**LETTERS TO THE EDITOR**

**Asthma care**

Neville and Higgins in their review of the provision of asthma care in a recent issue of *Thorax* 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 if they 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.

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**AUTHORS’ REPLY**

Drs Pearson and Bucknall are currently being explored. The questions into general practice software available in the future. Ways of incorporating secondary care and would encourage their use for patients with asthma in both primary and secondary care.

**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 placement 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 (clinical 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 cephalic 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.

**Screening for polymorphisms in exon 5 of the glutathione S-transferase P1 gene**

A recent paper by Ishii et al1 suggested an association between glutathione S-transferase P1 (GSTP1) polymorphism in exon 5 (Ile105Val) and the development of 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 polymorphism in exon 5 in 157 healthy 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 *BsmI* 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, 88 (44%) were heterozygous Ile105Val and 13 (6.5%) were homozygous Val105. This percentage was similar to that observed by Ishii et al in Japan and Harris et al in a Caucasian population in the UK, but differed from a study by Moir et al2 in a Caucasian population in the Netherlands.

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′-CCCTATGGGAAGACATTAGCCACCTGAGGTTAAG-3′) were designed from the GSTP1 sequence (Genebank U12472). The PCR reaction was performed as previously described.3 The SSCP procedure and silver staining were performed 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.4 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 GSTP1 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

**References**


3 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
single step method that does not require diges-
tion of PCR products with restriction enzymes,
thus avoiding the inaccuracies resulting from
incomplete digestion that can occur with PCR-
RFLP. Moreover, PCR-SSCP is less expensive
incomplete digestion that can occur with PCR-
tion of PCR products with restriction enzymes,
single step method that does not require diges-
tion, reasonable specificity. This screening test
should be used in patients with marginal air-
flow 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 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 air-
flow 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 smoking 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.

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This book is a theoretical and practical over-
vie 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 vol-
ume 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 tech-
niques, 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 dy-
amic principles in word form and have supple-
mented this text with considered, well
constructed graphs, tables and illustrative dia-
grams which underline and clarify the points
made. There are frequent highlighted “bullet
point” text boxes and succinct chapter conclu-
sions to allow the reader access to clear sum-
maries 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, pae-
driatic pulmonary function, pulmonary func-
tion testing in the intensive care unit, and
domiciliary oxygenation and assisted ventila-
tion demonstrates the potential and scope
that this field has to offer.

Being accessible and clearly composed,
the text has the potential to be used as a “ref-
ence manual” but its editors have steered
the emphasis towards promotion of a com-
prehensive understanding of the theory
behind commonly used pulmonary function
tests which is where its great strength lies.
This should allow readers to develop a prag-
matic, realistic and clinically applicable basis for
the interpretation of their results.

This book comes thoroughly recom-
mended to technicians and respiratory physi-
cians alike, and goes a long way towards revi-
talising an important area of respiratory
tests which is unfortunately in danger of
being overlooked as our attention is taken by
newer scientific advances. — ILJ

Therapeutic Applications of Leukocyte Filtration

A one-day workshop on Therapeutic Appli-
cations 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
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ference Centre, Imperial College of Science
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