Resolving the controversies in *Pseudomonas* serology will depend on more research in PA-free and initially PA infected children with CF using improved serological methods applied longitudinally with greater frequency. Monitoring PA antibody titres in children with CF diagnosed through newborn screening offers many advantages: (1) they begin PA-free; (2) the titres are initially very low and constant; (3) seroconversion per se indicates PA infection with a host immune response and not colonisation. However, the greatest difficulty in studying young children with CF—that is, the problem of culturing lower respiratory secretions—will continue to plague these investigations. Although either nasopharyngeal/tracheal techniques or oropharyngeal techniques may be used, their sensitivity and reliability can always be challenged when standard microbiological culturing methods are employed. Consequently, interpretation of the data published in the two current papers and all the literature becomes very difficult. For these reasons, non-culture based methods such as serological tests or polymerase chain reaction require further research and evaluation.

To discover the truth about the value of *Pseudomonas* serology in children with CF, we need to have more comprehensive research with better microbiological and serological techniques. We also need to identify an optimal panel of redundant complementary PA antigens that are clinically significant virulence factors. Ultimately, a combination of PA microbiology and serology will probably be used—serology will not replace microbiology. In the meantime, the implications of earlier studies[4–7] which are supported by the data of Kappler *et al*[9] as well as other publications[1 8 14] remain intriguing and interesting.

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Chronic cough in children

Diagnosing chronic cough in children

M D Shields

Further scientific evidence for the usefulness of signs and symptoms in predicting a specific cause of chronic cough in children

Problem coughing is common in children and can be produced by almost all the respiratory disorders that affect them. Rather than applying a comprehensive battery of tests to all children, most doctors use clinical pointers in the history and examination to determine the need for and targeting of investigations. Indeed, experienced clinicians usually use more than one single feature or diagnostic test and bring together bits of the history, clinical examination, and selective investigative tests to arrive at a diagnosis. Typical clinical cues recommended to be used in evaluating cough include (1) age of symptom onset, (2) quality of the cough, (3) triggers, periodicity and timing of cough, and (4) associated features such as wheezing.[1]

Recent evidence suggests that parents do not report the frequency or severity of cough accurately.[2 3] However, work from Professor Chang's unit has shown that parental reporting of wet versus dry cough is likely to be accurate.[4] Most of the clinical characteristics or pointers used to predict specific diseases causing cough in children have not been rigorously subjected to assessment as would be required for a diagnostic test[5] and, typically, historical case series have been used. For example, a bizarre loud and honking cough which increases with increased attention and abates at night in an otherwise well child who shows ''la belle indifference'' to the cough suggests a psychogenic origin. This

pattern of cough is described in the literature and in textbooks but has not been subjected to rigorous evidence based assessment for its predictive value in diagnosing psychogenic cough.[1]

In this issue of *Thorax* Marchant *et al*[6] have provided further scientific evidence of the usefulness of signs and symptoms for predicting a specific cause of chronic cough in children. The researchers investigated 100 children referred to a tertiary unit with chronic cough lasting more than 3 weeks. Each child was taken through an investigative pathway until a diagnosis was made. This included history and examination, chest radiography, spirometry, bronchoscopy and analysis of lavage fluid, and oesophageal pH studies. In addition, sweat testing/cystic fibrosis gene analysis, immunoglobulins, and *Mycoplasma pneumoniae* and *Bordetella pertussis* IgA titres were measured. A validated cough diary card was completed to assess the response to any treatment. The authors found that the best predictor for a specific cause being found for the cough was observed or parentally reported moist cough (odds ratio >9.0, sensitivity 86%, positive predictive value 80%). Abnormalities on chest examination or on the chest radiograph were also predictive of a specific cause (odds ratios 3.4 and 2.9, respectively).

There are some limitations to apply when interpreting the results from this study. Firstly, the sample size was not sufficient to determine which specific pointers relate to which specific conditions. The causes of cough have been classified into ''non-specific'' and ''specific'' with each group holding a variety of overlapping conditions. Secondly, it is important to note that the children studied were referred to a tertiary respiratory centre and it is possible that certain children with ''classical cough'' such as pertussis were filtered out at primary or secondary care. Diagnostic test properties can differ depending on the setting, so diagnostically powerful pointers can be used up as children are referred from primary to secondary care. Children may have been referred because they had specific features (or not referred because they lacked such features). Thirdly, in this study not all children underwent all of the investigations. Verification bias is therefore possible since the gold standard diagnostic tests were not applied to all children. In addition, in some the response to treatment helped to confirm a specific diagnosis. It is known that children referred with persistent cough often subsequently improve irrespective of the duration of the cough. Conducting a high quality diagnostic test (or evaluation of clinical pointers) is difficult[5] and, in particular, it is difficult to justify ethically the use of invasive tests in children when the researcher's previous knowledge suggests that the test has a very low probability of confirming a specific disease.

While this may be the first study to evaluate the use of clinical pointers for specific causes of cough, the overall results produced no surprises and expert opinion has been largely confirmed to be correct.[1 7]

A particularly interesting finding in this study was the high frequency of ''protracted bacterial bronchitis'' (45% of those with a specific cough). These children had chronic moist cough, a positive bacterial culture, and a response to antibiotics. The presence of a paediatric chronic bronchitis syndrome has been neglected by paediatricians and, in the past (when asthma and cystic fibrosis were underdiagnosed), its very existence has been questioned. This is an area of paediatric respiratory medicine that requires further research. It is not known what the natural history of ''protracted bacterial bronchitis'' is, and whether it might eventually lead to idiopathic bronchiectasis (a condition that must have a prodromal phase) or adult COPD.

Non-specific cough is a holding term for a group of children who otherwise appear well, do not seem to have a serious underlying disorder, but in whom no specific diagnosis has been made. Adult guidelines would suggest that cough variant asthma, allergic rhinitis/post nasal drip, and gastro-oesophageal reflux account for many of these, but it is unlikely that these disorders are a cause of cough in children. As non-specific cough is probably a common situation in primary care, further research is needed to clarify the underlying conditions that contribute to this group and to determine clinical pointers which are useful for turning a non-specific diagnosis into a specific diagnosis. This information would help to prevent the use of inappropriate medications such as asthma drugs and target potential future treatments if and when they are needed.

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Conflict of interest: In the last 12 months the author has received honoraria by Merck Sharp & Dohme and GlaxoSmithKline for lectures given and attended an advisory board meeting for Altana. In the past 5 years he hase given lectures and attended conferences as a guest for AstraZeneca, GlaxoSmithKline, Merck Sharp & Dohme, and 3M.

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