Pediatric Pulmonology 31:150±164 (2001)

State of the Art

Pediatric Bronchoscopy

T. Nicolai, MD*

Summary. Diagnostic flexible endoscopy for pediatric respiratory diseases is performed in many centers. Technical advances have resulted in performance of interventional bronchoscopies, and new diagnostic indications are being explored. Indications with documented clinical benefit include congenital or acquired progressive or unexplained airway obstruction. Pulmonary infections in immunodeficient children who do not respond to empirical antibiotic treatment may be diagnosed by bronchoscopy and bronchoalveolar lavage (BAL). The potential usefulness of bronchoscopy and BAL for managing chronic cough, wheeze, or selected cases with asthma or cystic fibrosis requires further study. The use of transbronchial biopsies (TBB) is established in pediatric lung transplantation. The role of TBB in the diagnosis of chronic interstitial lung disease in children remains to be determined. For a number of interventional applications, rigid endoscopy is required, and pediatric bronchoscopists should be trained in its use. Complications in pediatric bronchoscopy are rare, but severe nosocomial infection or overdosing with local anesthetics has occurred. The issues of quality control, video documentation, interobserver variability of findings, and educational standards will have to be addressed in the future as bronchoscopy use becomes less restricted to only large pediatric pulmonary units. Pediatr Pulmonol. 2001; 31:150±164. ß 2001 Wiley-Liss, Inc.

Key words: bronchoscopy; children; biopsy; lavage.

INTRODUCTION

The use of the flexible endoscope in investigating pediatric respiratory problems like stridor in infants or pulmonary infections in immunosuppressed children has become routine in many centers. A number of recent books1–3 review articles, and position statements have been published on this subject.4–7 The investigational use of bronchoscopy and bronchoalveolar lavage (BAL) has led to significant insights into various pulmonary disease processes. Retrospective studies indicate a high diagnostic yield,8–11 but the benefit for the patient will depend on careful evidence-based patient selection. The decision to bronchoscope a child is best guided by anticipating the parent’s view regarding possible therapeutic consequences of the procedure. For a surprising number of clinical situations there is either a lack of prospective data or a lack of consensus on the utility of airway endoscopy. New information is now available regarding possible complications of fiberoptic bronchoscopy such as nosocomial infection or consequences of the overuse of local anaesthetics. The issues of quality control, video documentation, interobserver variability of findings, and educational standards will have to be addressed in the future as bronchoscopy use becomes less restricted to large pediatric pulmonary units.

While the use of flexible bronchoscopy is regarded as a standard diagnostic tool in reviews from North America,7 a recent monograph from Europe12 still regards the rigid scope as the everyday workhorse; this difference may have to do with local practices. However, the availability and cost of a flexible bronchoscope compared with and added to that of rigid equipment (which will allow foreign body extraction as well as many diagnostic interventions) play a role in many parts of the world. On the other hand, lack of ready access to an operating theater or anesthetist, or a tradition of limiting rigid endoscopy to surgeons, will favor the use of a flexible instrument by pediatric pulmonologists. The use of the flexible endoscope is indispensable if functional assessment of the airway is required (stridor, suspected tracheobronchomalacia). The ease of its use under sedation and local anesthesia has made it the first choice for most diagnostic endoscopies. The main weaknesses of flexible endoscopy are the sub-

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optimal delineation of the immediate subglottic area and insufficient visibility if sedation is not adequate.

Rigid endoscopy is ideal for the documentation of glottic and subglottic pathology (cleft, high fistula) and for interventions (e.g., foreign body extraction, stents, laser surgery). If surgical intervention becomes necessary, high-resolution delineation of the airway structures will often be required by the surgeon. It may be necessary to decide whether a stenosis is rigid or flaccid by directly probing the lesion. The use of the laryngoscope, with a short-acting anesthetic, and inspection through an ultra-thin rigid telescope, can rule out a subglottic foreign body in severe or atypical group without touching mucosal surfaces. This may sometimes be the safest option. Rigid bronchoscopy may also be necessary in some cases for transbronchial biopsy, fistula detection, and airway recanalisation in tuberculosis (TB) or tumors. While the number of children requiring rigid endoscopy is not large, a place for both techniques will remain in the future; the relative strengths of both methods are summarized in Table 1. While it is easy to predict that many more pediatricians will be trained in flexible rather than rigid endoscopy, proficiency at both would be ideal.

ANESTHESIA/SEDATION

While rigid bronchoscopy always requires the use of general anesthesia, flexible endoscopy can be done under sedation. Guidelines have been laid down by the American Academy of Pediatrics regarding the monitoring and management of children during sedation. Very young children will often need deep sedation or anesthesia for the examination to be done with a similar degree of comfort and painlessness, as is the current standard for other therapeutic and diagnostic procedures in children. It is unacceptable to bronchoscope a toddler under light sedation and restraints, thus obtaining only suboptimal endoscopic information due to movement, coughing, and obstructed views. Some groups, therefore, prefer to perform flexible bronchoscopies in children under general anesthesia.

The progression from consciousness to deep sedation and anesthesia is gradual when repeated doses of commonly used drugs like midazolam are given. The bronchoscopist must anticipate that protective airway reflexes may no longer be present and that normal respiratory control may have ceased. A second physician should be present to monitor the patient, because it is very difficult for the bronchoscopist to observe the child while he/she performs the procedure. A published statement only requires that someone skilled in i.v. line placement be present during pediatric bronchoscopy. However, dangerous situations may arise, which may be difficult to manage without already established venous access. Commonly used sedative procedures are shown in Table 2, but their application requires experience.

With flexible bronchoscopy, the use of a local anesthetic is routine (Table 2). It is usually applied to the region of the vocal cords, then to the trachea above the carina and the bronchi. It is important to adhere to safe doses for these agents, because lethal complications of overdoses have been reported. Inhalation of topical anesthetics via a facemask is used in adults before bronchoscopy and has been reported in children, but we have found this difficult in children due to the bad taste of lidocaine. When a flexible endoscope with a suction channel is used, the local anesthetic can be sprayed directly onto the larynx. However, lidocaine has been shown to exaggerate laryngomalacia and should therapeutically administered.

### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ATS</td>
<td>American Thoracic Society</td>
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<tr>
<td>BACTEC</td>
<td>Radiometric detection of tuberculosis organisms in fluid culture media</td>
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<td>BAL</td>
<td>Bronchoalveolar lavage</td>
</tr>
<tr>
<td>BPD</td>
<td>Bronchopulmonary dysplasia</td>
</tr>
<tr>
<td>CCD</td>
<td>Charge coupled device</td>
</tr>
<tr>
<td>CF</td>
<td>Cystic fibrosis</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>CPAP</td>
<td>Continuous positive airway pressure</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>DNASe</td>
<td>Desoxyribonuclease</td>
</tr>
<tr>
<td>ECP</td>
<td>Eosinophil cationic protein</td>
</tr>
<tr>
<td>EM</td>
<td>Electron microscopy</td>
</tr>
<tr>
<td>EPX</td>
<td>Eosinophil protein X</td>
</tr>
<tr>
<td>ERS</td>
<td>European Respiratory Society</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive care unit</td>
</tr>
<tr>
<td>ILD</td>
<td>Interstitial lung disease</td>
</tr>
<tr>
<td>LLLMI</td>
<td>Lipid-laden macrophage index</td>
</tr>
<tr>
<td>LTC4</td>
<td>Leukotriene C4</td>
</tr>
<tr>
<td>LTB4</td>
<td>Leukotriene B4</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>NICU</td>
<td>Neonatal intensive care unit</td>
</tr>
<tr>
<td>OLB</td>
<td>Open lung biopsy</td>
</tr>
<tr>
<td>PCP</td>
<td>Pneumocystis carinii pneumonia</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
</tr>
<tr>
<td>PEEP</td>
<td>Positive end expiratory pressure</td>
</tr>
<tr>
<td>TBB</td>
<td>Transbronchial biopsy</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TNF-alpha</td>
<td>Tumor necrosis factor alpha</td>
</tr>
<tr>
<td>TXA2</td>
<td>Thromboxane A2</td>
</tr>
</tbody>
</table>

### TABLE 1—Relative Strengths of Flexible and Rigid Bronchoscopy

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Flexible</th>
<th>Rigid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchoscopy1</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>Preoperative assessment</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Fistula; cleft</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Bronchoalveolar Lavage</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Evaluating laryngeal function</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>Interventions</td>
<td>(foreign body, laser)</td>
<td>–</td>
</tr>
</tbody>
</table>

1+ +, excellent; +, good to fair; –, less suitable to not possible.
fore be applied only after assessment of the larynx in infantile stridor.

Oxygen delivery or the application of continuous positive airway pressure (CPAP) during flexible endoscopy will make the procedure safer and prevent desaturations particularly in small children. For this purpose, oxygen administration through nasal prongs or through the suction channel has been used. If the latter method is used, the endoscopist should be aware that local increased intra-airway pressure and possibly pneumothorax can develop if the endoscope is passed into smaller airways. Other groups have developed ventilation masks with appropriate ports for the endoscope; commercially available swivel adapters with a port may also be used with a conventional anesthesia mask. The application of a mask will sometimes require more sedation than the passage of the endoscope through the nose after local anesthetic alone. A laryngeal mask airway has been used by others, but deep sedation or anesthesia is needed to tolerate this device. While all information on upper airway dynamics is lost, contamination of the bronchoscope is decreased; this technique is suitable for BAL or interventional bronchoscopies.

The use of inhalation anesthesia for rigid bronchoscopy can result in occupational exposure of the personnel above accepted safety limits. Appropriate technical measures can avoid this (e.g., scavenging systems blowing fresh air from above the patient’s head) and exposure may be less during flexible endoscopy. Intravenous medication is preferable in many cases. Low-dose propofol has been used for sedation and higher doses for anesthesia. Propofol is not approved for children below age 3 years in some countries. Higher doses can cause apnea, and an anesthetist should be present when this drug is used. Usually, some analgesia is also required, and short-acting opioids appear appropriate, as no postprocedure pain is expected (Table 2).

Monitoring during bronchoscopy has been improved greatly by the use of pulse oximetry. If pulse oxymetry fails due to technical or other reasons, one should not go ahead with bronchoscopy. Endexpiratory CO2 monitoring will allow the early detection of significant airway obstruction or apnea (no PECO2 detected) or hypoventilation (increasing PECO2) during fiberoptic endoscopy, although absolute values will usually differ from blood gas analyses.

**TABLE 2—Sedation/Analgesia for Fiberoptic Bronchoscopy**

<table>
<thead>
<tr>
<th>Nothing per os</th>
<th>6 h food, 4 h clear liquids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premedication: Age &gt; 1 year:</td>
<td></td>
</tr>
<tr>
<td>Atropin</td>
<td>0.02 mg/kg (p.o., p.r.)</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.5 mg/kg (p.r., p.o.)</td>
</tr>
<tr>
<td>Sedation</td>
<td></td>
</tr>
<tr>
<td>i.v. line</td>
<td>Establish before start of procedure</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.1 mg/kg/dose i.v., total maximum dose 0.2–0.3 mg/kg i.v., flush well; second dose: only if insufficient after 1–5 min</td>
</tr>
<tr>
<td>And/or Propofol</td>
<td>0.5 mg/kg/dose, repeat until adequate sedation (maximum 3.5 mg/kg), followed by (or replaced by) 0.1 mg/kg/min (apneas, hypoventilation possible)</td>
</tr>
<tr>
<td>Additionally (if required to suppress cough)</td>
<td></td>
</tr>
<tr>
<td>Pethidin</td>
<td>0.5–2 mg/kg i.v. or</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>0.5 mcg/kg/min or</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>0.05–0.1 mcg/kg/min</td>
</tr>
<tr>
<td>No codeine except possibly for CF patients &gt;6 years, 7.5–15 mg</td>
<td></td>
</tr>
<tr>
<td>Topical anesthesia</td>
<td></td>
</tr>
<tr>
<td>Lidocaine 2%</td>
<td>0.5–1 mL/dose (each with 9 mL air in 10 mL syringe); maximal total dose 4 mg/kg, i.e., 0.2 mL/kg of 2% solution</td>
</tr>
<tr>
<td>First dose intranasally, second dose to vocal cords, then carina, bronchi as required</td>
<td></td>
</tr>
</tbody>
</table>

1 Caveat: propofol and opiates (and rarely midazolam) may cause apnea. Propofol not allowed < 3 years in some countries. Postprocedure surveillance for 2–4 h, discharge only if accompanied by adult.

**DOCUMENTATION**

Video cameras and displays have become widely available, and findings should be documented in all cases by description, still photographs, and video. Video documentation will allow reexamination of the films after the procedure, demonstrate the results to other physicians (e.g., if surgery is planned), and aid in discussing the results with parents. Also, changes over time will make comparisons possible, and this is much preferable to still shots with a conventional camera. It is useful to have a microphone for simultaneous recording of breath sounds indicating phases of respiration, and voice recordings regarding sedation status or the patient’s responses to procedures. This will allow precise documentation of diagnoses like vocal cord paralysis or dysfunction.
COMPLICATIONS

Many centers perform pediatric bronchoscopies frequently (up to 600/year/center), and data from larger surveys regarding the safety of the procedure have become available. Complications of flexible bronchoscopy are rare, but two pediatric fatalities have been reported. Local anesthetic overdose has been implicated in the death of a young healthy volunteer, and an adult died from sepsis after BAL. In hospitals with smaller numbers of endoscopies or for procedures done in outpatient offices, the complication rate has only rarely been documented. Some children are at greater risk than others, e.g., transient hypoxia was reported in 23%, and one of 30 patients experienced a bradycardic event, when children with wheeze underwent bronchoscopy and BAL. While modern sedatives may tempt one to bronchoscope in any setting, the risks involved should not be underestimated.

Recently, it has become clear that infection control is an important consideration in flexible endoscopy, as transmission of bacteria has been reported. The greatest problem is usually proper disinfection of the thin suction channel and valves. If endoscope surfaces become brittle from use, bacteria may penetrate into the cracks around the optic fibers and cables. Therefore, leak detection with appropriate devices must be performed regularly, and manual cleaning with the use of brushes for the suction canal is important immediately after each endoscopy. Washing/disinfection machines for endoscopes will not obviate the need for the manual removal of secretions from the critical surfaces. Regular surveillance programs to detect bacterial contamination are necessary at every institution performing pediatric bronchoscopies.

While rigid bronchoscopies may cause bacteremia, flexible bronchoscopy with BAL in immunocompetent children may induce high fever but not usually bacteremia. One case of rapidly fatal septic shock in a child with primary immunodeficiency and pneumonia followed BAL, this indicates that antibiotics should be considered at least immediately after the procedure in children who are not immunocompetent and who have acute pulmonary infections. However, most of these children will be on empirical antibiotics even before BAL and the rapid development of sepsis is unlikely.

DIAGNOSTIC BRONCHOSCOPIES

Clinical Indications

Inspiratory Stridor

The diagnostic utility of bronchoscopy is well-established for airway obstruction of unknown origin, and the most frequent indication is congenital stridor. For example, in a retrospective analysis of 53 bronchoscopies for noisy breathing, it was documented that a clinically meaningful result was found in 96% of cases. While this is a very high yield, it does not indicate that every child with infantile stridor will benefit from bronchoscopy, similar restrictions hold for many other applications of bronchoscopy or BAL. Most authors agree that noisy breathing should be investigated endoscopically when it is progressive or causes apneas, difficulty in feeding, or growth retardation, or when symptoms point to a diagnosis other than infantile laryngomalacia. During the initial clinical evaluation, the posterior part of the tongue should be palpated at least if apneic episodes are reported by the parents, because a thyroglossal cyst can cause sudden asphyxiation. It is now known that the endoscope must be advanced beyond the vocal cords, even if inspiratory collapse of the supraglottic structures is seen and felt to be responsible for stridor. Laryngomalacia can be associated with subglottic or tracheal obstructions such as hemangioma or tracheomalacia in up to 15% of children. Vocal cord paralysis has been implicated as the second most frequent cause of neonatal stridor. Children with Chiari malformation and respiratory difficulties may have vocal cord paralysis, which improves after decompression surgery.

Vocal cord dysfunction was recently recognized in atypical asthma in children and adolescents (e.g., refractory to standard therapy despite good compliance, or with severe unexplained episodes of stridor or dyspnea). In adults, deep inspiration sometimes allows for direct observation of inspiratory glottic closure, but this is more difficult in children. A paradoxical inspiratory narrowing of the anterior portion of the vocal cords has been demonstrated in pediatric patients as well. However, it is currently unknown whether this is a pathognomonic phenomenon. A normal laryngoscopy during a symptom-free interval does not exclude the diagnosis.

Expiratory Wheezing or Rhonchi

Expiratory wheezing or rhonchi will also be an indication for endoscopy, if other causes such as asthma or cystic fibrosis (CF) have been ruled out, or if the obstruction is unilateral. Foreign bodies, tracheobronchial or vascular malformations, and intrathoracic airway malacia or stenosis are occasionally found. Tracheomalacia is common after esophageal atresia and tracheo-esophageal atresia, and is easily identified by the often almost total collapse of the tracheal lumen at the site of the crossing brachiocephalic artery. Other diagnostic options such as a lateral chest X-ray, computed tomography (CT) scan, and magnetic resonance imaging (MRI), will often not give sufficient information to obviate endoscopy. Compression of the left main stem bronchus was the focus of a recent article, and the most frequent cause seems to be an abnormal prespinal position.
of the descending aorta, which compresses the bronchus against the left pulmonary artery. Left atrial enlargement can also compromise the lumen of the left main-stem bronchus.

A particularly difficult diagnosis is bronchomalacia,\textsuperscript{50,51} and no generally accepted diagnostic criteria are available. While central airway closure during quiet spontaneous breathing must be considered abnormal, the same would be normal when the patient coughs or uses expiratory muscles during bronchoscopy. It has been suggested that in normal airways the cross-sectional area will not decrease by more than 25\% during spontaneous breathing.\textsuperscript{52} However, this study used an unspecified clinical diagnosis of tracheobronchomalacia as the gold standard and analyzed only seven cases and eight controls, which makes it difficult to generalize the findings. The endoscope itself may cause increased resistance with forced inspiration and active expiration, leading to a false diagnosis of tracheobronchomalacia, or to inadvertent positive end-expiratory pressure (PEEP) and stenting of the airway (masking real tracheobronchomalacia). No data are available on the normal in vivo stability of children’s airways during bronchoscopy (e.g., transmural pressures vs. changes of airway size and collapse), but animal experiments show a greatly increased collapsibility of immature airways.\textsuperscript{53} It is difficult to make a firm diagnosis of tracheobronchomalacia from a bronchoscopic examination alone at the present time.

**Chronic Cough, Wheezy Bronchitis**

Bronchoscopy is often included in the diagnostic workup of unexplained chronic cough and wheeze, but the diagnostic yield will depend largely on patient selection. Other diseases, such as CF, asthma, immunodeficiency, gastroesophageal reflux, and chronic aspiration, should be ruled out before endoscopy, and cough variant asthma will be a frequent diagnosis.\textsuperscript{54} A recent study found that a diagnosis can be made with simple clinical approaches including a therapeutic trial (e.g., with bronchodilators or antacids) in most children with chronic cough.\textsuperscript{55} However, a few important diagnoses such as a nonobstructing unsuspected foreign body or tracheomalacia/stenosis will be made only by endoscopy. In our experience, this justifies bronchoscopy in children with chronic cough or wheeze after careful clinical investigations have failed to achieve a diagnosis. A retrospective case series used bronchoscopy and BAL to investigate 30 young children with recurrent wheeze poorly responsive to bronchodilators, who mostly had been tentatively labeled asthmatic.\textsuperscript{55} Tracheomalacia was found in 12 and treated with aortopexy in one; the findings from BAL culture and cytology were more difficult to interpret. Bacteria (11\%) and viruses (33\%) were isolated, and abnormal cell differential was reported in 41\% of cases. However, it was not reported how the treatment was adjusted based on the BAL results, and what change in clinical outcome was achieved on the basis of BAL and bronchoscopy. Therefore, the clinical utility and possible benefit from BAL in this situation remains to be determined.

The diagnostic value of bronchoscopy in suspected chronic aspiration or gastroesophageal reflux associated respiratory symptoms has been reviewed.\textsuperscript{56} In infants, endoscopy (sometimes combined with esophagoscopy) may be necessary if aspiration is strongly suspected and a lateral chest X-ray in the prone position with contrast filling of the esophagus has ruled out a fistula (e.g., to identify a laryngeal cleft).\textsuperscript{57} While BAL and the lipid laden macrophage index (LLMI) have been advocated as a useful indicator for chronic aspiration,\textsuperscript{58} others have found considerable overlap with various bronchopulmonary disorders and normal children, making the LLM of questionable value.\textsuperscript{59,60} It appears that the lipids in the lipid-laden macrophages may represent endogenous digested lipids from inflammatory processes rather than exogenous aspirated material. One study investigated children <18 months old with recurrent wheeze which was poorly responsive to bronchodilators,\textsuperscript{35} and while four patients with proven reflux had an elevated LLMI, two of these also had adenovirus cultured from the airways, making the LLMI findings difficult to interpret. Increases in LLMI have also been found after lipid infusions\textsuperscript{61} and in a child with veno-occlusive disease of the lung. Interestingly, aggressive surgical management of suspected reflux-associated respiratory disease defined by LLMI and other tests has been advocated by one group in a study of highly preselected patients, while no controls or conservative treatment trials were included.\textsuperscript{62}

There is no consensus whether bronchoscopy or BAL has a diagnostic role in the absence of anatomical abnormalities such as fistulas or clefts in these children. The LLMI can only provide some additional information in the wider clinical assessment leading to a diagnosis of chronic aspiration. Other tools such as nuclear (milk) scans, two-point pH-metry of the esophagus, or a therapeutic trial with proton pump inhibitors\textsuperscript{63} may be more important than bronchoscopy. The use of methylene blue-colored feeds and subsequent bronchoscopy has been proposed for the diagnosis of salivary aspiration in children with neurological abnormalities.\textsuperscript{64} However, it is unclear whether salivary aspiration alone causes pulmonary damage. Therefore, the clinical value of this technique remains unproven.

The diagnosis of primary ciliary abnormalities usually requires a stepwise approach excluding other diseases before airway epithelium is directly investigated. Early chronic upper (rhinitis, sinusitis, and otitis) and lower respiratory tract involvement is almost universally seen, and situs inversus is expected in 50\% of cases of
Kartagner’s syndrome. After a nasal brush biopsy and direct observation of the movement of cilia during an infection-free period has repeatedly shown the absence of normal beating, an airway biopsy (4–8 specimens) for electron microscopy (EM) is required. No data are available to suggest increased efficiency of bronchial over nasal biopsies for this purpose. In children, the carinal edges are the easiest bronchial regions to biopsy; however, they contain few ciliated cells. Due to the cost and time required to make the diagnosis by EM, bronchial biopsies for EM cannot be the standard of care in the evaluation of children with chronic respiratory problems. A recent report has shown that a careful clinical assessment before biopsy and EM can avoid unnecessary and expensive investigations. With this approach, primary ciliary abnormalities were found in about one third of samples taken. Also, screening the biopsy samples under light microscopy for ciliated epithelium before EM can prevent the expensive misadventure of processing specimens containing no ciliated epithelium.

### Bronchoscopy in the Intensive Care Unit (ICU)

Considerable progress has been made in the use of bronchoscopy in intubated children in intensive care. With small flexible endoscopes (e.g., 2.2 mm OD), even premature infants can be endoscoped through the endotracheal tube. While these endoscopes often have no suction channel, conventional suctioning through the tube immediately before endoscopy will usually allow sufficient visualization. Proposed uses have been to check for tube obstruction, obviating the change of the endotracheal tube, demonstrating the exact position of the tip of the tube, and the diagnosis of airway obstruction in lobar overinflation. However, significant oxygen desaturation and even transient bradycardia were observed in 14% of such procedures despite the use of an adapter allowing uninterrupted ventilation. While these problems may decrease with even smaller endoscopes, bronchoscopy has yet to become a universally accepted diagnostic procedure and is not routine in many neonatal ICUs (NICUs). The frequently detected granulation tissue after deep suctioning has led to restricting the use of suction catheters to the lumen of the endotracheal tube. In our experience, bronchoscopy is a very useful technique in selected cases. However, its routine use to locate the tip of the endotracheal tube in newly intubated neonates is unnecessary, because these children will usually require a chest X-ray for other reasons.

Airway endoscopy (particularly laryngoscopy) is useful in failure to extubate due to stridor. Granulations may be removed or respond to local application of corticosteroids, while cicatricial lesions or subglottic cysts may be incised surgically or with a laser. Vocal cord paralysis may resolve or have an intracranial etiology, and arytenoid dislocation can be identified. In selected cases with severe acute stridor, flexible pharyngoscopy may be done in an ICU setting without sedation to identify a retropharyngeal abscess, purulent tracheitis, and the now rare epiglottitis.

Bronchoscopy can be useful in children with airway obstruction after cardiac surgery. Typical findings include the obstruction of the left main-stem bronchus due to shunts or an enlarged pulmonary artery or left atrium. After a Fontan procedure, plastic bronchitis, consisting of chylous condensates forming bronchial casts, may require extraction by suction. This condition may respond to heparin, but not to locally applied lytic substances.

A recent report described the successful use of DNAse after bronchoscopic diagnosis of unilateral endoluminal obstruction in a carefully documented case of a ventilated child, with lobar atelectasis in status asthmaticus, which was refractory to conventional maximal therapy.

### Tracheostomy

Surprisingly little objective information exists regarding the management and monitoring of pediatric tracheostomies, but a consensus paper has recently been published by the American Thoracic Society (ATS) and the European Respiratory Society (ERS). Surveillance bronchoscopies (rigid or flexible) are usually done every 6–12 months, and more often in infants. However, few data are available to support any recommendation. If decannulation is not planned, only the trachea around and below the tracheostomy tube needs to be inspected. No anaesthetic or sedation is needed for this purpose if the flexible endoscope is passed through the cannula and then slowly pulled out together with the tracheotomy tube. A recent paper describes the use of bronchoscopy in children with burns, to determine when early tracheotomy is indicated to avoid tube placement in a severely inflamed subglottic area.

### Techniques

#### Bronchoalveolar Lavage

The use of BAL for diagnostic purposes appears attractive, as it is a relatively simple procedure with few side effects. A recent report by an ERS task force regarding technical aspects and normal values has been published. Some details of BAL (aliquot volume and number as well as exact processing techniques of the samples) have not been universally accepted, although it is unlikely that using less than 3 mL/kg will return sufficient material for examination in small children. The first aliquot may be analyzed separately. Normal values should in principle be established for each laboratory and endoscopy unit, but this could be difficult due to ethical and practical reasons. Normal values for cell
content, surfactant components, and proteins have been established for children.\textsuperscript{60,87–89} However, prospective studies analyzing the complication rate and benefit in various situations (e.g., unexplained chronic or recurrent cough/bronchitis in young children) are lacking. The diagnostic efficiency will be greatly influenced by patient selection and will therefore vary between studies, unless stringent entry criteria are applied.

Reported indications include pulmonary infections of the immunodeficient or immunosuppressed child, e.g., with HIV,\textsuperscript{90} or after bone marrow transplant (52% positive)\textsuperscript{91,92} refractory to standard empirical treatment. A retrospective analysis of 21 immunocompromised children identified fungi in 47% and bacteria in 25%, and reported a clinically meaningful result in 76%.\textsuperscript{9} However, the achievable clinical benefit will depend on the overall prognosis of these severely ill patients. In children with cancer and pulmonary infiltrates, the yield was lower (12/60 or 27%), and the authors noted that while positive BAL results will be helpful, negatives have to be interpreted with caution.\textsuperscript{93} Only positive BAL results, with pathogens that do not normally colonize the respiratory tract (\textit{Pneumocystis carinii} (PCP), Legionella, and \textit{Mycobacterium tuberculosis} (TB)) can be considered diagnostic,\textsuperscript{20} and negative results should not delay empirical antimicrobial therapy if clinically indicated. While it has been suggested that early BAL may achieve more positive samples,\textsuperscript{20,94} no prospective study has been carried out examining the relative benefit of both approaches as children are treated prophylactically against PCP and cytomegalovirus (CMV) (i.e., BAL before vs. after empirical treatment has been tried). Many oncologists currently adhere to the latter practice, and BAL is only needed in a few patients in our experience. BAL may also aid in the diagnosis of immunocompetent children with unexplained respiratory distress and pulmonary infiltrates, e.g., eosinophilic pneumonia\textsuperscript{95} or previously unsuspected pathogens.\textsuperscript{96}

The diagnostic use of BAL with modern microbiological methods (radiometric detection of TB organisms in fluid culture medium, BACTEC; or polymerase chain reaction, PCR) for the detection of acid fast bacteria\textsuperscript{97} may be indicated when standard methods of isolation (gastric lavage) fail, or a resistant strain is suspected and cannot be isolated from other sources. The sensitivity of detecting TB organisms in BAL specimens seems to be lower than that in gastric aspirates.\textsuperscript{98,99} If endobronchial disease is seen, the yield with BAL may be higher.\textsuperscript{100} It seems to be reasonable to endoscope children with TB when endobronchial disease or airway compression is suspected. This will aid in deciding whether to give steroids,\textsuperscript{101,102} and BAL should be included if the organism has not yet been identified by other means.

No study has directly compared the results of BAL with histological findings in biopsy-proven chronic interstitial lung disease (ILD). Some data indicate that BAL may give useful diagnostic information in these children in about 20% of cases,\textsuperscript{103} and BAL has been recommended in all children with this diagnosis.\textsuperscript{20} It may be diagnostic in histiocytosis (> 5% CD1a+ cells\textsuperscript{104}), alveolar proteinosis (neonatal surfactant protein B deficiency\textsuperscript{105}), and hemosiderosis.\textsuperscript{106} BAL could be useful in allergic alveolitis and for monitoring activity in sarcoidosis.\textsuperscript{107,108} However, at present BAL is not diagnostic in most cases of ILD.\textsuperscript{109} In our experience, many parents will more easily agree with a stepwise diagnostic plan including BAL before biopsy than with a first-line surgical lung biopsy.

\textbf{Transbronchial Biopsy (TBB)}

The use of transbronchial biopsies in children has been advocated after lung transplantation if rejection is suspected and cannot be differentiated by other means from complications such as infection. A sensitivity for acute vs. chronic rejection of 88% vs. 60% with a specificity of 91% vs. 100% has been reported.\textsuperscript{110–112} Methods have been described to easily inflate biopsy samples by applying negative pressure in a syringe during fixation in order to achieve optimal specimens.\textsuperscript{113} As repeated open lung biopsies after lung transplantation are impractical, TBB is the established standard procedure in this clinical situation, although no direct comparison with open lung biopsy (OLB) has been or probably ever will be performed.

The use of TTB in chronic ILD has been described, but a prospective comparison with OLB would be eventually needed to clarify its role. While one study reported similar proportions of diagnostic samples for TBB and OLB, the patients were not selected randomly to undergo either procedure; rather, TBB was performed when it appeared likely to give useful information.\textsuperscript{103} The main problem with TBB in ILD is the relatively small size of the tissue sample, which is due to the small biopsy forceps fitting through the thin working channels of pediatric bronchoscopes. Ingenious methods have been described to circumvent this problem in younger children. A suction catheter can be endoscopically placed\textsuperscript{114} and the larger biopsy forceps advanced through its lumen. However, the reported results were mostly (probably correctly) negative, and it is unclear for what diagnostic purposes TBB may be useful, given the fact that even open lung biopsy in small children with ILD often remains inconclusive or nonspecific (10/13 cases\textsuperscript{105}).

\textbf{Bronchography}

The need for bronchography to detect bronchiectasis has been greatly reduced by the use of CT. The latter is usually sufficient if surgical resection of a destroyed lobe is considered.\textsuperscript{9} However, the sensitivity and specificity of
CT vs. bronchography in children for the diagnosis of bronchiectasis has not been formally studied. The usefulness of fiberoptic tracheobronchial contrast delivery in children has been demonstrated. In children with cardiovascular anomalies, tracheoangiography can demonstrate the exact location and mechanism of the airway compression. If a cardiac catheterization is indicated for cardiologic evaluation, the combined technique may obviate the need for a CT scan or MRI.

**Other Diagnostic Uses**

Severe or recurrent hemoptysis is rare in children except in CF, and endoscopy is indicated in non-CF children after supraglottic bleeding sources or coagulation anomalies have been ruled out. Sometimes foreign bodies or vascular malformations (e.g., Osler’s syndrome, varices) are found, or pulmonary hemosiderosis may be diagnosed via BAL analysis.

Airway abnormalities (stenoses, malacia, granulation tissue) have been described in a high proportion of children with chronic lung disease of prematurity or bronchopulmonary dysplasia (BPD), in whom aspiration may contribute to a prolonged course. The usefulness of bronchoscopy in BPD has been described, this report stated that management was somehow directly affected by the results of the procedure in 41%. However, the exact therapeutic consequences and the clinical benefits were not described. Many of the children in this report were intubated or tracheotomized and may not be comparable to today’s typical presentation of this disease. Also, it was not reported what proportion of children with BPD they represented and why the decision to endoscope was exactly made. This makes it difficult to recommend bronchoscopy for children with severe BPD as a routine tool. In our experience, endoscopy will only be useful in rare and selected cases with BPD when localized stenosis (usually tracheal or subglottic) is a clinically suspected problem.

Bronchoscopy has been used to gain new information regarding the composition and cellularity of BAL fluid in CF, particularly in asymptomatic infants and to detect early infection. While this is a promising tool for future directions in cystic fibrosis research and treatment, its routine application for therapeutic decisions is not established. Recent papers have described a discrepancy in microbiological findings between oropharyngeal and lower airway cultures which may be of clinical significance. However, cultures were not taken during clinical exacerbations, and a confirmation of the results and their practical consequences for the management of cystic fibrosis will be necessary. It has been suggested that children may be treated according to their oropharyngeal culture, and bronchoscopic lower airway culture is performed if no rapid response to appropriate therapy is observed. A recent small study reported BAL in 9/16 children with CF clinically useful (e.g., to exclude Pseudomonas infection). However, therapeutic interventions for mucus clearance have rarely resulted in objective sustained improvements. Currently, the use of bronchoscopy for therapeutic interventions in CF is not supported by the evidence, but it may have a role in diagnosis of infections.

BAL has been used in pediatric asthma to validate markers of airway inflammation (e.g., circulating inflammatory mediators or breath condensate composition), and for guidance of therapy, at least in severe or steroid-resistant cases. However, bronchoscopy in asthma remains investigational at present, because it is unknown how to interpret cell and mediator content of alveolar fluid in clinical practice.

**INTERVENTIONAL AIRWAY ENDOSCOPY**

**Foreign Bodies**

At present there appears to be little reason to change from rigid to flexible bronchoscopy for foreign body extraction. Many foreign bodies are friable (e.g., nuts), and a method that pulls them into the distal opening of the rigid bronchoscope and en-bloc extraction of broncho-scope and foreign body allows a quick removal without the use of forceps, which tend to break soft foreign bodies into pieces. It seems reasonable to use a flexible bronchoscope to explore those children who have a rather low likelihood of foreign body aspiration, and switch to rigid bronchoscopy when one has actually been found. It is important that pediatric intensive care is available to deal with possible complications of foreign body aspiration and the extraction procedure.

**Laser Therapy of Airway Stenoses**

Interventional airway endoscopy is used to treat obstructions of the laryngeal region or trachea. No consensus exists as to the optimal treatment of subglottic hemangioma, and tracheostomy is still the treatment favored by some groups. Others have reported the application of intralesional steroids in children with subglottic hemangiomas, which is done during laryngoscopy and followed by intubation for some days. Careful CO₂ laser resection of a part of the hemangioma is usually sufficient to avoid tracheostomy or intubation in most children, even with large subglottic hemangiomas.

The use of lasers for the deroofing of thyroglossal or laryngeal cysts, and cicatricial subglottic narrowing, have been described. Large subglottic cysts can develop after endotracheal tube injury, may complicate BPD and can be resected easily with a laser. Lasers with mostly superficial and minimal deep tissue energy coupling should be used. This will avoid damage to the delicate
structures of the larynx as well as the perichondrium of the airway, and the development of secondary stenoses. The construction of small rigid ventilating endoscopes with a mirror system to direct a CO₂ laser beam, which has minimal deep tissue penetration but must be applied through a mirror system, has made it possible to treat such lesions even in the larynx of neonates, and in the trachea of older children. Also, the use of KTP lasers through a rigid endoscope has been described. Comparisons of different types of lasers for subglottic hemangiomas suggest less scarring with CO₂ than with Neodym YAG lasers.

Lasers have been employed to remove granulation tissue (e.g., at the site of a tracheostomy before decannulation), or infectious tumors (e.g., nontuberculous mycobacterial granulomas), and cicatrical obstructing lesions in the trachea. Bronchogenic cysts have been incised endoscopically with lasers, and transthoracic surgical removal may be aided by intraoperative flexible endoscopy.

Endoscopic Drug Application

The use of laser or forceps for the removal of laryngeal (or tracheobronchial) obstructing papillomas is a routine application of pediatric airway endoscopy. No data are available to suggest which method of removal is superior. As the surgical removal cannot cure papillomatosis, intralesional application of interferon or cidofovir is currently being investigated, as well as photodynamic therapy. This requires the use of rigid endoscopy, special needles, and the availability of pediatric intensive care in case of secondary swelling or other complications.

Stents

The use of airway stents has become routine in adults with malignant airway stenosis, and was recently described in a series of children after tracheoplasty. Also, children with severe tracheobronchomalacia or obstructing malignancies have been successfully treated with temporary stents, but serious questions remain as to their long-term safety, particularly when extrinsic compression of the airway by a vessel is to be relieved by the stent. Technical improvements and better materials may make them an attractive alternative to other interventions, such as aortopexy in children with intractable airway symptoms after repair of esophageal atresia, or in selected cases after cardiac surgery. However, their use remains experimental at present and should only be used as a last resort.

Other Endoscopic Interventional Procedures

Fiberoptic intubation of the difficult airway can be of great help, particularly in neonates with mandibular hypoplasia and other facial abnormalities. The endoscopic closure of esophagotracheal fistulas with glue and laser has been tried with success, but a high initial recurrence rate is reported. However, many isolated fistulas can be effectively and safely closed without thoracotomy in a relatively short operation from a cervical approach. In these cases, the advantages of the endoscopic technique appear small compared to the considerable morbidity due to delayed endoscopic closure and prolonged gavage feeding. Endoscopic balloon dilatation of airway stenoses, particularly in BPD patients, has been described. However, no systematic prospective study has delineated the clinical importance of stenotic lesions and the utility of interventional bronchoscopy in children with BPD. In our experience, such interventions are only rarely necessary.

Extensive BAL in alveolar proteinosis has been described in small children, and the use of balloon catheters with a distal opening (e.g., pulmonary wedge pressure catheters) will allow massive unilateral lavage through an endotracheal tube. In our experience, endoscopic control of the exact position and tight fit of the balloon with a very thin endoscope enhance the safety of this intervention.

Investigational Use

Bronchoscopy has been used to advance our understanding of pediatric lung diseases mainly by gaining lavage fluid and cells. Insulin-like growth factor II and its binding protein were increased in BAL fluid in children with ILD. Bronchiolitis obliterans, chronic organ rejection after lung transplantation, and the development of BPD after neonatal respiratory distress have all been investigated with the use of BAL. Eosinophils were present in a small study in asymptomatic atopic asthma but not in recurrent wheeze with infections, while the eosinophil activation markers eosinophil cationic protein (ECP) and eosinophil protein X (EPX) in BAL correlated with lung function and airway reactivity. Tumor necrosis factor (TNF)-alpha was released spontaneously by macrophages in the BAL of wheezy infants. During acute asthma attacks in children, leukotriene C4 (LTC4) and B4 (but not thromboxane A2 (TXA2)) were found to be increased. Abnormal levels of surfactant proteins and decreased glutathione have been found in CF with infection, and may contribute to lung disease. Recently, persistent airway obstruction after an acute viral illness was linked to chronic adenoviral infection. Adenovirus was isolated from some young children with chronic wheeze, although its pathogenetic relevance remains unclear. In a recent paper, bronchoscopy was used to assess the delivery of inhaled DNase into the airways of children with CF; this elegant method may be applicable to other inhaled substances. All these
EDUCATIONAL ISSUES

Technical training for diagnostic endoscopy is currently provided using self-made phantoms, animal models, and supervised clinical endoscopies. Further improvement would be possible with the use of recently developed virtual simulation trainers for adult bronchoscopy, which could be adapted to the pediatric age group. A real endoscope is used to intubate a simulated respiratory system which can be observed on a video screen; these systems include breathing movements, bleeding, secretions, etc., and it responds to the manipulations of the scope by the endoscopist.

A major issue remains quality assessment at each level (indication, diagnostic yield, complications, quality of documentation, and overall cost-effectiveness). Surprisingly few data are available to answer these questions. Achievable quality of care in different clinical settings (e.g., smaller outpatient clinics compared to larger teaching hospitals) has not been determined. One of the training and quality control issues which has only rarely been assessed is intra- and interobserver variability. A recent study analyzed intraobserver variability and found that only a >30% change in airway obstruction was detectable with sufficient accuracy.172

FUTURE DIRECTIONS

Prospective multicenter studies on the efficacy and safety of bronchoscopy for some of the more frequently encountered clinical situations will allow improved clinical decision-making, based on a higher level of evidence. While many of the published studies report the diagnostic yield on all patients endoscoped, lavaged, or biopsied, the eligible patient population and the selection criteria are not uniformly reported. This makes it impossible to generalize the findings and a high diagnostic yield will not automatically translate into a reasonable benefit for patients. The most suitable outcome variables will therefore have to be carefully selected in future studies. Also, studies should be extended to settings other than large pediatric respiratory centers in order to reflect clinical reality. This will allow us to better adhere to the advice given by Schellhase and Fan in 1995173: “Bronchoscopy should only be performed if the information to be gained or the expected therapeutic benefit outweigh the potential risk to the child, however small.”

Better techniques for transbronchial biopsies and their interpretation in small children may justify the use of TBB instead of open lung biopsies for an extended range of situations other than the patient after lung transplantation (e.g., chronic ILD). Pediatric airway endoscopy allows for local delivery of drugs. The segmental instillation of surfactant has been used in adult ARDS and may be tried in children with BPD and long-standing segmental atelectasis. In children with severe airway papillomatosis, the infiltration of antiviral drugs could become a useful method. New indications for interventional techniques like stent placement or removal may ensue with the development of better stent materials. However, further study is required to establish their use in situations other than after surgical airway reconstruction.

Technological advances in the future may change pediatric bronchoscopy. Ever smaller endoscopes with working channels are being developed.174 The use of charged couple device (CCD) cameras at the tip of the endoscope rather than fiberoptic transmission of the picture has been used in gastroenterological endoscopies; a prototype is currently being tested. Intrabronchial ultrasound to delineate peribronchial tissue has become available for adults, and with further miniaturization may be applicable to extrinsic airway compression in children as well.

Video libraries with specific diagnoses or training sequences would be of great help. Such databases could be made available through Internet sites of recognized pediatric respiratory societies and could contribute to improve the overall quality of pediatric bronchoscopy.

The use of electronic media for obtaining second opinions or expert advice on video-documented endoscopies will save time, and avoid repeat examinations or travel to a distant center. Also, information for parents and patients may be made available in this way.

CONCLUSIONS

Pediatric bronchoscopy has come of age and is being used for diagnostic and therapeutic purposes in an increasing number of clinical situations. In the future, it will be necessary to analyze its effectiveness and patient benefit in prospective studies, while concurrently improving its technical possibilities. It has become an increasingly important research instrument probing pathophysiologic concepts, monitoring, and possibly applying therapies locally. The use of electronic media as a training facility, and to present scientifically sound information regarding diseases diagnosed or treated by bronchoscopy, will require additional effort, as well as scientifically and clinically sound guidance. However, it promises better treatment and information for patients and parents, and may provide additional services for the appropriately trained pediatric pulmonologist.

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