persistent bacterial bronchitis/persistent endobronchial infection. This is indeed the case in adults, but producing sputum at will or giving a clear history of expectorating yellow/green sputum but, in younger children who do not expectorate or who are at an early stage of the disease progression, diagnosis rests largely on the history. The only reliable way to make the diagnosis unambiguously is to undertake bronchoscopic examination, but the number of patients is such that this is not currently our first line investigation, particularly as many will resolve completely with one or two courses of antibiotics. Common things are common, and we do try hard to determine whether asthma is the sole diagnosis or a contributory factor through appropriate trials of treatment.

Fortunately our primary care physicians are very good and it is uncommon for a child to be referred who has not been assessed as possibly having asthma. Overdiagnosis or failure to recognise a co-morbidity is much more common. If inhaled therapy and/or oral steroids fail to lead to a resolution and we have dealt with obvious confounders such as compliance, we then start children on a trial of treatment for 2 weeks and contact the parents at the end of the course before planning future interventions.

We would entirely agree that the inappropriate use of antibiotics should be discouraged but, equally, inappropriate treatment due to failure of an accurate diagnosis leading to unnecessary morbidity is also unacceptable.

Trying to ensure that a correct diagnosis is made and that appropriate treatment is provided does take care and regular review. The lag phase between being a “chesty” child and an adult with bronchiectasis will mean that adult physicians will only slowly start seeing numbers increasing in the next decade unless their paediatric colleagues and, indeed, primary care physicians recognise the potential size of this problem.

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References


Outcomes in children treated for persistent bacterial bronchitis

We write with regard to the retrospective chart review by Donnelly recently published in Thorax. The review covers a 5 year period and it is presented as a cross-sectional survey of their personal practice of children with persist-ent bacterial bronchitis. We are unsure how often their patients would have had time to benefit from the review and it does not examine outcomes longitudinally.

We agree that there is a lack of clarity regarding the definition of chronic bronchitis. However, like all diagnoses of exclusion, it is a difficult diagnosis to make. The definition of chronic bronchitis in adults is more specific: “the presence of chronic productive cough for 3 months in each of two successive years and a patient under whom other causes of chronic cough have been excluded”1. Comments regarding the diagnosis from two recently published paediatric respiratory text books are illuminating. In the first the adult definition of chronic bronchitis is given but “whether this definition can be applied to childhood chronic bronchitis remains unclear” and “it has the potential to divert the paediatrician from detecting a more specific respiratory condition”. The authors of the chapter suggest that: “The diagnosis of chronic bronchitis should occur in two phases. The first is consideration and identification of several well defined respiratory disorders according to a defined management protocol. The second but simul-taneous phase is elimination or modification of exogenous factors that produce or maintain the child’s illness.” The second paediatric text2 also notes that “the definition of chronic bronchitis in children is less clear ...”. Our concern with this paper, based on our own experience, is that the label of “chronic bronchitis” is given to children without ade-quate exclusion of other diagnoses. We acknowledge that our centres may differ because of the referral pattern, with most of the patients referred to secondary care rather than secondary care. The definition in this article is very reliant on a persistent “wet cough”, with no other anomalies. However, in this group of 81 children, 68% had abnormal chest radiographs (of the 98% in whom they were done), but only 17% had chest CT scans and 23% underwent bronchoscopic examina-tion. The other paper3 with which the authors align themselves had 15 patients diagnosed with chronic bronchitis, but all of these had a negative chest CT scan and all had positive bronchoscopies so a more accurate diagnosis is likely. One of the diagnostic criteria used in this article was response to antibiotics—ana-logous to response to asthma treatment. However, while only asthma responds to asthma treatment, many conditions may respond to antibiotic treatment and time alone may lead to some symptom resolution, so it is not a discriminating diagnostic characteristic. We agree that persistent bacterial bronchitis is often misdiagnosed as asthma although the two conditions may coexist and, although 30% of families smoked, there was no discussion on the impact this may have had.

We agree that chronic bronchitis is a real entity and that it may be underdiagnosed at the current time. Untreated, this condition may progress to bronchiectasis in an (unknown) percentage of children and prospective work in this area is needed to confirm this. However, we need to proceed cautiously so as not to miss already established bronchiectasis or other diseases without adequate investigations. It is hard to label all of these children as chronic bronchitis when 59% had symptoms for more than 4 weeks, and only 8% had 4 courses of antibiotics and 6 weeks of antibiotics before improvement, and so few had chest CT scans or bronchoscopic examinations. Those that improved after two courses of antibiotics with no chest radiographic change would be understandable to label as more likely to have chronic bronchitis. In this paper, however, that would amount to 51% of the patients.

In addition, we disagree that the children with an underlying immunodeficiency frequently have bronchiectasis that resolves. The only groups in which this has happened regularly are those with bronchiectasis secondary to foreign body inhalation or those diag-nosed during immunosuppressive treatment for an oncological disease; other examples of published circumstances are referenced.

The authors state later in the text (not referenced) relating to idiopathic bronchiectasis focus on diagnosis and management and ignore the antecedent stages of the disease; this is not true.1,2 Interestingly, while both the paediatric texts cite a number of differential diagnoses that require exclusion before using the term “chronic bronchitis”, neither specifically mentions bronchiectasis although both mention cystic fibrosis, yet the former is far more common in our experience and in other populations.1,2

The diagnosis of chronic bronchitis still needs to be made with care. While we believe it is a true and often under-recognised entity, there is still a risk of incorrectly ruling out other underlying problems which may well result in a child re-presenting with greater lung damage at a later stage. We recognise that it remains a difficult decision between assuming chronic bronchitis or subjecting a child to the radiation of a high resolution CT scan and the possible morbidity associated with bronchoscopy. In a child with persistent wet cough for more than 4 weeks, the features we believe should indicate more aggressive ascertainment of a definitive diagnosis would be:

• repeated antibiotic courses (>3 in 1 year) with only partial or temporary resolution of symptoms;
• persistent chest radiographic changes;
• a definitive episode of two or more pneu-monias requiring hospital admission;
• referral from hospital or community paediatric-tricians rather than primary care.

We agree that research and discussion need to continue in this area with regard to development of disease, diagnosis and nomenclature.

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Authors’ reply

We thank Drs Byrnes and Edwards for their comments regarding our paper and would certainly agree that the diagnosis of persistent bacterial bronchitis/persistent bacterial endobronchial infection can be difficult to make. However, without recognition that the condition exists, the diagnosis cannot be made. In our earlier letter (see page 921) we highlight the difficulties in reaching a correct diagnosis in a child with a chronic cough due to the limited repertoire of responses shown by the lungs when inflamed. Failure to identify children with persistent endobronchial infection results in a huge burden of unnecessary morbidity due to the disease and due to inappropriate treatment. In a significant proportion it probably leads to bronchiectasis, although this may take decades. Our experience is that persistent endobronchial infection in children is curable irrespective of the CT appearance, providing there is not a significant ongoing underlying problem such as cystic fibrosis or severe immunodeficiency. Bronchiectasis is not a diagnosis; rather, it is reversible. Our pathological finding at one end of the spectrum from normality through minor peribronchial wall thickening and patchy non-specific changes. We have major concerns regarding the use of CT scans by those who do not understand the natural history of the disease. We have seen a number of patients who were noted to have significant quantities of secretions on bronchoscopy and a heavy growth of one or two organisms in the lavage fluid who were then largely left untreated because the CT scan did not show bronchiectasis.

The letter from Drs Byrnes and Edwards highlights the concern about using a non-specific term such as “chronic bronchitis”. This is why we and Anne Chang’s group have deliberately adopted the terms “persistent bacterial bronchitis/persistent bacterial endobronchial infection” which highlight the fact that this is persistent bronchial bacterial 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 which is caused by the same organisms 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” infect 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 reported in the literature. Patients did not take up to six courses of prolonged antibiotics to improve. This was the time taken to affect a cure and a few will take longer. As previously noted, in the vast majority of cases the cough resolves within 10–14 days on high-dose antibiotics and failure to show a dramatic response calls the diagnosis into question. However, a small minority do take longer and occasionally do not clear even with 2 weeks of intravenous antibiotics, but have subsequently cleared with nebulised colistine which is active against Haemophilus. Our approach is based on the belief that the lack of a cough suggests that there is no active inflammation and that, under these conditions, the airways are healing themselves. When the typical cough returns, we aim to treat it aggressively and early until the condition resolves. We believe the main focus of research should be in how to identify the condition early in order to prevent the need for long and, in some cases, recurrent courses of antibiotics once the infection has been present for months or years.

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References


HIV-related TB and adverse drug events

Breen and coworkers 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://rcc.tech-res-intl.com), grade III adverse events are likely to cause inability to perform usual social and functional activities while grade IV adverse 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 regarding the discontinuation of treatment regimens. 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.

In contrast with previous studies, anti-TB drug-related hepatotoxicity was observed at a similar rate in HIV-infected and HIV-negative patients. Differing abilities to control socio-demographic and clinical profounders—such as malnutrition, alcohol use, drug abuse, hepatitis B/C, anti-retroviral drugs—could account for the differences, especially with the limited sample sizes of these studies. 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 subjects than those conducted among HIV-infected individuals. As hepatotoxicity is a major factor leading to interruption of anti-TB treatment, the similar incidence of hepatotoxicity in HIV-infected and HIV-negative patients is perhaps reassuring.

However, while the awaiting clinicians might be unwilling to interrupt the anti-TB treatment among HIV-infected subjects even in the face of severe vomiting and peripheral neuropathy, 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, 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.

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