LETTERS TO THE EDITOR

COPD Guidelines

The BTS guidelines on COPD[1] exhort GPs to diagnose COPD early, preferably in the presymtpomatic stage. In effect what is being promoted is "secondary prevention" (screening) through the use of spirometry. In most early cases this would involve two readings at an interval of four to five years. The intended outcome is that the patient stops smoking.

At first sight this appears a sensible proposal (although not one included in the ATS[2] or ERS[3] guidelines). However, the same outcome can be achieved without the screening process, so before GPs adopt this recommendation wholesale it is worth noting that there is no direct evidence to support screening.

Literature abounds on the costs of persuading smokers to stop smoking. If by screening for COPD one could achieve a lower cost per quitter amongst susceptible smokers, then an argument could be made on cost effective grounds. But as simple advice from a GP is one of the most cost effective interventions in health care, this is unlikely.[4]

One is therefore left to consider the incremental stop rate achieved by superimposing screening and advice on a programme of advice alone. Most smokers are already aware of the risk of lung cancer and ischaemic heart disease. It is not known what difference the distant threat of COPD makes to smoker quit rates.

If the costs of screening are distributed solely to the increment of true positives who stop with the enhanced programme one arrives at a true marginal cost of this preventative measure. The costs to be considered should include the direct health service costs of equipment and training, and the opportunity cost to society of the time spent by GPs and nurses.

Screening is intended to improve well being (the ethic of "maximising public welfare"), yet there is the paradox of identifying disease (and therefore reducing perceived well being) in pre-symptomatic individuals when the majority derive no benefit. Intangible costs become relevant as do indirect costs (with well people often having to miss work for screening). Intangibles include the anxiety created by screening and the even greater anxiety in the true positives who then fail to stop smoking. One also has to decide what to tell the true negatives (those shown not to be at risk of COPD).

A broader cost-utility analysis would permit comparisons with the benefits of other screening interventions in primary care. Cervical cytology, mammography, and newer technologies such as colorectal cancer screening compete for development monies.

Lieberman offers a model for measuring cost effectiveness of colorectal cancer screening programmes.[5] The sensitivity analyses considered are patient compliance, varying costs of procedures, frequency of surveillance, costs of downstream care, cancer detection rate, and cancer prevention rate. The parallels for COPD screening might include patient response rate to invitation, varying costs of equipment and staff time, frequency of surveillance, costs of treating diagnosed COPD, COPD detection rate, and smoker quit rates. A full analysis might also consider the discount rate for costs and benefits over time. In a programme that detects disease 10 years before it becomes symptomatic, an accepted discount rate of 6% per annum compounds considerably.

Spirometry is invaluable in the diagnosis and management of COPD. GPs should welcome the guidelines but must consider the opportunity costs to their activities before embarking on screening pre-symptomatic patients.

MATTHEW PERRY
Albrighton Medical Practice, Shaw Lane, Albrighton, Nr Wolverhampton WV7 3DT, UK

1 British Thoracic Society. BTS guidelines for the management of chronic obstructive airways disease. *Thorax* 1997;**52**(Suppl 5):S1–28.
2 American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995;**152**:s77–120.
3 Siafakas N, Vermiere P, *et al*. Optimal assessment and management of chronic obstructive pulmonary disease (COPD): European Respiratory Society Consensus Statement. *Eur Respir J* 1995;**8**:1398–420.
4 Buck D, Godfrey C. Helping smokers give up—guidance for purchasers on cost-effectiveness. London: Health Education Authority, 1994.
5 Lieberman D. Cost effectiveness model for colon cancer screening. *Gastroenterology* 1995; **109**:1781–90.

AUTHORS' REPLY With regard to the points raised by Dr Perry we would comment that there may be little direct evidence about screening for early COPD, but the indirect evidence was sufficient to persuade the guidelines committee. The natural history of COPD, elegantly described by Fletcher and Peto,[1] is that a proportion of cigarette smokers (15–20%) have an annual loss of FEV_1 that is larger than for non-smokers. Initially such losses, while measurable in large group studies, are too small to be detected in the individual. After 20–40 years the cumulative excess loss of FEV_1 is large enough for an individual's FEV_1 to be below the lower limit of the predicted normal value and thus be detectable. Thereafter, with continuing smoking, the subject will progress from mild impairment through moderate to severe impairment. The only proven treatment that slows this inevitable decline in function is stopping smoking.[1 2]

Most patients only present to the health service with moderate to severe disease at a stage when jobs are threatened or lost, and lifestyle limited. Since the damage is irreparable, it is logical to consider prevention at an earlier stage and preferably before symptoms develop.

Dr Perry is correct to point out that cost effectiveness studies should consider the wider picture, but it is important not to extrapolate from studies based on different principles. Simple advice from a GP is effective in a very small proportion of subjects (2–5%) and is cost effective only because it is so cheap. The health benefit of adding nicotine patches and nurse counsellor advice,[3] which increases the quit rate significantly (21%), are both clear and desirable, but the extra treatment costs have left doubt about the cost effectiveness of such additional work. However, studies in unselected smokers will include those not susceptible to COPD, cardiac disease, or lung cancer (perhaps half of all smokers).[4] The extra costs of treating all smokers (30% of the population) when only some can benefit makes the cost effectiveness equation less favourable. It also presupposes that non-symptomatic patients will agree to come and see their GP. Targeting smokers in their 50s with a reduced FEV_1 (who amount to less than 1% of the population) would result in a very different calculation. Now only 15% of smokers in a defined age range are being targeted for non-smoking advice/support which reduces the cost implication of the more effective treatment and, moreover, the health benefit is greater because every person who gives up smoking is being prevented from developing symptomatic COPD, with its costs to both the individual and the health service. A formal study should be done to confirm such estimates, but progress cannot always wait for absolute confirmation, particularly when the health benefits to this defined subgroup are so clear cut.

Dr Perry is concerned at the adverse effects of screening when many will derive no benefit. Those with a normal FEV_1 should still be advised to quit on the grounds of the risk from heart disease and lung cancer, but on cost effectiveness grounds they may not qualify for more intensive help. Their anxiety levels are unlikely to be raised by this any more than by the frequent publicity about smoking in the media.

Spirometry is not an expensive procedure, costing less than a chest radiograph and probably less than a fasting lipid measurement. Radiographs are of limited value in COPD yet are often requested, whereas measurement of the FEV_1 informs diagnosis, treatment and prognosis and has been grossly underused in both hospital and general practice. Finally, it should be pointed out that a recent paper in the *BMJ* describing the prospective Renfrewshire population[5] showed that FEV_1 was a stronger predictor of premature death than serum cholesterol measurements and as strong a predictor as cholesterol when only heart disease was considered. It concluded with the recommendation that anti-smoking activity be targeted on those with a low FEV_1.

M G PEARSON
P M A CALVERLEY
COPD Guidelines Committee

1 Fletcher CM, Peto R, Tinker C, *et al*. *The natural history of chronic bronchitis and emphysema.* Oxford: Oxford University Press, 1976.
2 Anthonisen NR, Connett JE, Kiley JP, *et al*. The Lung Health study: effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV_1. *JAMA* 1994;**272**:1497–505.
3 Campbell IA, Prescott RJ, Tjeder-Burton SM. Transdermal nicotine plus support in patients attending hospital with smoking related diseases: a placebo controlled study. *Respir Med* 1996;**90**:47–51.
4 Doll R, Peto R, Wheatley K, *et al*. Mortality in relation to smoking: 40 years observation on male British doctors. *BMJ* 1994;**309**:901–10.
5 Hole DJ, Watt GCM, Davey Smith G, *et al*. Impaired lung function and mortality in men and women: findings from the Renfrew and Paisley prospective population study. *BMJ* 1996;**313**:711–5.

COPD Guidelines

The British Thoracic Society is to be congratulated on the new COPD guidelines[1] which are clear and will prove a major boon to patients and their carers in primary care.

Spirometry lies at the heart of these guidelines, perhaps most importantly in screening for asymptomatic cases amongst smokers. After all, there is no cure. In our practice we perform such screening on smokers over 40 years old. To be effective, screening must be largely opportunistic. We own both a simple vane spirometer costing around £300 which states only FEV_1 and FVC values, and a more accurate device costing £1400. This produces a full range of results, interpretation, and quality checks. The guidelines state that a volume/time plot is mandatory, thus condemning cheaper varieties.

Both of these devices have their place. The cheap one is ideal for screening by general practitioners and respiratory nurses; it is quick and simple to use. The recommended expensive variety is wholly unsuitable for this purpose as it takes at least 10 minutes to set up and calibrate let alone print out the result. We use it only to check those with abnormal results on screening, as well as in "asthma/COPD" clinics where it is set up and used repeatedly.

It is unrealistic to expect most practices to purchase two types of spirometer and our experience would suggest that the cheap spirometers are preferable for routine primary care use with abnormal results being checked by an open access spirometry service. Furthermore, such a service is no substitute for performing spirometric measurements in house. If cheap vane spirometers are condemned, opportunities for preventing this devastating disorder will be lost.

RUPERT JONES
Roborough Surgery,
1 Eastcote Close,
Plymouth PL6 6PH, UK

1 British Thoracic Society. BTS guidelines for the management of chronic obstructive airways disease. *Thorax* 1997;**52**(Suppl 5):S1–28.

Travel by air for patients with COPD

Publication of the long awaited BTS guidelines on the management of COPD has been welcomed by all concerned and will go a long way towards providing a practical guidance on management of patients with COPD.

However, I would like to comment on the section on travel (page S14).This informs us that aircraft are pressurised to the equivalent of 900–2400 metres above sea level and that a Pao_2 of less than 6.7 kPa should be considered as a relative contraindication to air travel.

A Pao_2 of 6.7 kPa at sea level will equate to a Pao_2 of 4.6 kPa at an altitude of 2400 metres using Gong's nomogram, and this is unacceptably low.

I wonder if you would agree with me that the recommendation should specify that a predicted Pao_2 for the given altitude (and not at sea level) of less than 6.7 kPa should be considered as a contraindication to travel by air. Using Gong's nomogram a Pao_2 of 6.7 kPa at an altitude of 2400 metres is equal to a Pao_2 of 9.3 kPa at sea level. Therefore, a Pao_2 of less than 9.3 kPa, not less than 6.7 kPa, measured at sea level should be regarded as a contraindication to air travel unless supplemental in-flight oxygen is provided.

In practice, if the Pao_2 at sea level is less than 9.3 kPa, the flow rate of oxygen that would increase the Pao_2 to 9.3 kPa or above should be determined and recommended for administration during flight.

R K SINHA
Neath General Hospital,
Pant-yr-Heol,
Neath SA11 2LQ, UK

AUTHORS' REPLY The problem of knowing whether it is safe for an individual to travel by air is difficult. Breathing air with a reduced oxygen content should produce an additional degree of hypoxia, which might be expected to carry a risk of either cardiac or respiratory difficulty. However, there are few reports of patients with COPD encountering specific difficulties other than the well documented (but still uncommon) risk of pneumothorax. The prediction nomogram described by Gong was derived from experiments in a laboratory on the ground inhaling 15.1% oxygen and may not compare with actuality under hypobaric conditions. Although the American guidelines[1] do recommend preflight assessments, they specifically do not recommend the Gong nomogram and avoid stating any specific levels of hypoxia as of concern. With marked hypoxia (6.7 kPa) there must be concern that supplemental oxygen is likely to be of benefit, hence the recommendation—albeit one for which there is no strong evidence. With mild hypoxia there is suspicion but no evidence. This is an area where further research would be helpful to clarify the benefits and risks of travel with and without supplementary oxygen.

Many patients with COPD can and do travel apparently safely by air. Until there are more substantive data to the contrary, we must be careful not to place any additional constraints on COPD patients over and above those already present due to their limited exercise tolerance.

M G PEARSON
P M A CALVERLEY
COPD Guidelines Committee

1 American Thoracic Society. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1995;**152**:S77–120.

Guidelines on pulmonary embolism

The new guidelines for the practical approach to management of pulmonary embolism (PE) are clearly welcome to help all clinicians dealing with such patients.[1] I would, however, like to take issue with the statement advising the administration of hydrocortisone in conjunction with streptokinase to reduce the risk of allergic complications.

Allergic reactions are a well recognised adverse effect of intravenous streptokinase treatment and are probably due to immediate hypersensitivity reactions mediated by IgE antibodies to streptokinase.[2] The incidence of allergic reactions is low (1.7–18%)[2] and was only seen in 3.6% of patients entered into the Third International Study of Infarct Survival (ISIS-3) trial.[3] Indeed, only 0.3% of patients in ISIS-3 had allergic reactions causing "persistent symptoms".[3]

Patients at risk of allergic and anaphylactic reactions can be identified rapidly by intradermal streptokinase skin testing, which correlates with elevated levels of IgE to streptokinase.[2] This test will give results in approximately 15 minutes but is not widely utilised. At risk patients include those who have received prior streptokinase treatment, including those who have had previous intradermal streptokinase skin tests. The intradermal skin test will not, however, detect patients with IgG antibodies to streptokinase who are at risk of delayed reactions and may not have effective thrombolysis due to IgG neutralising antibodies.

Antihistamines and hydrocortisone may help to reduce the effects of immediate hypersensitivity reactions, but steroids are not routinely administered in the major cardiovascular thrombolytic trials or in most UK coronary care units. As patients with pulmonary embolism are at no greater risk for allergic reactions to streptokinase, there does not seem to be good evidence for the statement in the guidelines. It may be more appropriate to consider alternative thrombolysis if there is genuine concern regarding allergic reactions in individual patients.

CHRISTOPHER W H DAVIES
Osler Chest Unit,
Churchill Hospital,
Oxford Radcliffe Hospitals,
Headington, Oxford OX3 7LJ, UK

1 British Thoracic Society, Standards of Care Committee. Suspected acute pulmonary embolism: a practical approach. *Thorax* 1997;**52**(Suppl 3):S3.
2 Dykewicz MS, McGrath KG, Davison R, *et al.* Identification of patients at risk for anaphylaxis due to streptokinase. *Arch Intern Med* 1986; **146**:305–7.
3 ISIS-3 (Third International Study of Infarct Survival) Collaborative Group. ISIS-3: a randomised comparison of streptokinase vs tissue plasminogen activator vs anistreplase and of aspirin plus heparin vs aspirin alone among 41,299 cases of suspected acute myocardial infarction. *Lancet* 1992;**339**:753–70.

AUTHORS' REPLY Although indeed unusual, an allergic reaction to streptokinase in a patient with massive pulmonary embolism who, by definition, is already critically ill and hypotensive (unlike most myocardial infarction patients) could be disastrous, which is our reason for advocating the routine addition of hydrocortisone. This is not a problem with other thrombolytics; some hospitals, including mine, have already agreed that this advantage of alteplase in massive pulmonary embolism justifies its much greater cost. Our third suggestion, urokinase, is both safe and cheap, but although many pharmacies stock it for unblocking central venous catheters, few have the much higher dose formulation required for acute pulmonary embolism.

ANDREW MILLER
Chest Clinic,
Mayday Hospital,
Croydon, Surrey, UK

Malignant neoplasms in pulmonary sarcoidosis

As its authors intended—by limiting their analysis of the association to instances in which recognition of malignancy succeeded a diagnosis of sarcoidosis by more than one year—the study by Seersholm *et al*[1] rigorously tested the hypothesis proposed by

|Brincker and Wilbek[2] that persons with respiratory sarcoidosis are predisposed to develop malignancies. Several authors have hypothesised the reverse, that malignancies give rise to sarcoidosis. For example, Suen *et al*[3] reported six patients (four with lymphomas) in whom sarcoidosis followed chemotherapy with a median interval of nine months, and Pandha *et al*[4] found 48 cases reported in the literature in which sarcoidosis presented concomitantly or following a diagnosis of testicular cancer.

The subject is of considerable conceptual interest. Several authorities have suggested that the production of systemic non-caseating granuloma might reflect a peculiar reactivity of the host to a variety of causative agents. Epidemiological corroboration of the observation that patients with malignancies are prone to develop sarcoidosis would suggest aetiological heterogeneity. One hopes that the authors, who have at their disposal a large database, will test this hypothesis.

JEROME M REICH
Kaiser Foundation Hospitals, Center for Health Research, 3800 N Kaiser Center Drive, Portland, Oregon 97227-1098, USA

1 Seersholm N, Vestbo J, Viskum K. Risk of malignant neoplasms in patients with pulmonary sarcoidosis. *Thorax* 1997;**52**:892–4.
2 Brincker H, Wilbek E. The incidence of malignant tumours in patients with respiratory sarcoidosis. *Br J Cancer* 1974;**29**:247–51.
3 Suen JS, Forse MS, Hyland RH, *et al*. The malignancy-sarcoidosis syndrome. *Chest* 1990; **98**:1300–2.
4 Pandha HS, Griffiths H, Waxman J. Sarcoidosis and cancer (editorial). *Clin Oncol* 1995;**7**:277–8.

AUTHORS' REPLY Dr Reich raises an interesting hypothesis that previous malignancy and, in particular, treatment with chemotherapy may cause sarcoidosis. In our study, however, we found no cases of malignancy prior to the diagnosis of sarcoidosis, which would have been the case if the hypothesis is correct. A larger study of the risk of sarcoidosis following chemotherapy may reveal an association but requires national sets of sarcoidosis rates in order to calculate the expected number of cases. Unfortunately a national registry of the incidence of sarcoidosis is not available.

N SEERSHOLM
J VESTBO
K VISKUM
Munkely 12, DK-2860 Soborg, Denmark

BOOK REVIEW

Lung Biology in Health and Disease Series, Volume 109. Treatment of the Hospitalized Cystic Fibrosis Patient. David M Orenstein, Robert C Stern. (Pp 448; $165.00). New York: Marcel Dekker Inc, 1997. 0 8247 9500 8.

As the title suggests, this volume covers the care of inpatients with cystic fibrosis, but it is not restricted to this alone. It provides a clear account of the management of all aspects of cystic fibrosis, from initial diagnosis to terminal care, with the emphasis on the practical approach. The book consists of a collection of chapters by different cystic fibrosis physicians, mostly paediatric. All the common complications of cystic fibrosis are discussed in depth and from the perspective of each author. Optimal treatment regimens are suggested in the text, supported by objective data where possible. Some of the topics overlap, such as the management of pneumothorax which is discussed by several authors including cystic fibrosis physicians and a thoracic surgeon. The text is therefore more a source of reference to be dipped into than to be read from cover to cover. The book is aimed at physicians caring for patients with cystic fibrosis and does have a paediatric slant. Certain sections would also be of interest to nurses, dieticians, pharmacists, social workers, and other health care professionals working with patients with cystic fibrosis.

The volume is almost pocket sized and contains many handy investigation and management tables to aid the busy physician. Highlights include an excellent section on pharmacokinetics which clearly explains the principles of treatment in cystic fibrosis and attempts to tease out evidence-based medicine from cystic fibrosis folklore in dosing and drug monitoring. The chapter on cystic fibrosis related diabetes mellitus (CFRDM) is also very good, explaining how the management of CFRDM contrasts with classical treatments for diabetes mellitus.

The book is American in style and content, most evident in the transplant chapter where current practice differs from that in the UK. The volume also includes a chapter presenting a personal view of one physician to the hospitalised patient with cystic fibrosis which seems out of keeping with the rest of the text. At $165.00 the book is more expensive than its contemporaries, but it does cover a wider range of topics in greater depth. It also includes numerous relevant illustrations. Overall, this short text is an excellent source of reference and will benefit all health professionals who care for patients with cystic fibrosis.—HCR

NOTICES

MICRO 98

MICRO 98, the International Microscopy Conference and Exhibition organised by the Royal Microscopical Society, will be held on 7–9 July 1998 at the Novotel, Hammersmith, London. For further details please contact Allison Winton, RMS, 37/38 St Clements, Oxford OX4 1AJ, UK. Telephone: +44 (0)1865 248768; Fax: (0)1865 791237; email info@rms.org.uk; web page http://www.rms.org.uk

INTERASMA 98

A joint meeting of Interasma 98 and the VIth Congress of the Moroccan Society of Allergology and Clinical Immunology will take place in Marrakech on 8–11 October 1998. Further information can be obtained from Professor M Bartal, SMAIC, B.P. 1754, Derb Ghallef, Casablanca, Morocco. Fax (212 2) 222355/296850.

Pharmacology of Asthma

A course on the pharmacology of asthma will be held at the Imperial College School of Medicine at the National Heart & Lung Institute in collaboration with the Royal Brompton Hospital on 23–26 November 1998. For further information please contact the Postgraduate Education Centre, National Heart & Lung Institute, Dovehouse Street, London SW3 6LY, UK. Tel: 0171 351 8172. Fax: 0171 376 3442.