LETTERS TO THE EDITOR

Reform of the Public Health Act

We agree with Richard Coker1 that the vast majority of non-compliant cases of tuberculosis can be dealt with by a mixture of directly observed therapy (DOT) and inducements. However, when DOT fails in a few cases each year, despite intensive team effort and carrots such as housing or food vouchers, the Public Health Act may have to be invoked. We have had recourse to this measure four times in the past six months but, though providing a more measureable breathing space, it is extremely costly and proved ineffectual as a solution each time.

Once the patient is admitted there are still potential problems. Treatment cannot be enforced and patients can abscond. There have also been instances of patients assaulting staff, physically and sexually, issuing death threats, breaking hospital property, and terrorising other patients, even interfering with other patients’ therapy. Dealing with such patients puts hospital staff and patients under unacceptable pressure and requires extra staffing for security purposes. NHS hospitals were not designed for, nor are they staffed adequately for, custodial purposes.

There is an urgent need to review the Public Health Act and make provisions for small specialist units staffed by nurses with training in and an aptitude for interpersonal skills. Admission to the unit would usually only be required for short periods of time until precipitating circumstances were resolved and alternative arrangements made. The threat of compulsory admission, or a short period thereof, may induce a behavioural change in the patient, allowing DOT to be successful. The threat of hospital property, and an aptitude for interpersonal skills.

Pulsed dose oxygen delivery system

Dr Garrod and colleagues have described a pulsed flow oxygen delivery system for use during exercise by patients with chronic obstructive pulmonary disease (COPD).1 They found the device to be four times as economical as nasal cannulae for the same increase in walking distance in patients with COPD compared with the other devices which were tested.2 3

The Haldane type mask fell out of use because, with a limited demand and low price, the manufacturer had little incentive to maintain a stock. Now, with greater awareness of the likely benefit, there might be a case for trying again.

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Simian virus 40 and human pleural mesothelioma

Mulatero et al1 report failure to detect Simian virus 40 (SV40) DNA in 12 British mesothelioma. They propose that their negative results indicate that the previous positive findings are probably a consequence of PCR contamination. Since Mulatero et al1 submitted their paper, several laboratories have further confirmed the association of SV40 with human mesothelioma and other types of human tumours.2 3 Furthermore, the International Mesothelioma Interest Group has published results of their multilaboratory investigation confirming consistent association of SV40 DNA with mesothelioma.4 Additional recent studies (reviewed by Butel and Lednicky)5 have shown SV40 DNA to exist in an integrated form in human tumours and to be associated with expression of SV40 large T antigen as demonstrated by RNA in situ hybridisation, Western blotting, and immunostaining. These results therefore contradict the PCR contamination theory. The negative findings of Mulatero et al1 may be explained by technical or demographic differences.6 7 The authors state that the sensitivity of their assay is one SV40 genome per cell based on a PCR methodology capable of detecting HPV. This level of sensitivity is below the threshold for detecting SV40 in human mesothelioma, partly because of the usual low proportion of tumour cells included in mesothelioma biopsy specimens and partly because of the low copy number (<10 copies) of SV40 DNA estimated to be associated with this tumour type.8 9 In this context, the adequacy of method sensitivity claimed by the authors based on its comparison with sensitivity of an assay capable of detecting HPV in cervical cancer is potentially misleading. Cervical cancer is not only a more cellular tumour but is known to be associated with several to hundreds of viral genomic copies per tumour cell. We therefore suggest that the specimens of Mulatero et al1 should be re-tested using a more sensitive methodology to establish whether their negative findings are related to technical or demographic differences.

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AUTHORS’ REPLY

Dr Jasani misquotes us when he says we suggested that laboratories positive findings are probably a consequence of PCR contamination; we listed laboratory contamination of samples as one of several possible explanations for differing results.

Dr Jasani suggests that our failure to identify SV40 may be due to inadequate sensitivity and he states that the sensitivity of our assay, which we reported at one copy of SV40 per cell, is below the threshold for detecting SV40 in human mesothelioma. All laboratories who have rejected the possibility that he may be correct, but he does not identify any evidence to support his assertion. The studies which have identified SV40 in malignant mesothelioma all refer, including one of which he was a co-author,6 did not report sensitivity of more than one copy per cell.

The multi-institutional study to which Dr Jasani refers1 examined only 12 cases of mesothelioma from one hospital in New York, but the samples were analysed in four laboratories including one in Finland which had previously reported negative results for SV40 in local mesothelioma. All laboratories who have identified SV40 in 10 of the 12 New York cases. However, in their discussion the authors stated that the Finnish group subsequently confirmed the absence of SV40 in mesothelioma cases from Finland and speculated that this was because SV40 contaminated vaccines had not been used in Finland. This evidence points to demographic differences rather than lack of sensitivity as a more likely explanation for differing results from different series.

It appears from the collective results of various studies that the prevalence of SV40 in mesothelioma may be greater in the USA than in Europe, possibly as a consequence of

1. Coker RJ, Carrots, sticks and tuberculosis. Tho-

more widespread use of contaminated polio vaccine in the USA. However, epidemiolog- 
ic evidence indicates that the incidence of mesothelioma in the USA has peaked, 
where a continuing increase in incidence over the next 20 years is expected in Europe. 
These observations, together with evidence that so far there is no increase in the incidence of mesothelioma in individuals who received SV40 contaminated polio vaccine, 
do not suggest that SV40 is important in the causation of human mesothelioma.

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1 Pepper C, Jasani B, Navab H, et al. Simian virus 
40 large T antigen (SV40LTAg) primed specific 
DNA hybridization in human pleural meso-

2 Testa JR, Carbone M, Hirvonen A, et al. A multi-institutional study confirms the presence 
and expression of simian virus 40 in human 
tumours of mesothelioma. Cancer Res 1998;58: 
4505–9.

3 Price B. Analysis of current trends in United 
States mesothelioma epidemic. Br J Cancer 

4 Strickler HD, Rosenberg PS, Devesa SS, et al. 
Contamination of poliovirus vaccines with 
simian virus 40 (1955–1963) and subsequent 

Acronyms 
I write to protest against the use of unex-
plained acronyms in your editorial entitled 
“EUROSCOP, ISOLDE and the Copen-
aghen City Lung Study”. Acronyms are useful and 
often necessary because they simplify and 
accelerate modern communication. But when 
first mentioned in any biomedical journals, 
acronyms must be explained fully. Further-
more, abbreviations are prohibited in a title.

Specialists often take for granted that certain “trade terms” are so evident that they 
do not bother to define them. I thought that 
cardiologists, of which I am one, are ordi-
nary for using or inventing acronyms. Acro-
nymia is contagious. Please do not let our 
colleagues in respiratory medicine catch this terrible disease.

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1 Sherwood Burge P. EUROSCOP, ISOLDE and the 
Copenhagen City Lung Study. Thorax 

2 Cheng TO. Acronyms of clinical trials in 
cardiology—1998. Am J Heart 
1999;137:726– 
5.

3 International Committee of Medical Journal 
Editors. Uniform requirements for manu-
scripts submitted to biomedical journals. 

4 Cheng TO. No abbreviations in title, please. 

Cystic fibrosis and diabetes 
Yung et al present important data on 
cystic fibrosis related diabetes (CFRD) and suggest 
a selective approach for screening and diagnosis. Although the majority of patients 
with CFRD may be identified using this approach, over 8% would remain undiag-
nosed.

CFRD is associated with substantial mor-

bidity and mortality. Analysis of 21 000

patients followed by the Cystic Fibrosis 
Foundation Registry shows a sixfold increase in mortality for CFRD with more severe pul-
monary disease.

Once insulin treatment begins, FEv, and 
FVC increase and are comparable to non-
diabetic patients. By this time, the number of 
pulmonary infections with Haemophilus influ-
enzae and Staphylococcus aureus fall and body 
mass index increases sharply within three 
months of starting treatment. Consequently, 
many may judge the risk for patients undiag-
nosed by the selective approach to be too high.

Recommendations from the 1998 Consen-
sus Conference on CFRD state that the fast-
ging glucose and oral glucose tolerance test 
(OGTT) should be performed in all patients 
with symptoms of diabetes, particularly as 
measurement of glycosylated haemoglobin 
(HbA1c) has been shown to be unreliable in 
the diagnosis of new CFRD. The major 
disparities between the findings of Lanng et 
al. and the Brompton group emphasises this 
point.

Clear distinction needs to be made be-
tween screening for the disease and diagnosis. Many tests of 
glucose control in CFRD lack the sensitivity 
and specificity to identify most new cases. 
The approach used by Yung et al may prove to 
be a suitable screening test since the majority 
of cases were identified.

The OGTT is currently recommended as 
the test of choice in the diagnosis of CFRD 
which aids in prompt and accurate identifica-
tion of the disease. Otherwise, an entirely 
treatable cause of pulmonary decline may be 
missed.

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1 Yung B, Kemp M, Hooper J, et al. Diagnosis of 
cystic fibrosis related diabetes: a selective 
approach in performing the oral glucose toler-
ance test based on a combination of clinical and 

2 Moran A. Highlights of the February 1998 con-
sensus conference on CFRD. Pediatr Pulmonol 

3 Lanng S,Thorsteinsson B, Nerup J, et al. Diabetes mellitus in cystic fibrosis: effect of 
insulin therapy on lung function and infections. 

Methacholine challenge and 
sputum induction 
Spanevello and colleagues claim that a 
methacholine inhalation challenge carried 
out one hour before sputum induction in 
patients with stable asthma does not signifi-
cantly alter the cellular, eosinophil cationic 
protein (ECP), or albumin constituents of 
spum. These results, if correct, are impor-
tant for both clinical practice and clinical 
trials where information regarding airway 
hyperresponsiveness and inflammation is 
needed. Being able to perform a metha-
choline challenge and sputum induction on 
the same day would be convenient.

Sixteen subjects with asthma were studied 
on two days within a week. Sputum induction 
was performed alone on one day and one 
hour after a methacholine challenge on the 
other. Cell counts and the biochemical mark-
ers of the two sputum samples were 
compared using the Wilcoxon signed rank test 
and a value of p<0.05 was considered statisti-
cally significant.

The small sample size, variability in the data, and 
p values near significance for neutrophils (p = 0.06) 
and macrophages (p = 0.08) led us to determine the power of the study. The results of a power analysis for 
paired continuous data showed that the study 
only had a 36%, 29%, 10%, 6.6%, and 19.5% 
chance of detecting a di-

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composition of sputum induction. Thorax 
rhDNase in cystic fibrosis

Cystic fibrosis is a disease that is relatively rare but expensive for patients, families, and carers. The introduction of rhDNase has been associated with controversy as to its benefits and costs. Milla describes the experience in a centre that prescribed this drug to patients, 60% of whom had an FEV₁ or more than 80% predicted at the time of prescription. Overall, the group had an accelerated decline in lung function following its introduction. This study illustrates the importance of patient selection and follow up in the prescription of rhDNase.

Paediatricians and chest physicians from the South & West Region of the UK have audited their use of DNase as part of their contribution to the South & West Cystic Fibrosis database. In 1995 78 (12%) of the 664 patients receiving care within the region had been prescribed DNase. This had risen to 143 (22%) in 1996. We subsequently defined criteria for its use: patients over five years of age, FEV₁ <70% predicted, and more than one course of intravenous antibiotics during the previous year. In 1995 12 (17%) of patients receiving DNase did not appear to meet these clinical criteria. A further 36 patients who were eligible under these criteria were not receiving the drug.

Innes rightly emphasises the responsibility of carers to target this treatment effectively—it is also important that treatment is seen to be equitable and not dependent on postcode. Our experience illustrates that a regional cystic fibrosis database can be a clinically relevant and cost effective device for targeting appropriate treatment. The annual cost of DNase for two patients would be sufficient to fund a regional audit to monitor and influence this and other expensive treatments in patients with cystic fibrosis.

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(On behalf of the South & West CF Group)


BOOK REVIEW

Up to Date in Pulmonary and Critical Care, Steven E Weinberger. USA: American Thoracic Society.

Up To Date in Pulmonary and Critical Care, a product from the stable of the American Thoracic Society, is one of a rising tide of PC based medical texts. The programme is based on the concept of providing quick and authoritative answers to common specific questions that arise during specialist clinical practice but not as a resource to use when faced with a rare disease.

Presented on CD-ROM for Windows or Macintosh and supported by clear installation instructions, it ran efficiently on a 266 MHz based laptop, from the hard disc or CD-ROM drive. The search functions were easy to use with helpful cross referencing links and section content outlines. The initial cost is approximately £300 for the first year with the CD-ROM being regularly updated throughout the year.

Have they succeeded in their aim? Overall, the answer is yes.

Useful practical advice is given on simple but irritatingly difficult questions to answer— for example, provision of oxygen during air travel, the choice of agent for chemical pleurodesis, the role of inhaled steroids in chronic obstructive pulmonary disease, etc. However, the programme is slanted toward the American market, as highlighted in the section on long term oxygen therapy (LTOT) which gives, in detail, the billing mechanism. Similarly, nasal calcitonin suggested for the treatment of steroid induced osteoporotic bone pain is not licensed in the UK.

Its functionality makes it a valuable tool in the outpatient setting, being described by one trainee as “really helpful”. This programme would be best suited to hospitals and practices with adequate provision for computing facilities in the clinical area, ideally over a local area network and not locked away in the library. The added bonus for the chest physician with a commitment to general medicine is that the disc also has sections on cardiology, gastroenterology, and other main streamline disciplines of similar quality. This programme sets a formidable standard for the UK government’s proposed NICE (National Institute for Clinical Excellence) clinical information system.—SPH

NOTICE

MICRO 2000

Following the success of MICRO 98, the Royal Microscopical Society has announced that a MICRO 2000 international microscopy exhibition and conference will be held on 11–13 April 2000 in London. Further information will be available shortly from the Exhibition Organiser, Royal Microscopical Society, 37/38 St Clements, Oxford OX4 1AJ, UK. e-mail: exhibitions@rms.org.uk