persistent bacterial bronchitis/persistent endo-
bronchial infection. This is indeed the case in an adult with bronchiectasis and, indeed, pri-
aves and 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 and excluded as a result of
diagnostic uncertainty or failure to
recognise a co-morbidity is much more common.
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 inappropri-
ate 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 pro-
vided 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 increase over the next decade unless
their paediatric colleagues and, indeed, pri-
mary care physicians recognise the potential
size of this problem.

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Outcomes in children treated for persistent bacterial bronchitis
We write with regret to the retrospective chart
review by Donnelly published recently in Thorax.1
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 long
the patient has been on antibiotics prior to the
time of 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 idea to standardise. 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”.2 Comments
regarding the diagnosis from two recently
published paediatric respiratory text books are
illuminating. In the first3 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 condi-
tion”. 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 suratul-
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 text4
also notes that “the definition of chronic bronchitis
in children is less clear …”.

Our conclusion to 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 being referred, very occasionally
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 paper5 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
bronchoalveolar lavage so a more accurate diagnosis
is likely. One of the diagnostic criteria used in
this article was response to antibiotics—analog-
gous 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 1 year, 67% required 3 or more courses of 4
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
changes 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 groups in which this happens regularly
are those with bronchiectasis secondary
to foreign body inhalation or those diag-
nosed during immunosuppressive treatment
for an oncological disease; other examples of
reported circumstances are referenced.6
The authors state that the conditions (not referenced) relating to idiopathic bronch-
chectasis focus on diagnosis and management
and ignore the antecedent stages of the
disease; this is not true.7,8 Interestingly, 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.9,10

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 broncho-
scopy. In a child with persistent wet cough for
more than 4 weeks, the features we believe
should indicate more aggressive asertment
of a definitive diagnosis would be:

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

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

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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 large 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 a morphological 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 one of the problems using a non-specific term such as “chronic bronchitis”. This is why we and Anne Chang have deliberately adopted the terms “persistent bacterial bronchitis/persistent bacterial endobronchial infection” which highlight the fact that this is persistent 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. However, in children 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’ infection 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. 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 but we do not believe 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 colistin which is active against Haemophilus. Our approach is to wash out over a period of 10 days 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 severe (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://rrc.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-threating. 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 modification 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 difference, 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 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, 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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Outcomes in children treated for persistent bacterial bronchitis

Catherine Byrnes and Elizabeth Edwards

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