Many adult patients with chronic obstructive bronchitis adopt the terms ''persistent bacterial endobronchial infection'' which highlight the fact that this is probably not a bacterial bronchial infection and is quite distinct from adult ''chronic bronchitis'' associated with cigarette smoke. Many adult patients with chronic obstructive pulmonary disease (COPD) are plagued by recurrent/persistent bacterial endobronchial infection. We see in children but this, as in the children, is a secondary phenomenon resulting from impaired mucociliary clearance. These patients have two ongoing pathologies—one (COPD) predisposing to acquisition of the second (persistent endobronchial bacterial infection). We would go further and speculate that the continuing symptoms and decline in lung function in a significant proportion of ex-smokers is due to ongoing inflammation secondary to persistent endobronchial bacterial infection.

As noted above, we believe that persistent endobronchial bacterial infection is not a primary diagnosis but represents colonisation secondary to impaired clearance of the airways. This may be due to cystic fibrosis or an immunodeficiency but, most commonly, is secondary to a ''hit and run'' insult such as a significant viral lower respiratory tract infection or—much less commonly—these days—pertussis. Other causes of impaired clearance such as mucus plugging in asthma, tracheomalacia or even pulmonary vascular congestion with congenital heart disease may allow Haemophilus influenzae in particular to colonise the lower airways.

Finally, we would wish to clarify some of the misconceptions in the letter by Drs Byrnes and Edwards. We did not say that bronchiectasis frequently resolves in those with immunodeficiency but mention that it has been recorded on full recovery from a respiratory tract infection or—much less commonly—these days—pertussis. Other causes of impaired clearance such as mucus plugging in asthma, tracheomalacia or even pulmonary vascular congestion with congenital heart disease may allow Haemophilus influenzae in particular to colonise the lower airways.

In contrast with previous studies, anti-TB drug-related hepatotoxicity was observed at a similar rate in HIV-infected and HIV-negative patients.4 Differing abilities to control socio-demographic and clinical provoking factors—such as malnutrition, alcohol use, drug abuse, hepatitis B/C, anti-retroviral drugs—could account for the difference, especially with the limited sample sizes of these studies.1,2 In this regard, it is interesting to note that use of rifampin plus pyrazinamide in the treatment of latent TB infection was associated with apparently higher prevalences of hepatotoxicity in clinical trials conducted among HIV-negative subjects5 than those conducted among HIV-infected individuals.6 As hepatotoxicity is a major factor leading to interruption of anti-TB treatment,7 the similar incidence of hepatotoxicity in HIV-infected and HIV-negative patients is perhaps reassuring.

However, while the attending clinicians might be unwilling to interrupt the anti-TB treatment among HIV-infected subjects even in the face of severe vomiting and peripheral neuropathy,8 patient cooperation could be jeopardised and drug adherence would then be difficult to ensure outside the setting of directly observed therapy. Non-adherence, frequent regimen modifications and treatment interruptions certainly increase the risk of treatment failure and relapse with acquired resistances. With the recent report of highly fatal cases of drug resistant TB among HIV-infected patients,9 there remains a need for heightened awareness of possible adverse drug events, as well as vigilance in the prevention, detection and management of such events.

References

HIV-related TB and adverse drug events
Breen and coworkers4 showed that, in the era of effective antiretroviral therapy, discontinuation of anti-tuberculosis (TB) treatment occurred with a similar frequency in HIV-infected and HIV-uninfected individuals despite a greater rate of serious grade III/IV adverse events among HIV-infected individuals.

According to the Division of Aids table for grading the severity of adult and pediatric adverse events (http://ccrtech-res-intl.com), grade III adverse events are likely to cause inability to perform usual social and functional activities while grade IV events are potentially life-threatening. However, among HIV-infected patients with grade III/IV adverse events in the above study, treatment was interrupted only in a minority of patients, except for those with hepatotoxicity, and no mention was made of modifications in the treatment regimen. With the retrospective study design, it might be difficult to exclude some degree of subjective bias in symptom reporting/grading/interpretation, especially among HIV-infected individuals, despite the use of a standardised grading scheme.
over 35 years were regarded as having airway obstruction (COPD) if the forced expiratory volume in 1 second (FEV1/FVC) ratio was <0.70. This conforms with the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines adopted by various organisations, albeit that no data were obtained after bronchodilatation. Even the GOLD group acknowledges there is evidence that this cut-off point signifies clinically validated airway obstruction and that “the use of this fixed ratio may result in over-diagnosis of COPD in the elderly, especially of mild disease. Using the lower limit of normal (LLN) values for FEV1/FVC that are based on the normal distribution and classify the bottom 5% of the healthy population as abnormal is one way to minimize the potential misclassification.”

In the 1995/6 study of a representative sample of the English population, valid spirometric data were obtained in 11 894 men and 13 554 women. Measurements in 6035 non-smoking white people with no reported diagnosis of asthma or respiratory symptoms were used to derive prediction equations for the FEV1/FVC ratio and its LLN. For an adult woman of 160 cm (method A) or below the LLN (method B). Figure 1 illustrates the inappropriateness of using a fixed ratio, airway obstruction will hence be under-diagnosed below those ages and over-diagnosed above those ages.

Using data on 25 408 subjects, we established how often FEV1/FVC <0.70 (method A) or below the LLN (method B). We expressed the difference between A and B as a percentage of B. Thus, 0% means equal prevalence, 100% means that the fixed ratio for FEV1/FVC identified twice as many subjects with airway obstruction as the LLN method (50% false positives), and ~80% means that the fixed ratio method failed to identify 8 out of 10 subjects with airway obstruction (80% false negatives). Using the NHANES III database and data from a Dutch population, sample findings were comparable with those in fig 1: the 2001 Health Survey for England data used by Shahab et al produced results nearly identical to those in fig 1. The trend in non-smoking men and women with no reported diagnosis of asthma or respiratory symptoms (a healthy reference group) is the same as that in the whole population.

The findings in a healthy reference group illustrate the inappropriateness of using a fixed FEV1/FVC ratio for establishing airway obstruction. Applying that criterion to the whole population leads to substantial over-diagnosis of airway obstruction in middle-aged and elderly subjects, particularly in men, and unacceptably large under-diagnosis in younger adults. We recommend that organisations like GOLD, the American Thoracic Society, European Respiratory Society, British Thoracic Society and the National Institute for Clinical Excellence—who all recommend an FEV1/FVC ratio of <0.70 as evidence of airway obstruction—return to evidence-based medicine and revise their guidelines.

Shahab et al recently reported significant under-diagnosis of chronic obstructive pulmonary disease (COPD) in England. Adults

Diagnosis of COPD

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