Bronchial biopsy

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Introduction

It is important at the start of this summary to emphasise the difference between bronchial biopsy (also termed endobronchial (EBB), mucosal or airway wall biopsy) and transbronchial biopsy. In the former, a relatively superficial sample of airway wall is obtained under direct vision; in the latter, the bronchoscope is wedged in an airway and the forceps are advanced distally with the deliberate aim of piercing the airway wall and sampling the alveolar region more distally. Indications for the two procedures differ completely and there are also significant differences in their safety profiles. This summary and lecture will deal entirely with endobronchial biopsy and not at all with the transbronchial technique.

Indications

In contrast to the frequency with which EBB is employed in adults, largely in the investigation of suspected malignancy, the technique is employed relatively infrequently in paediatrics. Indeed, in a recent State of the Art article on Pediatric Bronchoscopy by Nicolai, the technique was barely mentioned. Centres conducting programmes of clinical research, such as our own, will often perform endobronchial biopsies opportunistically at the time of a clinically-indicated bronchoscopy. Purely clinical indications for EBB include both focal and generalised conditions. Examples of the former would be suspected endobronchial tuberculosis, polyps and other granulomatous growths, and less common conditions such as papillomatosis. More commonly, samples will be taken from throughout the airway to aid diagnosis of a generalised, non-focal disorder. In asthma, there is a move towards phenotype-driven treatment, which can utilise either bronchoscopic samples or less invasive samples such as induced sputum and or exhaled breath. In conditions such as cystic fibrosis
(CF), there is increasing recognition that changes in the bronchial lumen measured by bronchoalveolar lavage (BAL), may not mirror those in the airway wall itself. This has led to the inclusion of airway wall biopsies in some research studies, although the clinical relevance of such sampling remains to be determined.

**Technical issues, limitations and interpretation**

Paediatric bronchoscopy and biopsy must be performed by someone specifically trained and experienced in the techniques; success in obtaining samples of sufficient quality to be processed and interpreted will be critically dependent on the skill of the operator.

Many designs of forceps are available including alligator jaw, rat-tooth, cup etc. Choice of forceps will depend in part on the familiarity of the operator and possibly also the question being addressed, although rigorous comparisons of biopsy quality with the different types of forceps has not been published. The size of forceps used will be completely dependent on the size of child. In small children, in whom a 3.6 mm bronchoscope has to be employed, the biopsy channel is only 1.2 mm in diameter; larger bronchoscopes have a 2.2 mm channel, although even these are significantly smaller than the 2.8 mm channels in the majority of adult-sized bronchoscopes. Interestingly, paediatric studies conflict with regard to whether larger forceps necessarily generate biopsies of better quality, although this seems intuitively likely to be the case.

In experienced hands, several biopsies can be performed within a period of a few minutes; technical difficulty and hence the time required to obtain adequate samples, is increased greatly by the presence of significant amounts of mucus within the airway, such as seen in CF. In chronic inflammation, the airway may be rather friable, which will also increase the challenge if surface bleeding reduces visibility. A further limitation is that one samples only the proximal (maybe to 7th or 8th generation) airways; smaller airways will not be accessible and processes which preferentially affect the more distal respiratory tree may therefore be less easily assessed. In addition, because of the nature of the forceps, it is difficult, if not impossible to sample from a flat surface; samples will be obtained from either a carina or a lesion which projects into the airway lumen. It is unknown whether changes at a carina
(where there is thought, for example, to be a high proportion of epithelial progenitor cells), accurately reflect those at other areas within the bronchial tree.

**Safety issues**

Significant risks, in particular pneumothorax, have been associated with *transbronchial biopsy (TBB)*. In contrast, *endobronchial biopsy* carries very little theoretical risk of harm and few, if any, reports of significant side effects have appeared in the published literature. Unlike with TBB, the biopsy forceps remain in sight for the whole of the procedure; positioning can be accurately determined and areas of increased risk, for example those with abnormal vasculature, will be avoided. One might consider that inflammatory airway conditions might pose an increased risk of bleeding due to a hyperaemic mucosa, although a recent report from our group in children with CF, many of whom had significant airway inflammation, showed this not to be the case. We have also reported a good safety profile of bronchoscopy with airway wall biopsy in children with asthma and preschool wheeze.

*What can endobronchial biopsies tell us?*

With basic stains, such as haematoxylin and eosin (H&E; see figure), many histological structures can be visualised. If the biopsy is of sufficient quality, the ciliated respiratory epithelium, together with mucus-containing cells such as goblet cells will be easily recognisable. These surface structures are often lost due to the method of obtaining the biopsy however. The reticular basement membrane (RBM) can be identified and measured; indeed it is from biopsy studies that we appreciate the relationship between RBM thickening and asthma. More recent work has shown this to be the case for other inflammatory airways diseases such as CF and PCD as well. The area occupied by smooth muscle can be quantified; this has been shown to be increased in asthma and to correlate with severity. We have also reported significant increases in smooth muscle mass in CF. Whilst this measurement is fairly straightforward, determining whether this increase is due to hypertrophy or hyperplasia (or both) requires more complex stereological-based analysis. Submucosal glands are clearly recognisable as such and the area they occupy can be quantified in a similar manner; mucus and serous cells can be differentiated by
processing with alternative stains such as PAS and alcian blue. Cells of the submucosa can be difficult to identify on basic stains such as H&E and will usually require the use of immuno-staining with antibodies directed at specific cell surface markers.

*Brush biopsy*

This is included here for the purposes of completeness, as some people refer to bronchial brushing as a ‘brush biopsy’. With this technique, a cytology brush is rubbed against the airway surface, in a fashion very similar to that employed in the nose in the diagnosis of PCD. Cell yield is usually largely epithelium and will vary greatly depending, in part, on the size of brush used. In adult practice, this is performed as part of the routine investigations for suspected malignancy. It can be useful in diagnosing endobronchial tuberculosis, as the sample can be placed onto a slide and stained for mycobacteria. Ciliary beat frequency can also be assessed from these samples, although in practice this is rarely necessary as nasal samples suffice. Cells can be placed into culture, although this is notoriously difficult; significantly different responses to viral infection by cells from asthmatic adults have been reported using these techniques. Several groups have reported safety and success of a non-bronchosopic alternative to sample such cells, which may have important implications in terms of time and resources.
Figure Legends

Sections of a good quality endobronchial biopsy stained with haematoxylin and eosin (H&E) and low (a) and higher (b) power, demonstrating recognisable histological features (kindly provided by Dr T Hilliard).
Further reading


