combination of patchwork fibrosis, fibroblast foci, and microscopic honeycombing as criteria they considered diagnostic of UIP, and some of their illustrations do show fields that could be UIP. But as the authors acknowledge, none of these findings individually has diagnostic specificity, and even this combination could be the result of a variety of processes, including drug reactions, chronic hypersensitivity pneumonitis, connective tissue diseases, or asbestosis. Pathologically, one could also argue that the combination of only patchwork fibrosis and honeycombing (one of Berbescu’s acceptable combinations for diagnosing UIP) in a small specimen has much lower specificity, and it is now recognized that fibroblast foci, often but not exclusively found in areas of dense fibrosis, occur in other interstitial lung diseases. As a further complication, cases of unequivocal UIP can have focal areas that look like nonspecific interstitial pneumonia, this problem is readily addressed in surgical lung biopsies but likely to cause tremendous confusion in TBB.

The strength of the report by Berbescu et al is that they do provide detailed pathologic descriptions of what UIP might look like in TBBs, descriptions that are virtually nonexistent in the literature, and thus they offer a set of criteria that can be tested. As the authors note, the real issue is not whether these criteria are accurate in patients with UIP established on surgical lung biopsy; rather, do they work applied in a prospective and blinded fashion? To this we would add two crucial questions: Do these criteria apply to patients who do not have the expected clinical and radiologic picture of IPF, because this is the setting in which a biopsy is of most importance, and are the features proposed by expert pathologists with a tremendous experience in this area usable by pathologists in the general medical community? These issues are worth investigating. But until such studies are performed, we suggest that the collective wisdom be followed and that TBB not be used to diagnose IPF/UIP.

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Pediatricians Are Not Just Small Internists

We pediatricians like to remind anybody who will listen that children are not just small adults. The diseases of childhood are those of growth and development, and response of the growing child to the external environment. Genetic diseases such as cystic fibrosis and primary ciliary dyskinesia are usually first diagnosed in the young child, and significant congenital abnormalities of the airways, thorax, and lung are diagnosed and treated initially in the first years of life. Therapy is directed at maximizing growth potential of the child, with the recognition by pediatricians that interventions early in life can benefit the growing child and the adult; the child is clearly the father to the man.

Not to put too fine an edge on it, diseases of adulthood and the elderly are often those of physiologic decay and chronic abuse. COPD, lung cancer, alcoholism, obesity-related disorders, coronary artery disease, and hypertension are all good examples. The goal of therapy in adults is often to slow the ravages of aging and to try and reverse the effects of too much food, drink, or tobacco smoke. Because of these differences, it is not unusual for the pediatri-
cian to always look at a disease or symptom through a different lens than the internist. However, this approach may not always be justified and occasionally it can be downright confusing.

In this issue of CHEST (see page 1132), Marchant and colleagues evaluate the epidemiology and therapy of chronic cough in children up to the age of 18 years, using what they refer to as a modification of the pathway developed by Irwin et al for investigating chronic cough in adults. Using this modified pathway, they report that the common causes of cough in adults, the so-called “big three” of upper airway cough syndrome (previously called postnasal drip syndrome), gastroesophageal reflux disease, and asthma, are uncommon causes of cough in young children and that a new disorder that these investigators call protracted bacterial bronchitis occurred in nearly 40% of their cohort, making this diagnosis more than four times as common as the combined prevalence of the big three. Because of this, the authors suggest that fiberoptic bronchoscopy may be the diagnostic test of choice in evaluating chronic cough in young children, and that the most effective therapy for the young child with chronic cough should be a 2-week course of antibiotics.

What are we to make of this study and these results? When the American College of Chest Physicians convened an expert panel to develop an evidence-based approach to managing cough in 1998, it was recognized by the pediatricians on this panel (including this author) that there were few high-quality studies evaluating the etiology of chronic cough in children or the response to therapy. However, published studies suggested that both asthma and gastroesophageal reflux disease were a common cause of chronic cough in children; by invoking biological plausibility, we made the assumption that the big three diagnoses in adults were likely to be among the more common causes of chronic childhood cough beyond the toddler years. We suggested that evaluation for inherited diseases such as cystic fibrosis, primary ciliary dyskinesia, and congenital abnormalities (eg, tracheomalacia) were an essential part of the evaluation of these children. Although published data strongly suggested that the big three causes of cough in adults were also most common in children, we strongly urged that this supposition be validated by well-controlled randomized clinical trials following as closely as possible the algorithm developed by Irwin and colleagues, which has been so successful in evaluating and managing cough in adults.

It is laudable that Marchant and colleagues have taken up this challenge and conducted an evaluation of 105 very young children seen for chronic cough in a referral practice in Queensland, Australia. This is one of the first and certainly the most complete study to do this prospectively in the pediatric population. Unfortunately, what these investigators call a modified adult-type pathway is radically different from the pathway described by Irwin and colleagues. As shown in their Figure 1, all children underwent chest radiography and spirometry (in the older children), and except for the few (n = 2) with resolution of the cough before a bronchoscopy session could be booked, all underwent bronchoscopy and BAL (n = 102) or sputum induction (n = 4) before any further tests were performed. This was despite the fact that only approximately one half of the children had had an undefined trial of inhaled corticosteroids, and a smaller number had received a trial of therapy for either upper airway cough syndrome or gastroesophageal reflux disease. In children with asthma, it is important to clearly identify that medication has been used correctly and appropriately before assuming that this therapy is ineffective. The authors do not report having done this, so it is unclear how many of these children may have had asthma.

In response to a reviewer’s query, the authors stated that in Queensland, parents and physicians prefer performing fiberoptic bronchoscopy under general anesthesia with BAL to having the child undergo esophageal pH probe testing, primarily because the bronchoscopy takes a shorter period of time and does not require restraint of the young child to prevent removing the esophageal pH probe for the 12-h duration of the study. They also stated that parents in Queensland would refuse to accept an empiric treatment course for gastroesophageal reflux disease without first having confirmatory data from an esophageal pH probe study. Thus, it is unclear how many of these children had symptomatic gastroesophageal reflux disease.

This hierarchy of evaluation is the opposite of expectations in North America, where a 1-month course of reflux therapy is thought preferable to conducting a pH probe study, which, in turn, is more acceptable to families than having a child undergo general anesthesia for diagnostic bronchoscopy and lavage because of the risks of bronchoscopy relative to either the pH probe or to the empiric therapy. Most parents in North America would also accept a course of therapy for asthma—including oral corticosteroids—before they would accept a bronchoscopy under anesthesia. Thus, in nearly half of the children in this study, the final diagnosis was made on the basis of an initial bronchoscopy, and this procedure suggested a newly described diagnostic entity of protracted bacterial bronchitis.

The diagnosis of protracted bacterial bronchitis was based on the “history of a moist cough” and either microorganisms (bacteria or virus) in the BAL.
fluid or a "positive response" to antibiotic therapy. However, the term moist cough is subjective and carries no physiologic significance. The authors\(^\text{1}\) suggest that this implies that secretions are moving in the large airway, and they claim that a moist cough in a child is the same as a productive cough in the adult. Nevertheless, in the one publication\(^\text{9}\) that identifies a condition similar to protracted bacterial bronchitis in adults with a chronic cough, none of these adults had a productive cough despite all having copious grossly purulent tracheobronchial secretions. These pediatric patients with protracted bacterial bronchitis did not appear to have copious, purulent tracheobronchial secretions at bronchoscopy.

The adult pathway defines chronic cough as a cough that persists for \(>8\) weeks. This timing was set to decrease the possibility of diagnosing a prolonged postinfectious or subacute cough that would resolve spontaneously. In this pediatric study,\(^\text{1}\) a prolonged cough was defined as a cough lasting for \(\geq 3\) weeks, and thus it is likely that some of these children had postinfectious cough or mechanically induced airway inflammation from the act of coughing itself.

The authors\(^\text{1}\) declare that elevated BAL neutrophil count and the presence of microorganisms (viral or bacterial, pathogenic or nonpathogenic) was the key to the diagnosis of protracted bacterial bronchitis. It is immunologically unclear why children would be prone to have protracted bacterial bronchitis while this is rare in adults.\(^\text{9}\) Indeed, the presence of true protracted bacterial bronchitis in a child would cause most pediatricians to strongly consider the diagnosis of cystic fibrosis, primary ciliary dyskinesia, bronchiectasis, or immune deficiency.

Finally, the “response” to a 2-week course of oral antibiotics should not be considered evidence of protracted bacterial bronchitis without either a follow-up bronchoscopy showing resolution of bacteria and neutrophils or without a placebo-controlled arm to determine if the response to antibiotics was a placebo effect, post hoc ergo propter hoc. It is curious that none of the adults with cough due to unsuspected bacterial suppurative disease of the airways (protracted bacterial bronchitis) responded to a 3-week course of oral antibiotics directed at the organisms identified using a protected brush. Their cough only resolved with an additional course of IV antibiotics.

The authors\(^\text{1}\) began with the assumption that children would be different from adults and therefore the diagnostic protocol must be modified for use in children. Because of this, they did not evaluate the children for the big three before they underwent bronchoscopy and lavage, nor was therapy started that might have resulted in a different set of diagnoses in these children. Children are not little adults and, under the appropriate circumstances, this must be taken into account when designing studies or evaluating therapy. Because most of the subjects in this study were \(<3\) years old, these results probably cannot be generalized to the broader pediatric population. Furthermore, by failing to follow the adult pathway, they may have missed an opportunity to learn when children with true chronic cough can be treated as adults.

The authors\(^\text{1}\) are to be congratulated for undertaking this study, but we need to remember that when pediatricians invoke that "children are not adults" as a reason for significantly altering diagnostic and therapeutic pathways that have been successful in adults, the results of such studies may well be confusing. These results must be replicated in a prospective study of children with a true \((>8\)-week duration) chronic cough, and this new approach must be compared to the proven adult algorithm in a controlled, randomized study. Only then will we learn if pediatricians must treat their patients with a chronic cough differently from internists, as Marchant and colleagues\(^\text{1}\) suggest they should.

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REFERENCES

8 Rubin BK. What does it mean when a patient says, “My
“Make The Cough Go Away”

Cough is an important medical and economic problem. It is a common symptom of a number of respiratory and nonrespiratory disorders. It has a substantial impact on health; it represents the most common symptom leading patients to consult with their doctor.1

Traditionally, cough has been categorized as follows based on duration: acute cough, lasting <3 weeks; subacute cough, lasting 3 to 8 weeks; and chronic cough, lasting >8 weeks.2 Most of the published studies on cough have concentrated on chronic cough. In this issue of CHEST (see page 1142), Kwon et al3 make an important contribution and fill a void in the literature by prospectively looking at the causes of subacute cough. They report on 529 patients with a complaint of cough from Seoul, Korea, but focus on the 184 patients who met their criteria for subacute cough. Their initial approach included obtaining a medical history, and performing a physical examination, pulmonary function studies, including a methacholine broncho-provocation challenge (BPC), chest roentgenogram, and an induced sputum test measuring eosinophils. No initial therapy was given. Patients were seen 7 to 10 days later. Cough had spontaneously resolved in 62 of 182 patients (34%). A diagnosis of “postinfectious cough,” based on predefined criteria, was given to most patients with spontaneously resolving cough (74.3%).

At the second visit, 122 patients continued to complain of cough. In 97 of 122 patients, cough was thought to occur either secondary to postnasal drip (72 patients) or after infection (25 patients), and those patients were treated with a first-generation antihistamine-decongestant (chlorpheniramine, 4 mg, and pseudoephedrine, 30 mg three times per day) for 3 weeks. Sixty-eight of 97 patients (70%) showed significant improvement with the antihistamine-decongestant therapy. In the 29 patients who did not respond (plus 25 patients who initially had no findings of postnasal drip or postinfectious cough), the results of BPC analysis and induced sputum testing were reviewed. Thirty-eight of 54 patients had a positive results for BPC, induced sputum testing, or both, and all but 3 of these patients responded to therapy with inhaled corticosteroids. Cough-variant asthma was diagnosed in patients with a positive BPC finding, and eosinophilic bronchitis was diagnosed in those patients with a negative BPC finding but eosinophils measured on sputum samples. The 16 remaining patients with negative BPC and sputum (plus the 3 patients who did not respond to therapy with inhaled corticosteroids) underwent 24-h esophageal pH monitoring, CT scan of the chest, and bronchoscopy.

The authors came to several conclusions: One, cough after infection is the most common cause of subacute cough (48%), postnasal drip is the second most common (33%), and cough-variant asthma is the third most common (16%). Second, in a significant percentage of patients with subacute cough (34%), it is self-limited and will resolve without treatment. Third, most patients with subacute cough that spontaneously resolves had postinfectious cough (74%). The authors recommend that BPC be delayed until after an initial period of either no treatment or antihistamine-decongestant treatment for postnasal drip (unless asthma was strongly suspected).

Although we think that this study of subacute cough is a valuable contribution to the literature, we believe that some of their results are subject to a different interpretation. We think that the distinction between postinfectious cough and postnasal drip-induced cough is not nearly as clear-cut as they suggest. In this study, cough was diagnosed as being postinfectious when the etiology was believed to have been an upper respiratory tract infection (ie, a “common cold”). Because the best available evidence suggests that the predominant mechanism of acute cough from the common cold is postnasal drip,4 it is quite likely that many of the subacute coughs categorized as being postinfectious could alternatively have been due to a lingering postnasal drip. Furthermore, it has been reported that the diagnosis of postnasal drip (or at least cough responsive to antihistamine-decongestant therapy) cannot be eliminated based on a lack of symptoms or signs because up to 20% of patients whose cough responds to antihistamine-decongestant therapy have no manifestations of postnasal drip (called silent postnasal drip).5

Second, while it is helpful to know that subacute cough may resolve spontaneously, it does not follow that treatment with an antihistamine-decongestant should be withheld. Patients with cough are seeking help for a bothersome symptom. Because it is not possible to predict in which patients subacute cough will spontaneously resolve or how long it might take, it does not make sense to withhold treatment. The patient is suffering from the cough. The “up-front” use of an antihistamine-decongestant frequently abbreviates the cough with minimal side effects.4,5