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Paradigm shift in surgical approaches to spontaneous pneumothorax: VATS

The recently published BTS guidelines on the management of spontaneous pneumothorax by Henry *et al*[1] have stimulated some discussion among our respiratory physicians and thoracic surgeons. We found it interesting that the authors quoted a pneumothorax recurrence rate of 5–10% after video assisted thoracoscopic surgery (VATS). Numerous large series from around the world have recently reported recurrence rates of primary spontaneous pneumothorax following VATS bullectomy combined with surgical pleurodesis to be in the range of 1.7–5.7%.[2 3] Although the recurrence rates following VATS may be marginally higher than the open procedure, the benefit to the patient of a shorter postoperative hospital stay, less postoperative pain, and better pulmonary gas exchange in the postoperative period should be balanced against this. Furthermore, we found that patients who undergo VATS have significantly less shoulder dysfunction and pain medication requirements in the early postoperative period than after posterolateral thoracotomy.[4] Whether VATS can be ''established as being superior to thoracotomy'' will in part be decided by our patients and become clearer with future trials.

With the lowered morbidity and proven safety of VATS, even for elderly and paediatric patients,[2] the old surgical algorithms based on the morbidity of thoracotomy should be re-evaluated.[5] We feel there are two additional conditions that warrant inclusion in the list for ''accepted indication for operative intervention''. Firstly, patients presenting with the life threatening condition of tension pneumothorax, even for the first time, should be considered for VATS because of the potential grave consequences of its recurrence. Secondly, the presence of radiologically demonstrated huge bullae associated with spontaneous pneumothorax should be an indication for VATS because of the increased risk of recurrence. In addition, the huge bullae may continue to expand and impair lung function by causing compression of adjacent healthy lung tissue, and can be a manifestation of lung carcinoma or a focus for recurrent infection.[2 6]

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Authors' reply

We thank Dr Ng and colleagues for their comments on the recently published guidelines on the management of spontaneous pneumothorax.[1] Dr Ng points out that recurrence rates for pneumothorax after VATS preventative procedures were lower than those quoted in the guidelines. It should be pointed out that, in the multiple drafts of this document, it was recognised that recurrence rates after VATS were falling and that further improvements in these figures were likely as operator experience improved. This was recognised within the guidelines. It is fully expected that, as experience and provision of services improve, VATS will replace open thoracotomy for treatment of recurrent pneumothoraces.

In response to Dr Ng's second point regarding surgical treatment of tension pneumothoraces and hugh bullae, the guidelines obviously could not take into account every possible clinical scenario. As far as we are aware, there is no evidence to suggest that tension pneumothoraces are more likely to recur than ''non-tension'' spontaneous pneumothoraces. This does not mean, of course, that an individual physician should not decide that the clinical risk in an individual patient—either from rupture of a huge bulla or recurrence of a tension pneumothorax—should not warrant surgical intervention.

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Role of CFTR mutations in adult bronchiectasis

Over 1000 different mutations of the cystic fibrosis transmembrane conduction regulator (CFTR) gene have so far been identified. These mutations have been associated with a spectrum of clinical phenotypes ranging from classic cystic fibrosis (CF) presenting in early childhood to CFTR related conditions that may present in adulthood such as congenital bilateral absence of the vas deferens, chronic pancreatitis, and rhinosinusitis. In addition, the 5T variant in the polythimidine tract is felt to be important in atypical CF as it significantly reduces the amount of normal CFTR transcript because intron 8 is inefficiently spliced.[1]

Bronchiectasis in adults is most commonly idiopathic[2] and is a significant cause of chronic morbidity. The chief manifestation of CF is bronchiectasis, and the role of CFTR mutations in adult bronchiectasis is still not well defined. Several small studies have suggested that there is an increased prevalence of CFTR mutations in diffuse adult bronchiectasis,[3–5] and one large study found that there was a marginally higher prevalence of mutations in adult bronchiectasis.[6] Most of these studies have had little information on the patients' clinical status and family history of disease and have not assessed the 5T mutation.

A joint project was undertaken between Monash Medical Centre (MMC) and the Murdoch Children's Research Institute to assess the role of CFTR mutations in adult bronchiectasis. A sequential series of 100 adults with bronchiectasis confirmed on high resolution computed tomographic (CT) scanning was studied. The patients were screened for the 10 most common mutations in the local population (ΔF508, Δ1507, V520F, G542X, G551D, R553X, R117H, 621+1G→T, A455E and N1303K) responsible for 82% of cases of CF and the 5T mutation by previously published methods.[7 8] Ethical approval for the project was obtained from the ethics committee at MMC.

The group comprised 36 men and 64 women of mean (SD) age 61 (13) years. Most of the patients were white (n = 95), predominantly from a northern European background (n = 84). The main symptom was chronic mucopurulent sputum production which was present in 98 of the 100 subjects and, in most cases (n = 78), this had started in childhood. Chronic rhinosinusitis was also common (n = 75). Lung function tests showed moderate airway obstruction in the cohort. Most patients (n = 86) had multilobar disease on CT scanning, predominantly in the lower zone. The mean (SD) number of lobes with bronchiectatic changes on the CT scan was 2.5 (0.98). Nine of the patients had *Pseudomonas aeruginosa* isolated from their sputum and one of these isolates was a mucoid strain. The most common pathogen was *Haemophilus influenzae* (37%) followed by *Streptococcus pneumoniae* (10%). Screening for underlying causes of bronchiectasis showed that most patients (n = 84) had idiopathic disease. All subjects were asked about the presence of chronic respiratory illness in first degree relatives. There was not a high incidence of familial chest disease. No relative had a diagnosis of CF and only one had a history of bronchiectasis.

The patients did not have a high prevalence of features in addition to bronchiectasis and rhinosinusitis which are known to be associated with CF (none had pancreatitis, one had unexplained infertility, and three had predominantly upper zone bronchiectasis).

Screening of the cohort showed that none of the subjects was homozygous and four were heterogeneous for CFTR mutations (table 1). Three of the subjects had mutations of the most common CFTR mutation (ΔF 508) which is responsible for 67.5% of CFTR mutations in the local population and the other subject had the second most common mutation (G551D, 4.7%). Sweat tests on the heterozygote subjects showed normal chloride levels.

The prevalence of CFTR mutations in normal predominantly white populations based on several studies is approximately 1/25.[9 10] The expected level of heterozygotes in this group which had been screened for 82% of mutations was 3–4 subjects. Thus, in this group of subjects with bronchiectasis the

Table 1 CFTR mutations/sweat tests in 100 adults with bronchiectasis

Age	Sex	Allele 1	Allele 2	5T variant	Sweat test (chloride levels)
54	F	ΔF 508	−ve	+ve	38 mmol/l
70	F	ΔF 508	−ve	−ve	34 mmol/l
72	F	ΔF 508	−ve	−ve	36 mmol/l
69	M	G551D	−ve	−ve	Not done

number of carriers was the same as would be predicted in a normal population (95% confidence intervals (CI) 1.1 to 9.9). Similarly, the incidence of the 5T mutation was 7% which is similar to the incidence in a normal population[8] (95% CI 2.9 to 13.9).

These findings suggest that CFTR mutations do not have a major role in the pathogenesis of adult bronchiectasis and further investigation is needed to establish the predisposing factors involved in the development of this condition.

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BTS guidelines for investigation of unilateral pleural effusion in adults

We are pleased to see that formal guidelines for the investigation of the previously neglected and sometimes difficult area of pleural effusions have been published.[1] There have been many publications concentrating on the distinction of exudative from transudative pleural effusions as a means of aiding the diagnostic process, but not necessarily focusing on the underlying clinical aetiology.

We were, however, disappointed to find that the Pleural Disease Guidelines Group did not appear to have taken specialist advice about the clinical biochemistry investigations. This means that some of the important methodological aspects have not been commented on. For example, it is important to appreciate that most of the assays currently used in NHS laboratories in the UK have not been optimised and validated for use in fluid other than serum/plasma and may give inaccurate results. A review of the biochemical aspects of pleural fluid analysis was recently published in the *Annals of Clinical Biochemistry*.[2] Although pleural fluid testing accounts for a very small percentage of laboratory work, this area requires close collaboration between the clinician and the laboratory to ensure that the most appropriate tests for answering the clinical question are selected, rather than adopting a blanket approach.

The advice that there is no requirement to test bilateral effusions which, in the clinical setting, are strongly suggestive of a transudative process unless there are atypical features or a failure to respond to treatment is welcomed. We agree that the appearance of the fluid provides useful information and would suggest that this is included in the formal laboratory report.

We endorse the view that total protein is central to the investigation of an undiagnosed pleural effusion and that this is usually sufficient unless the pleural fluid protein lies in the range of 25–35 g/l. This recommendation is not made clear in the algorithm, which suggests that lactate dehydrogenase (LDH) and pH should be requested together with protein. Because of the problems of concurrent sampling, we were pleased to see that the use of a pleural fluid to serum ratio is not recommended. With respect to LDH, the use of modified Light's criteria as described by Heffner *et al* did not significantly improve the discrimination from that achieved using total protein alone.[3]

The recommendation that gives us most concern is that of measuring pleural fluid pH in all non-purulent pleural effusions. Although the pH of pleural fluid may vary depending on the cause of the effusion, there is no evidence that routine measurement adds value to the diagnostic process. The only situation for which clinical studies may support pH measurement is in aiding the decision about drainage of non-purulent parapneumonic effusions.[4] Aside from its clinical utility, the value of pH measurement is further compromised by analytical considerations. The samples must be collected anaerobically and analysed immediately under anaerobic conditions. This effectively means using a blood gas analyser. The suitability of pleural fluid samples for analysis by this method is unproven and, furthermore, brings concerns about whether such samples may cause blockage and instrument failure, especially since many blood gas analysers are now situated outside the laboratory and samples are run by non-laboratory personnel. This increases the concerns about compliance with Health and Safety regulations, especially since samples are often of high risk and the diagnosis of tuberculosis is specifically being queried. Additionally, such measurement would be outside the licensed indications for the analyser.

There are a few points to make about those tests used in specific clinical circumstances. We are pleased to see that the use of cholesterol and triglyceride is restricted to the investigation of suspected chylothorax, where high concentrations are likely, especially since cut-offs used in studies recommending cholesterol to separate exudates and transudates lie below the usual measuring range of routine assays. We are also pleased that the use of pleural fluid glucose is restricted to situations where the effusion is thought to be rheumatoid in origin and amylase where pancreatitis is the clinical query. We agree that creatinine is useful where a urinothorax is queried, that adenosine deaminase may be useful in TB pleurisy, and that ANA is not considered useful. Caution is advised, however, in using complement measurements on the basis of one positive reference, especially since the cut-off value quoted is 10 times less than the usual serum value and lies below the functional sensitivity of most assays.

While we acknowledge that the desire to minimise the number of invasive procedures leads to development of an all-inclusive algorithm, provided there is good liaison between the laboratory and clinician, a stepwise approach may be more cost effective without compromising patient management. In addition, good liaison and discussion will lead to a better appreciation of any test limitations and an individualised investigation strategy.

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