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Cough swabs less useful but induced sputum very useful in symptomatic older children with cystic fibrosis

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Microbiological surveillance continues to be an important aspect of cystic fibrosis care.[1,2] In young children, such surveillance is complicated by the inability to expectorate sputum. Thus, cough swabs are routinely used to obtain samples, and some cystic fibrosis centres use regular bronchoalveolar lavage or induced sputum sampling.

In *The Lancet Respiratory Medicine*, Katherine Ronchetti and colleagues[3] compared the diagnostic yield of bacterial culture results from 167 paired induced sputum and cough swab samples in patients aged 6 months to 18 years.[3] In a subset of their study they compared bacterial yield from induced sputum to bronchoalveolar lavage. Induced sputum samples had a significantly higher bacterial yield than cough swab samples: 86 different pathogens were isolated in total from the samples, and 79 [92%] of these were identified by sputum induction whereas 27 [31%] were on cough swab samples (p<0·0001). This difference suggests that induced sputum can detect pathogens from the lower airways that cough swabs cannot. A strength of this first stage of the study was high participant numbers: 124 patients were recruited from whom 167 paired samples were successfully taken. Children younger than 6 years were also well represented in this part of the study (n=72). In view of these results, induced sputum appears to be far superior to cough swab for detection of lower airway pathogens in patients with cystic fibrosis. These findings are useful and consistent with other studies that showed improved microbial yield of induced sputum over upper-airway sampling in children.[4,5] The poor diagnostic value of cough swabs is also consistent with other findings that oropharyngeal swabs bear little-to-no relation to lower-airway pathology in young children with cystic fibrosis.[6]

In a subset of largely symptomatic patients, Ronchetti and colleagues compared bacterial culture yield from 41 paired induced sputum samples and single-lobe, two-lobe, and six-lobe bronchoalveolar lavages. Sequentially more pathogens were isolated with bronchoalveolar lavage as more lobes were lavaged. Sputum induction isolated 27 (69%) of the 39 total pathogens detected by both techniques versus 22 (56%) on single-lobe bronchoalveolar lavage, 28 (72%) on two-lobe bronchoalveolar lavage, and 33 (85%) on six-lobe bronchoalveolar lavage. Because different pathogens were detected between induced sputum and bronchoalveolar lavage, Ronchetti and colleagues[3] advocate for a combination of induced sputum and six-lobe lavage as the new standard of care for lower airway pathogen surveillance. They also make a case for the use of induced sputum as a non-invasive surrogate for bronchoalveolar lavage in symptomatic patients and propose that bronchoalveolar lavage should be reserved for patients with persistent signs or symptoms not explained by sputum induction. In symptomatic patients, induced sputum will correctly describe pathogens in almost two-thirds of cases

and, if correctly used, might reduce the need for bronchoscopy.

Importantly, five (13%) of the total 39 pathogens identified were only detected by the induced sputum technique. This highlights an issue often encountered in diagnostic studies, of how to best define the gold standard. For example, bacteria found only from cough swabs, but not lower airway samples, will easily be discounted as normal commensal throat flora. The same suggestion could be made for induced sputum, as these samples pass the upper airways during collection. However, the authors suggest that the pathogens that were identified solely from induced sputum might be from the large intrathoracic airways, which are bypassed in a bronchoalveolar lavage procedure. This seems reasonable, particularly as bacterial bronchitis is common in symptomatic children with cystic fibrosis. Rather than discarding the pathogens that were exclusively found on induced sputum, the authors have included them in a combined gold standard, thereby highlighting the additional value that sputum induction might have for pathogen detection in symptomatic children with cystic fibrosis.

Care should be taken to not simply extrapolate results from the smaller subgroup of Ronchetti and colleagues' study.[3] Only small numbers of children younger than 6 years were recruited, and the sample was too small to enable a separate analysis of children younger than 6 years. Also, for most samples taken in the part of the study comparing sputum induction with bronchoalveolar lavage, participants were symptomatic (ie, had respiratory exacerbations).

The distinction between asymptomatic young children and symptomatic older children is important. Cystic fibrosis lung disease starts in the small airways and in young children, infection might be present in the absence of symptoms.[7] Induced sputum might miss infection that will lead to structural lung damage in young asymptomatic children. Indeed, the largest study thus far that compared 61 paired sputum induction and bronchoalveolar lavage samples from young asymptomatic children suggested that induced sputum samples only had a 36·8% (95% CI 16·3–61·6) sensitivity to detect microbiota from the lower airway in cystic fibrosis using bronchoalveolar lavage as the gold-standard method.[8]

Infancy and the early preschool years comprise a vital period when structural changes in the lungs of people with cystic fibrosis begins.[7] Therefore, while Ronchetti and colleagues[3] provide robust evidence for the usefulness of sputum induction in symptomatic older children with cystic fibrosis, future efforts should be focused on developing an accurate non-invasive method for microbiological surveillance in young asymptomatic children.

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