima, the media, and the adventitia. During vasculogenesis the first layer to appear is the intima, and the tunica media develops once a stable vascular pattern has been formed (by interaction of the epithelium and the mesenchyma). In cases of congenital dilatation the venous layer to be affected is the media, as opposed to acquired dilatation (i.e. varicose veins) where there is a fibrosis beneath the endothelium.[12] To confirm this hypothesis it is necessary for a histological study to be performed to detect alterations in the venous endothelium.

In patients with an azygos venous aneurysm a frontal chest radiograph may demonstrate a prominent azygos vein or an abnormal mediastinal density. On a frontal chest radiograph, characteristically, the size of the aneurysm changes with the respiratory movements (especially with Valsalva manoeuvre), as happened in our case.[1] In the past, venography used to be performed to suggest the diagnosis.[2 6] Nowadays, dynamic enhanced CT scanning and MRI not only provide non-invasive methods for the evaluation of vascular abnormalities,[5 13] but can also rule out other entities which may produce enlargement of the azygos vein. However, the blood flow in the aneurysmal vein is sometimes so slow that MRI may provide an image similar to a solid mass.[5] The signal

Table 1 Characteristics of venous aneurysms reported in the literature

	Age	*Sex*	*Symptoms*	*Size of mass*	*Arch involved*	*Diagnostic test*
Mabitang *et al*[6]	35	F	Incidental finding	Not reported	Dilatation of whole arch	Surgical
Stern *et al*[4]	19	M	Asymptomatic	3 cm	Dilatation of whole arch	Surgical
Rockoff *et al*[1]	59	F	Incidental finding Thoracic pain	2.5 cm	Paratracheal	Venogram
Seebauer *et al*[2]	54	F	Obstruction of SVC	12 cm	Confluency with SVC	Surgical
Kurihara *et al*[5]	62	M	Asymptomatic	Not reported	Paratracheal	Surgical CT
Lena *et al*[7]	70	M	Incidental finding Lung cancer	3 cm	Paratracheal	Surgical Transoesophageal Echography
Metha *et al*[8]	70	F	Incidental finding Pulmonary nodule	3 cm	Paratracheal	CT
Pobielsky *et al*[9]	68	F	Asymptomatic	4 cm	Confluency with SCV	Surgical CT

intensity of the lesion, in our case, varied depending on whether upflow or downflow were saturated, thus confirming its vascular nature.

Although this entity is very rare, we believe that it should be borne in mind for the differential diagnosis of a mediastinal mass. Moreover, it should be stressed that, for an accurate diagnosis, invasive tests are not necessary. Follow up of this lesion is important as an azygos vein aneurysm may grow.[2]

1 Rockoff SD, Druy EM. Tortuous azygos arch simulating a pulmonary lesion. *Am J Roentgenol* 1982;**138**:577–9.
2 Seebauer L, Prauner HW, Gmelnwleser J, *et al*. A mediastinal tumour simulated by a sacculated aneurysm of the azygos vein. *Thorac Cardiovasc Surgeon* 1989;**37**:112–4.
3 Fraser RG, Paré PD, Genereux GP. *Diagnosis of diseases of the chest*. Vol 4. Philadelphia: WB Saunders, 1991: 2879–84.
4 Stern WZ, Bloomberg AE. Idiopathic azygos pheblectasia simulating mediastinal tumor. *Radiology* 1961;**77**:622–5.
5 Kurihara Y, Nakajima Y, Ishikawa T. Case report: saccular aneurysm of the azygos vein simulating a paratracheal tumor. *Clin Radiol* 1993;**48**:427–8.
6 Magbitang MH, Hayford FC, Blake JM. Dilated azygos vein simulating a mediastinal tumor. *N Engl J Med* 1960;**263**: 598–600.
7 Léna H, Desrues B, Heresbach D, *et al*. Azygos vein aneurysm: contribution of transesophageal echography. *Ann Thorac Surg* 1996;**61**:1253–5.
8 Metha M, Towers M. Computed tomography appearance of idiopathic aneurrysm of the azygos vein. *J Can Assoc Radiol* 1996;**47**:288–90.
9 Podbielski F, Sam II AD, Halldorsson A, *et al*. Giant azygos vein varix. *Ann Thorac Surg* 1997;**63**:1167–9.
10 Willians PL. Embryology and development. In: *Gray's anatomy: the anatomical basis of medicine and surgery*. 38th edition. New York: Churchill Livingstone, 1995: 324–7.
11 Larsen WJ. Development of the vasculature. In: *Human embryology*. New York: Churchill Livingstone, 1993: 185–191.
12 Risau W. Vasculogenesis, angiogenesis and endothelial cell differentiation during embryogenic development. In: Feinberg RN, Sheror GK, Auerbach R, eds. *The development of the vascular system*. Philadelphia: Karger, 1991: 58–68.
13 Moncada R, Demos TC, Marsan R, *et al*. CT diagnosis of idiopathic aneurysms of thoracic systemic veins. *J Comput Assist Tomogr* 1985;**9**:305–9.

LETTERS TO THE EDITOR

COPD guidelines

Following the publication of the BTS guidelines on chronic obstructive pulmonary disease (COPD), questions were raised concerning the costs of spirometric screening in the detection and management of these patients.[1]

The guidelines state that a volume/time plot is mandatory for screening[2] and that such machines are considerably more expensive than a simple vane spirometer. This led one author to suggest that basic screening should be performed with the latter device and that patients with abnormal results should be sent for full open access spirometric testing at chest clinics for further evaluation.[3]

Since the publication of the guidelines the Chest Service at St George's Hospital has received many enquires about an open access spirometry service. We therefore conducted a postal questionnaire of the local GP practices to determine (1) their need for a spirometry service, (2) the level of priority they considered this need should be given, and (3) by whom the service should be provided.

The response rate was 70% (35 practices); 83% considered that there was a need for access to a spirometer following publication of the guidelines but the majority (55%) felt this need was only of medium priority. Most of the practices (83%) thought that a spirometry service should be provided by the Chest Clinic. However, when asked if they would support the allocation of local commissioning resources to establish such a service, only 70% agreed to this.

Clearly our local GPs would prefer a Chest Clinic based open access spirometry service. Whilst this service would be easy to establish, it would place an enormous drain on staff and clinic resources and separate funding would have to be made available.

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1 Perry M. COPD guidelines. *Thorax* 1998;**53**:624.
2 British Thoracic Society. BTS guidelines for the management of chronic obstructive airways disease. *Thorax* 1997;**52**(Suppl 5):S1–28.
3 Sinha RK. COPD guidelines. *Thorax* 1998;**53**: 625.

AUTHOR'S REPLY Objective measurement of lung function by spirometry is the single most important recommendation in the COPD guidelines.[1] However, the guidelines deliberately did not recommend how spirometry services should be set up because this will vary according to local facilities, finance, and politics. The guidelines do recommend a volume-time plot as inspection of the traces is the only practical way of ensuring a degree of quality control on the data, and the extra one-off cost of an appropriate device that should last for years is not a huge burden even for individual practices. The option of open access spirometry services (analogous to the chest *x* ray service) is already available in some districts and may have financial, and probably quality, benefits—but at the cost of being distant from the patient and the GP. In my own district outreach spirometric testing using hospital technicians to provide locality testing sessions is a compromise between the two that is presently being evaluated.

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Inhaled corticosteroids in COPD

Dr van Grunsven *et al*[1] refer to our study comparing inhaled beclamethasone 750 µg twice daily with placebo in the long term management of COPD (their reference 11) and were unable to find the full report. Its reference is *Bronchitis V* edited by D S Postma and J Gerritsen, published by Van Gorkum, Assen in 1994 (pages 280–4).

Our study followed up 74 patients at approximately two and five years after a double blind steroid trial. The mean (SE) decline in FEV_1 in those taking beclomethasone was 35 (21.5) ml/year at the two year follow up and 65 (10.3) ml/year at the five year follow up (not significant). In those not receiving inhaled steroids the mean (SE) decline in FEV_1 was 112 (23.3) ml/year at the two year follow up, decreasing significantly to 25.3 (19.5) ml/year at the time of the second follow up when they were given inhaled beclomethasone dipropionate. There was no relationship between the response to the initial steroid trial and the subsequent decline in FEV_1.

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1 Van Grunsven PM, Van Schayck CP, Derenne JP, *et al*. Long term effects of inhaled corticosteroids in chronic obstructive pulmonary disease: a meta-analysis. *Thorax* 1999;**54**:7–14.

AUTHOR'S REPLY We thank Dr Sherwood Burge for his comments on our study. Indeed, the results of their study have been presented not only in abstract form but also in more detail.[1] We apologise for this omission. As we stated in the discussion section of our study,[2] Weir *et al* investigated the long term effect of inhaled beclomethasone 1500 µg daily on the decline in FEV_1 in a therapeutic trial. This (uncontrolled) treatment followed an original randomised controlled trial of 107 patients including a group of patients with moderately severe COPD (FEV_1 <70% predicted), comparable to our study. In their original study patients were treated with prednisone 40 mg daily, inhaled beclomethasone 1500 µg daily, and placebo in a crossover design to assess the short term steroid response (defined as an increase in FEV_1, FVC or PEF of ≥20% from baseline). Seventy four patients were reassessed approximately two and five years after this original trial. Thirty two patients received beclomethasone only during the second follow up period, the remaining patients were treated with beclomethasone during the whole follow up period. In the former group of 32 patients the authors showed that the

decline in FEV_1 decreased significantly when the first follow up period (without the use of inhaled beclomethasone) was compared with the second follow up period (during treatment with inhaled beclomethasone). This result, although not achieved in a randomised controlled design and therefore excluded from our meta-analysis, supports our finding of a significant two year treatment effect of inhaled beclomethasone or budesonide in a daily dose of 1500/1600 µg compared with placebo of +0.034 l/year.[2]

Dr Sherwood Burge also pointed to the absence of a relationship between the response to the initial steroid trial and the subsequent decline in FEV_1 in their study. Indeed, an interesting finding of their study was that, although the majority (75%) of the original 23 steroid responders had been treated with beclomethasone during the whole follow up period, the mean (SE) decline in FEV_1 of 51.5 (10.3) ml/year did not differ from the 51 non-responders of which only 50% were treated with beclomethasone during the whole follow up period (53.1 (8.7) ml/year). The authors therefore concluded that the acute steroid response did not seem to be an adequate predictor of the long term response to inhaled steroids in patients with moderate to severe COPD. In our meta-analysis[2] only patients in the study by Renkema *et al* had been treated with a course of steroids in a dose of 40 mg daily during the eight days preceding the trial in order to assess steroid responsiveness (response as defined by an increase in FEV_1 of $\geq$20% from baseline). In their study only three steroid responders (of 58 patients with severe COPD) were identified.[3] In two studies in patients with mild to moderate COPD the presence of "asthmatic features" such as allergy and reversibility of obstruction resulted in a better long term treatment effect with inhaled corticosteroids.[4 5] In our meta-analysis we did not find this relationship.[2] This result could be explained by our selection of subjects with strictly diagnosed non-asthmatic and irreversible COPD, comparable to the subjects in the study of Weir *et al*. Forthcoming data of the ISOLDE trial which was initiated by Dr Sherwood Burge (ISOLDE is a three year randomised placebo controlled trial in 990 patients with severe COPD treated with 1000 µg fluticasone daily) may give a more definite answer to the question of the predictive value of a short course of oral prednisone (or other asthmatic features such as reversibility and allergy) on the clinical effects of long term treatment of patients with moderately severe COPD with inhaled corticosteroids.

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1 Weir DC, Wieland GA, Sherwood Burge P. In: Postma DS, Gerritsen J, eds. *Bronchitis V: Fifth International Symposium.* Assen: Van Gorkum, 1994: 280–4.
2 Van Grunsven PM, Van Schayck CP, Derenne JP, *et al*. Long term effects of inhaled corticosteroids in chronic obstructive pulmonary disease: a meta-analysis. *Thorax* 1999;**54**: 7–14.
3 Renkema TE, Schouten JP, Koeter GH, *et al*. Effects of long-term treatment with corticosteroids in COPD. *Chest* 1996;**109**:1156–62.
4 Kerstjens HA, Overbeek SE, Schouten JP, *et al*, and the Dutch CNSLD Study Group. Airways hyperresponsiveness, bronchodilator response, allergy and smoking predict improvement in FEV_1 during long-term inhaled corticosteroid treatment. *Eur Respir J* 1993;**6**:868–76.
5 Van Schayck CP, Van Grunsven PM, Dekhuijzen PNR. Do patients with COPD benefit from treatment with inhaled corticosteroids? *Eur Respir J* 1996;**9**:1969–72.

Rising incidence of SCLC in young women

There has been much media interest in the work of Thompson and Pearson[1 2] who demonstrated, via a hospital based study of 1044 patients undergoing bronchoscopic examination, that women of all ages are more likely to present with small cell lung cancer than men, and that younger women are more likely to present with small cell cancer than older women. Increasingly, women who begin smoking at an early age seem to be more susceptible to small cell lung cancer (two year survival about 5%).

We can extend and complement these findings in a study of population based data held by the Northern and Yorkshire Cancer Registry and Information Service (NYCRIS). Table 1 shows data for 7485 patients diagnosed between 1992 and 1994, 4823 (64%) of whom were men. A lower proportion of men (11%) than women (17.5%) had a histological diagnosis of small cell lung cancer. Rates of histological confirmation increased over time but were lower for older patients. Of those confirmed, younger patients of both sexes were significantly more likely to present with small cell lung cancer than older patients ($p<0.001$, logistic regression). However, young women in particular were more likely to present with small cell cancer than men of similar age ($p<0.001$).

The reasons for these patterns are not understood. It is suggested that changes in smoking habit, particularly in younger women, could play a part. Initiation of smoking at an early age has been shown to increase the risk of small cell lung cancer in men,[3] so it is reasonable to assume that a rise in young female smokers could be responsible. Should the incidence continue to rise, there are important future implications for both provision of care and the prognosis of younger patients with lung cancer. These data again emphasise the need for effective anti-smoking programmes, particularly targeting adolescents.

The authors are grateful to NYCRIS and members of The Yorkshire Cancer Management Study Group for making these data available.

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1 Thompson S, Pearson MG. Changing patterns of lung cancer histology with age and gender. *Thorax* 1998;**53**(Suppl 4):A10.
2 Kmietowicz Z. Women at double risk of small cell lung cancer. *BMJ* 1998;**317**:1614.
3 Khuder SA, Dayal HH, Mutgi AB, *et al*. Effect of smoking on major histological types of lung cancer in men. *Lung Cancer* 1998;**22**:15–21.

Airway hyperresponsiveness in asthma

The review by Brusasco *et al*[1] demonstrates that a simple causal hypothesis is insufficient to explain airway hyperresponsiveness in asthma. We have also refuted this hypothesis by identifying that airway eosinophilia can occur without airway hyperresponsiveness,[2] and that in asthma airway hyperresponsiveness can persist despite suppresssion of airway inflammation and pancytopenia induced by chemotherapy.[3] However, airway inflammation and airway hyperresponsiveness are so intrinsically linked in asthma that an alternative hypothesis must be provided.

My hypothesis is that airway inflammation can modulate the level of intrinsic airway responsiveness such that an increase in airway inflammation from, for example, allergen exposure will lead to an increase in airway responsiveness, and a decrease in airway inflammation from, for example, corticosteroid therapy will lead to a reduction in airway responsiveness. The absolute level of airway responsiveness, and hence whether it is categorised as normal or increased, will depend upon two factors—the starting level of airway responsiveness and the magnitude of change.

This hypothesis is consistent with the observed data. Exposure to respiratory sensitisers induces airway inflammation and increases the level of airway responsiveness. This occurs both in the "asthmatic range" and in the normal range of airway responsiveness (fig 1). Similarly, corticosteroid therapy reduces airway eosinophilia and this leads to an improvement in airway responsiveness, both in the normal range[2] and in the asthmatic range (fig 1). It is interesting to note that the magnitude of change in airway responsiveness induced by changes in airway inflammation is similar whether it occurs within the asthmatic or the normal range.

The mechanisms for the intrinsic airway hyperresponsiveness in asthma will differ from those resulting in a change in airway responsiveness induced by airway inflammation.

The consequences of airway remodelling such as airway wall thickening and alterations in smooth muscle mass and contractility may each be determinants of the underlying level of airway responsiveness, independent of any airway inflammation.

From a clinical perspective it is likely that airway inflammation will be suppressed by (low dose) corticosteroid therapy but airway hyperresponsiveness will persist. The optimal treatment in this circumstance remains to be defined, but the persistence of airway hyper-

Table 1 Proportions of lung cancer cell types by sex and age group (1992–4)

	Men (n = 4823)			*Women (n = 2662)*		
Lung cancer cell type	*<65*	*65–74*	*75+*	*<65*	*65–74*	*75+*
Histologically confirmed small cell	17%	13%	6%	25%	18%	11%
Other histologically confirmed cell types	68%	63%	47%	59%	54%	35%
Clinically diagnosed lung cancer	15%	24%	47%	17%	28%	54%
Ratio of small cell to other confirmed cell types	0.3	0.2	0.1	0.4	0.3	0.3

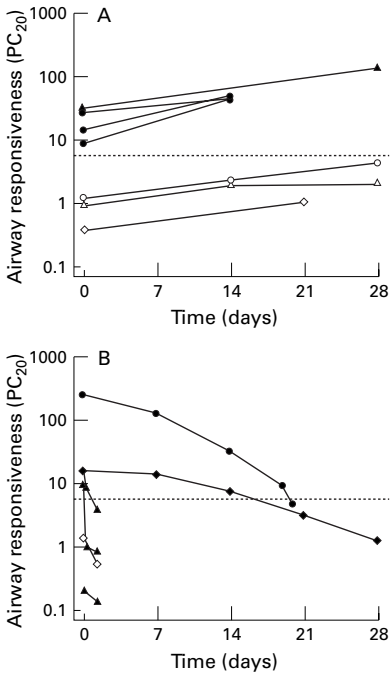

Figure 1 Modulation of airway inflammation is associated with changes in airway responsiveness both within the asthmatic range (below the dotted line) and beyond this into the non-asthmatic range. Closed symbols are individual patient data, open symbols are group mean data. (A) Improvement in airway responsiveness following inhaled corticosteroid therapy in subjects with asthma and chronic cough; (B) deterioration in airway responsiveness following allergen challenge (closed triangles), seasonal allergen exposure (diamonds), or exposure to an occupational sensitiser (closed circles). Reproduced from Gibson[4] with permission.

responsiveness in the absence of airway inflammation may explain the unanticipated benefit from the addition of long acting β_2 agonists to patients who remain symptomatic on inhaled steroids. It will be important to establish the relationship between changes in airway hyperresponsiveness, airway inflammation, and asthma symptoms and to use this information to assist in the rational choice of treatment in asthma.

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1 Brusasco V, Crimi E, Pellegrino R. Airway hyperresponsiveness in asthma: not just a matter of inflammation. *Thorax* 1998;**53**:992–8.
2 Gibson PG, Hargreave FE, Girgis-Gabardo A, *et al*. Chronic cough: eosinophilic bronchitis response to corticosteroid and examination for variable airflow obstruction. *Clin Exp Allergy* 1995;**25**:127–32.
3 Jones PD, Henry RL, Gibson PG, *et al*. Chemotherapy for malignancy induced a remission in asthma symptoms and airway inflammation but not airway hyperresponsiveness. *Pediatr Pulmonol* 1998;**25**:74–7.
4 Gibson PG. Cough in asthma. In: Barnes PJ, Grunstein MJ, Leff AR, *et al*, eds. *Asthma*. Volume 2. Philadelphia: Lippincott-Raven, 1998: 1456.

AUTHORS' REPLY We thank Dr Gibson for his interest in our review article on airway inflammation and airway hyperresponsiveness.[1] As already pointed out,[2] we do not deny a role for airway inflammation in the pathogenesis of airway hyperresponsiveness. As others, we have also found a close relationship between the increase in airway responsiveness and the influx of eosinophils after allergen inhalation.[3] Yet, in cross sectional studies the relationship between airway responsiveness and airway inflammation is very loose. In our view these observations suggest that chronic changes in airway structure and/or inherited factors play a major part in the pathogenesis of airway hyperresponsiveness, although this may increase transiently during episodes of acute airway inflammation. On the other hand, the changes in airway responsiveness induced by allergen inhalation are small compared with the interindividual differences at baseline. Regarding the effects of corticosteroids, we are not fully convinced that they can support a causal relationship between airway hyperresponsiveness and airway inflammation for two reasons. Firstly, the available data are not always consistent. Secondly, the fact that a given treatment affects two different variables is not proof that a direct causal relationship exists between them. In essence, we agree with Dr Gibson's hypothesis that airway inflammation can modulate airway responsiveness, which remains a very complex phenomenon relying on both immunological and non-immunological mechanisms. Any attempt to relate airway hyperresponsiveness to the presence of inflammatory cells and their mediator in the airways therefore seems an oversimplification.

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2 Brusasco V, Crimi E, Gianiorio P, *et al*. Allergen-induced increase of airway responsiveness and inflammation in mild asthma. *J Appl Physiol* 199;**69**:2209–14.
3 Crimi E, Spanevello A, Neri M, *et al*. Dissociation between airway inflammation and airway hyperresponsiveness in allergic asthma. *Am J Respir Crit Care Med* 1998;**157**:4–9.

Corticosteroids and ibuprofen in cystic fibrosis

Excessive lung inflammation is a major factor in the morbidity associated with cystic fibrosis. Despite the lack of evidence of convincing benefit,[1 2] corticosteroids are being increasingly prescribed to children with cystic fibrosis to reduce this inflammation, whilst ibuprofen has also been advocated as a useful anti-inflammatory agent. We wished to ascertain current prescribing practice in the UK, so carried out a postal survey of all specialist cystic fibrosis centres treating children under 18 years of age.

Surveys were returned from all 31 centres that collectively care for around 3500 patients and the results are shown in fig 1. Within centres, regular oral steroids were prescribed to a median (interquartile range, IQR) of 2.5% (0–7%) patients. There was a wide range (0–23%) and in seven centres over 10% of patients were prescribed them. The main indications were allergic bronchopulmonary aspergillosis and asthma/wheezing, although 83% of centres also prescribed them non-

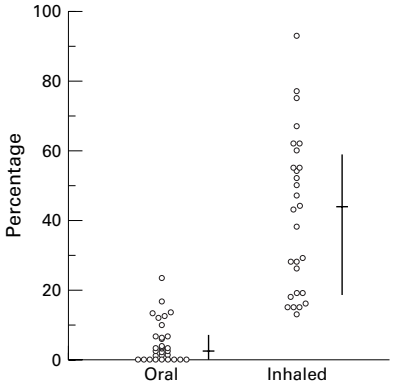

Figure 1 Percentage of patients using oral and inhaled corticosteroids. Each point represents a cystic fibrosis centre. Also shown are median values with interquartile ranges (bars and vertical lines).

specifically for severe lung disease. Inhaled steroids were more commonly prescribed (median 44%, IQR 18–59%) and again there was a marked variation between centres (range 10–93%). Most centres (87%) gave them for troublesome wheezing whilst 65% prescribed them as anti-inflammatory therapy. Only eight centres (26%) reported ever having prescribed ibuprofen for lung disease and in five this had been prescribed to a single patient only. The main reasons given for not using ibuprofen were concerns over safety and practical difficulties with assaying blood levels.

This survey has revealed wide variation in the practice of treating lung inflammation in cystic fibrosis with corticosteroids, whilst ibuprofen is hardly ever used. The figures are similar to those reported by Walters in her survey of adult patients in the UK,[3] and is also consistent with data from the (European) Epidemiologic Registry of Cystic Fibrosis which found that 36% of 3433 patients of all ages in the UK were prescribed inhaled steroids.[4] Further evidence is needed to remove the uncertainty surrounding the use of anti-inflammatory therapy in cystic fibrosis and this needs to be informed by well defined clinical trials.

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1 Cheng K, Ashby D, Smyth R. Oral steroids in cystic fibrosis (Cochrane Review). In: *The Cochrane Library, Issue 3*. Oxford: Update Software, 1998.
2 Balfour-Lynn IM. Inhaled corticosteroids in cystic fibrosis - in favour of their use. *Pediatr Pulmonol* 1998;Suppl 17:169–71.
3 Walters S. *Association of CF Adults (UK) Survey 1994*. CF Trust, 1995.
4 Koch C, McKenzie SG, Kaplowitz H, *et al*. International practice patterns by age and severity of lung disease in cystic fibrosis: data from the Epidemiologic Registry of Cystic Fibrosis (ERCF). *Pediatr Pulmonol* 1997;**24**: 147–54.

Medical students' knowledge of smoking

We read with interest the editorial and review on medical students' attitudes and knowledge of smoking in the January issue of *Thorax*.[1 2] We carried out a survey on a cross section of

NHS staff including regional specialist registrars in respiratory medicine.[3] The aim of this survey was to assess staff smoking habits and knowledge of the harmful and addictive effects of cigarette smoking. Respondents were questioned about their smoking habits, attitudes to smoking, knowledge on the harmful and addictive effects of smoking, and smoking advertising. The response rate was 62%; 68% of respondents were female and 53% were non-smokers, 27% smokers, and 20% ex-smokers. Nurses made up 44% of the current smokers. Eighty eight percent felt that a no-smoking policy should be policed and enforced at work. Knowledge of the harmful and addictive effects of cigarettes was poor. Only 13% of staff thought that all cigarettes were harmful and addictive. Most felt that only extra strong cigarettes were harmful or addictive and up to one quarter of respondents, including some doctors, were unable to answer the question. Of the 13 respiratory registrars only three thought that all cigarettes were harmful and addictive. Although the 13 specialist registrars were able to identify differences between tar and nicotine, only one associated harmful and addictive effects with all types of cigarettes.

Our survey suggests that the smoking habits of a cross section of NHS staff is similar to the general population and that knowledge of the harmful and addictive effects of cigarettes is poor. If our own staff have insufficient knowledge of the harmful and addictive effects of cigarettes and continue to smoke, what hope is there of educating patients to cease or refrain from smoking?

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1 Allen MB. Medical students' knowledge of smoking. *Thorax* 1999;**54**:2.
2 Richmond R. Teaching medical students about tobacco. *Thorax* 1999;**54**:70–8.
3 Bowen EF, Rayner CFJ. NHS staff knowledge and understanding of the harmful and addictive effects of cigarette smoking. *Thorax* 1998; **53**:(Suppl 4):A89.

Aspergillus fumigatus in sputum during acute EBV infection

Murayama *et al*[1] recently suggested that *Aspergillus fumigatus* may possess the ability to inhibit phagocyte function. We report a patient with transient neutropenia in whom *A fumigatus* was present in the sputum. She had a productive cough of two months' duration and presented with seven days of fever, sweats, myalgia, fatigue, and right supraclavicular swelling. There was no significant past history except smoking. Apart from supraclavicular lymphadenopathy the examination was normal. She was leukopenic (2.3×10^9/l) and neutropenic (0.96×10^9/l). The CD4 count was normal (1.44×10^9/l) and levels of C reactive protein (CRP) were 57 mg/l (normal <10). The chest radiograph and abdominal ultrasound were normal and blood and throat cultures were negative. A heavy growth of *A fumigatus* was found in the sputum without evidence of any other infection. HIV testing was negative. Despite a negative monospot test, Epstein-Barr virus (EBV) IgM was detected. Initial EBV IgG and EBNA were negative. The patient remained neutropenic for one week. EBV IgG was detected after two months.

Neutropenia is uncommon but well described during acute EBV infection. It is usually mild and self-limiting though fatalities associated with bacterial sepsis or pneumonia have been reported.[2] *A fumigatus* is an ubiquitous mould.[3] In immunocompetent patients it is an incidental finding. In immunocompromised patients it may cause serious infections, most commonly in acute leukaemia, bone marrow transplantation, and prolonged and intense neutropenia. This patient presented with a glandular fever-like illness, neutropenia, and a heavy sputum growth of *A fumigatus*. This was a confusing finding and HIV seroconversion illness was considered. However, with the rise in neutrophil count after one week *A fumigatus* disappeared from the sputum and the patient recovered. Acute EBV infection was confirmed serologically.

Neutropenia is uncommon in infectious mononucleosis but may occasionally precipitate bacterial co-infection. EBV should therefore be considered in any unexplained neutropenia, and may here have facilitated the colonisation of this patient's respiratory tract with *A fumigatus*.

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1 Murayama T, Amitani R, Ikegami Y, *et al*. Effects of *Aspergillus fumigatus* culture filtrate on antifungal activity of human phagocytes in vitro. *Thorax* 1998;**53**:975–8.
2 Neel EU. Infectious mononucleosis. Death due to agranulocytosis and pneumonia. *JAMA* 1975;**236**:1493–4.
3 Kwon-Chung KJ, Bennett JE. *Medical Mycology*. Philadelphia: Lea and Febiger, 1992.

AUTHOR'S REPLY Drs Schmid and Green present an interesting case and speculate that transient peripheral neutropenia caused by EBV infection may have facilitated the colonisation of this patient's respiratory tract with *Aspergillus fumigatus*.

We would not necessarily agree with their speculation. In our paper[1] we suggested that *A fumigatus* produces a variety of substances, some of which may suppress antifungal (anti-*A fumigatus*) activity of human phagocytes including neutrophils and alveolar macrophages in localised regions around the proliferating *Aspergillus* hyphae. It has been considered that selective protection against *Aspergillus* conidia by mononuclear phagocytes, especially alveolar macrophages, and against *Aspergillus* hyphae by neutrophils are critical host defences. In addition, mucociliary clearance should also play an important part in eradicating the fungi from the airways. It is therefore more likely that impairment of the mucociliary clearance associated with underlying bronchopulmonary disorders such as bronchiectasis, healed tuberculosis, and suppression of macrophage function is more closely related to the colonisation of the respiratory tract with *A fumigatus* than with peripheral neutropenia alone.

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1 Murayama T, Amitani R, Ikegami Y, *et al*. Effects of *Aspergillus fumigatus* culture filtrate on antifungal activity of human phagocytes in vitro. *Thorax* 1998;**53**:975–8.

NOTICES

24th International Conference on Lung Sounds

The 24th International Conference on Lung Sounds will be held in Marburg, Germany on 6–8 October 1999. For further information contact Dr Raymond L H Murphy Jr, Faulkner Hospital, 1153 Centre Street, Boston, MA 02130, USA (telephone +1 617 983 7000 ext 1968; fax +1 617 522 4156; e mail: rmurphy@faulknerhospital.org) or Professor Dr Peter von Wichert, Klinikum der Phillips-Universitat, Med. Poliklinik, 35033 Marburg, Germany (telephone +49 6421 286450; fax +49 6421 288987; e mail: penzel@mailer.uni-marburg.de).

Pharmacology of Asthma

A course on the "Pharmacology of Asthma" organised by Professor Peter Barnes will be held at the Imperial College School of Medicine at the National Heart & Lung Institute in collaboration with the Royal Brompton Hospital on 22–25 November 1999. For further information contact the Postgraduate Education Centre, National Heart & Lung Institute, Imperial College School of Medicine, Dovehouse Street, London SW3 6LY, UK. Tel: 0171 351 8172; fax: 0171 376 3442.

Enhanced Tuberculosis Surveillance

The Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC) is co-ordinating the implementation of an enhanced system for the surveillance of tuberculosis in England and Wales. Enhanced Tuberculosis Surveillance, introduced on 1 January 1999, aims to address deficiencies in routine tuberculosis surveillance by providing timely and more detailed information on the evolving epidemiology of tuberculosis. This system will make further intermittent national surveys, of the type carried out in 1998, unnecessary. The principles underlying the scheme are (a) to collect a minimum essential data set on all cases of tuberculosis; (b) to collect and collate information on tuberculosis cases locally, with regular transmissions to regional and national centres; (c) to link information about cases with their microbiological results (including susceptibility to antituberculosis drugs) and, ultimately, treatment outcome; (d) to safeguard patient confidentiality; and (e) to feed back information on the occurrence of tuberculosis to those providing the data. Information about Enhanced Tuberculosis Surveillance was sent last year to all chest physicians, medical microbiologists, regional epidemiologists, consultants in communicable disease control, and general physicians with an interest in respiratory medicine. The Management Group for Enhanced Tuberculosis Surveillance would like, however, to bring the new system to the attention of all doctors who might diagnose a case of tuberculosis. For more detailed information, please contact Ms Amanda Gatto at CDSC (tel: 0181 200 6868 ext. 4456).