LETTERS TO THE EDITOR

Asthma care

Neville and Higgins in their review of the provision of asthma care in a recent issue of *Thorax*[1] refer to a meeting at the Royal College of Physicians in London at which agreement on the form of three key questions about patients' asthma symptoms was reached. The form of the questions was wrongly quoted in their paper and the correct form is:

"In the last week/month:

(1) Have you had difficulty sleeping because of your asthma symptoms (including cough)?

(2) Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)?

(3) Has your asthma interfered with your usual activities (e.g. housework, work/school)?"

There is a trade off to be made between the better recall of events over the past week and the greater generalisability of events over the past month. The feeling of the meeting was that there was insufficient evidence upon which to base a decision about the best timescale and further evaluation of this issue is needed. It was agreed that these questions should be answerable by simple yes/no responses, with the possibility of scaled responses where these were positive. The full proceedings have now been published by the Royal College of Physicians.[2]

We hope that these questions will become a common currency for recording the outcome for patients with asthma in both primary and secondary care and would encourage their use in order that comparable data may be available in the future. Ways of incorporating the questions into general practice software are currently being explored.

M G PEARSON
Aintree Chest Centre, Fazakerly Hospital Liverpool L9 7AL, UK

C E BUCKNALL
Department of Respiratory Medicine, Gartnavel General Hospital, Glasgow G12 0XL, UK

1 Neville RG, Higgins BG. Providing better asthma care: what is there left to do? *Thorax* 1999;**54**:813–7.
2 Pearson MG, Bucknall CE, eds. *Measuring clinical outcome in asthma: a patient focused approach*. London: Royal College of Physicians, 1999.

AUTHORS' REPLY Drs Pearson and Bucknall are right to draw attention to the final version of the three key questions. In preparation of our article we had a copy of a draft report to work with, but not the final version. We thank Drs Pearson and Bucknall for correcting this and endorse their view that we need to encourage use of these questions.

R G NEVILLE
B G HIGGINS
Asthma Research Unit, Tayside Centre for General Practice, University of Dundee, Dundee DD2 4AD, UK

Ultrasound placement of peripherally inserted central catheters (PICCs) in adults with cystic fibrosis

Chronic *Pseudomonas aeruginosa* infection occurs in more than 85% of adults with cystic fibrosis. Recurrent courses of intravenous antibiotics are required to treat pulmonary exacerbations and the establishment of reliable intravenous access is necessary. Administration of multiple courses of antibiotics may require the insertion of long line or central venous catheters. Totally implanted venous devices are reserved for patients where alternative access is not feasible.[1] Peripherally inserted central catheters (PICCs) are increasingly used for the administration of antibiotics and chemotherapy. Ultrasound has been reported to assist the successful insertion of PICC lines.[2] We report our experience with the use of ultrasound to assist the placement of PICC lines where access has been difficult, using a standard technique via the antecubital fossa.

During the past 23 months a total of 124 PICC lines have been inserted in patients with cystic fibrosis (clinic population 110). In a subgroup of patients 22 placements of the PICC have been guided by ultrasound. The criteria for the use of ultrasound include inability to access the vein via the antecubital fossa by an experienced anaesthetist or ICU consultant; inability to advance the catheter due to venous obstruction; and no other viable venous access. The procedure was performed by an interventional radiologist and ultrasonographer with the catheter inserted in the basilic or brachial vein in the upper arm. Ultrasound was used to select which vein to access and was determined by vein position (not lying superficial or adjacent to artery), calibre (>2 mm diameter), and tortuosity (straight). The position of the catheter was confirmed by fluoroscopy.

We retrospectively reviewed PICC insertion utilising ultrasound. In all patients the PICC line was inserted successfully. The mean catheter dwell time was 17 days (range 9–51, median 14). No catheter sepsis, obstruction, or breakage have been documented and one localised thrombus within the axillary vein was detected 12 days after insertion (symptoms resolved completely on PICC removal). Venous access may be difficult in patients with cystic fibrosis who require regular antibiotic therapy. Infection, occlusion, or erosion through the skin may complicate totally implanted venous devices. Ultrasound guided placement of a PICC may be used as a bridge to the insertion of a totally implanted venous access device, but does require the expertise of an interventional radiologist and ultrasonographer.

JULIE BUNTING
Adult Cystic Fibrosis Unit

RICHARD E SLAUGHTER
Department of Medical Imaging

PHILIP J MASEL
Adult Cystic Fibrosis Unit

WAYNE J KROLL
Department of Medical Imaging

SCOTT C BELL
Adult Cystic Fibrosis Unit, The Prince Charles Hospital, Chermside, Queensland 4032, Australia

1 Rodgers HC, Liddle K, Nixon SJ, *et al*. Totally implantable venous devices in cystic fibrosis: complications and patients' opinions. *Eur Respir J* 1998;**12**:217–20.
2 Parkinson R, Gandhi M, Harper J, *et al*. Establishing an ultrasound guided peripherally inserted central catheter (PICC) insertion service. *Clin Radiol* 1998;**53**:33–6.

Screening for polymorphisms in exon 5 of the glutathione S-transferase Pl gene

A recent paper by Ishii *et al*[1] suggested an association between glutathione S-transferase P1 (GSTP1) polymorphism in exon 5 (Ile105Val) and the development of chronic obstructive pulmonary disease (COPD) in a sample from a Japanese population. The authors reported that GSTP1 homozygous wild type Ile105 polymorphism was found more frequently in patients with COPD than in controls (79% vs 52%).

In an ongoing COPD genetic study (unpublished preliminary results) we determined the prevalence of GSTP1 polymorphisms in exon 5 in 200 healthy Caucasian volunteers from the Barcelona area. Genetic variants were detected using polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP). The amplification products were digested with the restriction enzyme *BsmaI* at 55°C, subjected to electrophoresis, and visualised by ethidium bromide staining. Of the 200 healthy volunteers, 99 (49.5%) were homozygous wild type Ile105 (additionally, 88 (44%) were heterozygote Ile105Val and 13 (6.5%) were homozygous Val105). This percentage was similar to that observed by Ishii *et al* in Japan and Harries *et al* in a Caucasian population in the UK,[2] but differed from that observed by Morita *et al* in Japan[3] and Lieshoust *et al* in a Caucasian population in the Netherlands.[4]

We now report the successful application of PCR and single strand conformation polymorphism (SSCP) to the rapid detection of Ile105Val genotypes. DNA was isolated from EDTA blood samples using the QIAamp Kit (Qiagen Ltd, Crawley, UK). Gene specific primers to amplify a 190 bp fragment (5'-CTCTATGGGAAGGACCAGCA-3' and 5'-AGCCACCTGAGGGGTAAG-3') were designed from the GSTP1 sequence (Genebank U12472). The PCR reaction was performed as previously described.[5] The SSCP procedure and silver staining were carried out according to the manufacturer's instructions (Pharmacia Biotech. Sweden) with the following modifications: samples were denatured at 95°C for 15 minutes and electrophoresis was done at 15°C for two hours.

Using serum samples from 100 healthy volunteers, we compared in a blind experiment the results obtained by this method with those obtained by PCR-RFLP analysis. In all cases identical genotypes were obtained. Moreover, GSTP1 polymorphisms were confirmed by direct sequencing analysis of individuals predicted to be Ile105, Ile105Val, and Val105 from the assay results using a previously reported PCR sequencing method.[5] Figure 1 shows the results obtained with PCR-SSCP and PCR-RFLP.

Studies on large series are required to investigate further the pronounced interethnic differences in allelic frequencies in exon 5 of the GSP1 gene in normal populations. The simple PCR-SSCP method we propose, with comparable sensitivity and specificity to that obtained with the PCR-RFLP method, could be useful for GSTP1 genetic screening. PCR-SSCP is a

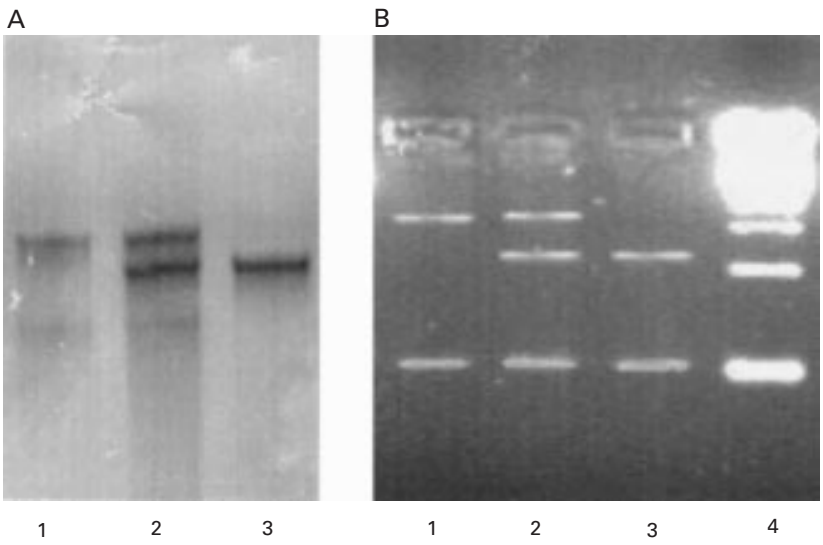

Figure 1 (A) PCR-SSCP based genotyping for GSTP1 polymorphism: (1) homozygous wild type Ile105, (2) heterozygous Ile105Val, and (3) homozygous Val105. (B) PCR-RFLP based genotyping corresponding to a patient (1) wild type, (2) heterozygous, and (3) homozygous for the Ile105Val mutation. Lane 4: 100 bp ladder molecular weight marker.

single step method that does not require digestion of PCR products with restriction enzymes, thus avoiding the inaccuracy resulting from incomplete digestion that can occur with PCR-RFLP. Moreover, PCR-SSCP is less expensive and time consuming than PCR-RFLP.

FRANCISCO RODRIGUEZ-FRIAS
CARLOS GONZALEZ
XOSE COSTA
FRANCISCO CAMPOS
MONTSE COTRINA
Department of Biochemistry

ROSENDO JARDI
MARC MIRAVITLLES
RAFAEL VIDAL
Department of Pneumology, Hospital Universitario Vall d'Hebron, Barcelona 08035, Spain

Correspondence to: Dr R Jardi
email: riardi@hg.vhebron.es

1 Ishii T, Matsuse T, Teramoto S, *et al*. Glutathione S-transferase P1 (GSTP1) polymorphism in patients with chronic obstructive pulmonary disease. *Thorax* 1999;**54**:693–6.
2 Harries LW, Stubbins MJ, Forman D, *et al*. Identification of genetic polymorphisms at the glutathione S-transferase P1 locus and association with susceptibility to bladder, testicular and prostate cancer. *Carcinogenesis* 1997;**18**:641–4.
3 Morita S, Yano M, Tsujinaka T, *et al*. Association between genetic polymorphisms of glutathione S-transferase P1 and N-acetyltransferase 2 and susceptibility to squamous-cell carcinoma of esophagus. *Int J Cancer* 1998;**79**:517–20.
4 Lieshoust EM, Roelofs HM, Dekker S, *et al*. Polymorphic expression of the glutathione S-transferase P1 gene and its susceptibility to Barrett's esophagus and esophageal carcinoma. *Cancer Res* 1999;**59**:586–9.
5 Jardi R, Rodriguez-Frias F, Miravitlles M, *et al*. Identification and molecular characterization of the new alpha-1-antitrypsin deficient allele P1 Ybarcelona (Asp256-Val and Pro391-His). *Hum Mutation* 1998;**174** (online).

AUTHORS' REPLY The data presented by Rodriguez-Frias *et al* confirm the polymorphism in exon 5 of the glutathione S-transferase P1 (GSTP1) gene in healthy volunteers. Because this polymorphism varies in Asians and Caucasians, the current study is helpful in determining the prevalence of GSTP1 polymorphism in healthy subjects. In addition, the results suggest that the prevalence of GSPT1 polymorphism in healthy volunteers does not differ significantly between Caucasians and non-Caucasians. This is an important observation for understanding the pathogenesis of chronic obstructive pulmonary disease (COPD) in relation to cigarette smoking, irrespective of race.

We agree that PCR-SSCP is a better method for determining GSTP1 polymorphism than PCR-RFLP, since an ideal screening test should be simple, inexpensive, time saving, and have a high sensitivity with reasonable specificity. This screening test should be used in patients with marginal airflow limitation who have not yet developed COPD, and would be particularly effective for detecting patients with a predisposition to COPD. Because only 20% of heavy smokers develop COPD, the genetic susceptibility of lungs to cigarette smoke may be determined. Our study and the work by Rodriguez-Frias and coworkers further contribute to an understanding of the genetic background of COPD in both Asians and Caucasians.

TAKEO ISHII
SHINJI TERAMOTO
Department of Geriatric Medicine, Tokyo University Hospital, 7-3-1 Hongo Bunkyo-ku, 113-8655 Tokyo, Japan

TAKESHI MATSUSE
Department of Respiratory Medicine, Yokohama City University, School of Medicine, Urafune General Medical Center, 3-46 Urafune-cho, Minami-ku, Yokohama City, 232-0024 Yokohama, Japan

Correspondence to: Dr T Matsuse
email: matsuse@vrahp.yokohama-cu.ac.jp

BOOK REVIEW

Lung Function Tests: Physiological Principles and Clinical Applications J M B Hughes, N B Pride, eds. (Pp 314; £25.00). London: Harcourt Brace, 1999. ISBN 0 7020 2350 7.

This book is a theoretical and practical overview of pulmonary function testing. As such it caters both for clinicians and technicians involved in the gathering of data and its interpretation.

Having evolved from the well renowned Hammersmith Hospital course on Clinical Applications of Pulmonary Function, this volume draws on the experience and expertise of its many contributors. They have successfully developed a textbook that takes its readers from the physiological basis of all aspects of pulmonary function testing, through the mechanical limitations of measurement techniques, aspects of evaluation of breathlessness and breathing control, to the often neglected areas of interpretation and presentation of results. All this is produced in a format made relevant to clinical practice.

The authors adeptly express complex dynamic principles in word form and have supplemented this text with considered, well constructed graphs, tables and illustrative diagrams which underline and clarify the points made. There are frequent highlighted "bullet point" text boxes and succinct chapter conclusions to allow the reader access to clear summaries of the issues discussed in each section.

A section including chapters devoted to the less routine aspects of lung function testing including sleep disordered breathing, paediatric pulmonary function, pulmonary function testing in the intensive care unit, and domiciliary oxygenation and assisted ventilation demonstrates the potential and scope that this field has to offer.

Being accessible and cleverly composed, the text has the potential to be used as a "reference manual" but its editors have steered the emphasis towards promotion of a comprehensive understanding of the theory behind commonly used pulmonary function tests which is where its great strength lies. This should allow readers to develop a pragmatic, efficient approach to the appropriate use of the tests discussed, together with a realistic and clinically applicable basis for the interpretation of their results.

This book comes thoroughly recommended to technicians and respiratory physicians alike, and goes a long way towards revitalising an important area of respiratory medicine which is unfortunately in danger of being overlooked as our attention is taken by newer scientific advances.—ILJ

NOTICE

Therapeutic Applications of Leukocyte Filtration

A one-day workshop on Therapeutic Applications of Leukocyte Filtration organised by Professor Ken Taylor and Dr Terry Gourlay will be held at the Hammersmith Hospital, Imperial College, London on 7 July 2000. For further details and registration forms contact Jean Bryant, Manager, Wolfson Conference Centre, Imperial College of Science Technology and Medicine, Hammersmith Hospital, Du Cane Road, London W12 0NN, UK. Telephone: 44 (0) 208 383 3117. Fax: 44 (0) 208 383 2428. Email: wcc@rpms.ac.uk