‘Semper aliquod novi Cystic Fibrosis adferre’

Cystic Fibrosis always Brings Us Something New – with Apologies to Pliny the Elder

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The major effect of cystic fibrosis (CF) has long been recognized to be on the lungs; much of the mortality and morbidity is related to chronic bronchial sepsis and inflammation, culminating in bronchiectasis, hypoxic cor pulmonale and death. When CF was first described, the major pathogen isolated was *Staphylococcus aureus*, and the major therapeutic goal the elimination of that micro-organism. With aggressive anti-staphylococcal therapy and better survival, *Pseudomonas aeruginosa* colonization became the next threat. Early treatment with ciprofloxacin, nebulised colomycin and other antibiotics, and intravenous treatment have greatly reduced the effects of this pathogen, while not eliminating it completely. New infections have set us management conundrums which would have been undreamed of thirty years ago. These include the various clinical phenotypes of the *Burkholderia* genomovars [1], atypical mycobacteria [2] and *Aspergillus fumigatus* [3].

New methods for investigating the respiratory tract have also appeared, and these have largely focused on the airway rather than the distal lung parenchyma. They have resulted in insights into the fundamental biology of the airway, as well as stirring up new controversy. The composition and tonicity of airway surface fluid [4, 5]; the mechanisms of *P. aeruginosa* adherence to the epithelium, be it upregulation of cell surface receptors [6], an effect of bacterial internalisation [7] or interference with

the anti-bacterial effects of cationic peptides [5, 8]; whether the CF airway is pro-inflammatory, and airway inflammation can occur in the absence of infection [9]: these are all exciting areas for further research. CF has traditionally been thought of as an airway disease, and investigations such as fibre-optic bronchoscopy have been directed at the bronchial tree. In this issue of *Respiration*, a new twist to the story of the pulmonary complications of this disease appears. Häusler et al. [10] described a young man with proven CF who developed a systemic illness initially thought to be due to *Mycobacteria abscessus* infection. To their surprise, an open lung biopsy (OLB), an unusual investigation to be performed in CF, showed not mycobacterial infection, but bronchiolitis obliterans/organizing pneumonia.

Treatment with prednisolone, which otherwise would probably not have been risked in the presence of atypical mycobacteria in the sputum, resulted in complete recovery. This paper reports an association which is of interest in itself, but also raises issues with regard to the investigation of the CF patient with atypical features or who is doing badly on conventional therapy. What will be the role for lung biopsy in the 21st century in CF, and what is the preferred technique?

It is likely that lung biopsy will rarely be employed in CF, but there will be clear-cut indications. These may include the assessment of positive cultures for organisms

that may do anything from being harmless commensals to causing devastating disease, such as atypical mycobacteria [2] or aspergillus [3]; the investigation of complications of new treatments, particularly if, as seems likely, more potent anti-inflammatory agents are used to damp down the exuberant host response in the CF airway; and in patients whose pulmonary disease is running an atypical course.

The preferred technique will vary with the age of the patient and the nature of the abnormality. In children, my own preference [11] would always be for an OLB, rather than transbronchial (TBB). In adults, although a TBB may be less invasive, in view of the risk of bleeding and pneumothorax which is already a part of CF, and the relatively small biopsies obtained, a video-assisted OLB may

be better. OLB is certainly a very safe technique in expert hands, even in sick patients with interstitial lung disease or hypertensive pulmonary vascular disease secondary to congenital heart disease.

‘Time does not wither, nor custom stale, my infinite variety’ quoted Sherlock Holmes. He was describing a clever trick to catch a criminal, but could equally have been talking about CF lung disease. If we are to give all our CF patients the best chance of longevity, we need to continue to be alert to new facets of CF lung disease, be flexible and open-minded in our approach, and use the most modern investigative techniques to obtain an accurate diagnosis. We should not be afraid to include OLB in this armamentarium if a clinical question arises in a CF patient that only this technique can answer.

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