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ADVANCES IN BRONCHOSCOPY

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The field of bronchoscopy has rapidly emerged as a major component of pulmonary and critical care medicine. It is perhaps the most commonly employed invasive diagnostic procedure in pulmonary diseases. The quality of instrumentation continues to improve and newer applications have evolved. Many recent developments are still in their infancy and their future remains to be seen. The following paragraphs provide brief summarization of recent and newer developments in both diagnostic and therapeutic bronchoscopy. It is important for the bronchoscopist to be aware of the newer developments and be cautious in applying the newer techniques in clinical practice. Both the advantages and disadvantages of the newer developments are discussed.

FLEXIBLE BRONCHOSCOPE (FFB)

FFBs with larger working channel permit the bronchoscopist to insert larger biopsy forceps, balloon catheters, laser fibers, and other instruments into the airways to obtain larger biopsies and higher quality specimens, thereby enhancing the diagnostic yield.

Ultra-thin FFBs are available in different diameters (as small as 1.2 mm). These have permitted the examination of the tiny airways of very small infants. The ultra-thin FFBs also enable the bronchoscopist to directly visualize eighth through twelfth branchings of the bronchial tree in adults. This has permitted detection of airway lesions in smaller airways missed earlier by the standard-size FFB. Investigators have been able to introduce an ultra-thin FFB, with a diameter of 1.8 mm, through the 2.6 mm channel of the conventional FFB to perform alveolobronchography. The ultra-thin FFB is useful in the placement and assessment of endotracheal tubes, particularly in patients with trauma, hemorrhage, or spinal instability. They are very helpful in examining the airways through the double-lumen endotracheal tubes. The disadvantages of these instruments include the lack of working channel (thus the inability to suction mucus and blood), smaller bronchoscopic image, somewhat flimsy movement of the distal (flexible) tip, delicate structuring that renders it to be easily damaged with routine handling, and thus the increased cost of maintenance.

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VIDEOBRONCHOSCOPE (VB)

The VB consists of a charge-couple device (CCD) at its distal tip. The CCD is essentially a miniature video camera located at the tip of the FFB. The image captured is digitally transmitted to a video processor for display on a television monitor. The image quality with the VB is now very near to that of the rigid bronchoscope-telescope system. The obvious advantages of VB include the much improved optics, ability to use video monitor to teach bronchoscopy students, light weight of the proximal end of the FFB (without the need to attach earlier heavy "teaching head"), and the ability to digitally record video images for teaching/publishing purposes. The images can be stored in a variety of video formats including 35 mm, video tapes, floppy diskettes, and laser disks. There have been some publications claiming that early mucosal (cancerous) changes can be discerned earlier. This assertion has yet to be documented by rigorous studies. It is true that the image quality is far superior and allows for a more accurate and detailed evaluation of mucosal surface, vascular patterns of tracheobronchial mucosa, mucosal folds, and tumor. The disadvantages include the added expense of purchasing video equipment, computer terminal, and larger working and storage space taken up by the bronchoscopy equipment. The ability to view through the head-piece of the FFB is totally lost and the bronchoscopist has to depend on the video monitor to visualize bronchoscopic findings. The image on the monitor is only as good as the monitor. Lack of faithful color images on the video monitor is a real and serious problem. Another concern is the gradual phase out of all the older FFBs that are still in good working order. As these are replaced by VB, service and repair work may become unavailable, thereby forcing the bronchoscopist to purchase the newer VB. It is important to point out that there are no studies that show that VB is better than the traditional FFB in clinical practice.

RIGID BRONCHOSCOPE (RB)

The RB, while maintaining the basic structural format, has also undergone serial changes to accommodate specialized procedures such as laser bronchoscopy, stent placement, and dilatation of tracheobronchial stenosis. The newer rigid bronchoscopes allow the passage of flexible bronchoscopes, thereby enabling the

bronchoscopist to take advantage of the capabilities of both instruments simultaneously. The major applications for RB include laser bronchoscopy, tracheobronchial stent placement, dilatation of tracheobronchial strictures using balloons and bougies, and removal of foreign bodies, particularly in children.

ANCILLARY INSTRUMENTS

Many new instruments designed to be used in conjunction with the FFB continue to appear in the market. Some are designed to increase the diagnostic yield while others are for entirely new applications. A new "needle brush" (a cytology brush with a needle at the distal tip) has been designed for procuring pathologic specimens from peripheral lesions. It is reported to have a higher diagnostic yield in malignant lung masses or nodules than the regular brush and forceps biopsy.

In a well-designed study it was shown that larger flexible biopsy forceps (cup size 3x2x0.9 mm) obtained significantly more tissue in 74% of 27 patients in contrast to small biopsy forceps (cup size 2x1.5x0.6 mm) which obtained more tissue in only 19% of 27 patients. Large forceps also obtained more alveolar tissue in 73% patients whereas small forceps obtained more alveolar tissue in only 27%. There was no difference in the post-BLB bleeding with either forceps. Potential problems with the use of larger forceps include the inability to pass the forceps through the working channel of smaller adult FFB and difficulty in getting the jaws to open in small peripheral airways.

BRONCHOSCOPIC (ENDOBRONCHIAL) ULTRASONOGRAHPY (BUS)

BUS includes an echographic camera, a bronchoscopic ultrasonic probe, a video monitor to obtain the echographic image, and the facility to develop ultrasonographic histograms and echo enhancement. BUS has been reported, in preliminary studies, to identify subtle submucosal changes and lesions adjacent (extrabronchial lymph nodes and other structures) to the airways. Early diagnosis of mucosal cancer and identification of paratracheal. hilar, or mediastinal lymph nodes by BUS may alter the current modes of therapeutic approach to bronchogenic carcinoma. Earlier work from japan has observed that BUS can clearly delineate the thoracic aorta, pulmonary artery, esophagus, and peribronchial tissues. The probe head's diameter of 6.3 mm limited its insertion into lobar bronchi. In patients with bronchogenic cancer, BUS detected invasion of vessel wall and paratracheal lymph nodes. In a prospective study, BUS identified the presence and estimated the size of subcarinal, tracheobronchial, paraortic and periesophageal lymph nodes better than CT, with diagnostic rate of malignancy in 72 percent. Lymph nodes behind air-containing organs (paratracheal lymph nodes) could not be identified. The major deterrent to the use of BUS is the inability to maintain fluid-bronchial mucosal interphase during the procedure. Therefore, the tumors within the lung parenchyma are difficult to identify. Some studies have shown that combination of BUS with needle aspiration (USTBNA) has a higher diagnostic yield. Mediastinal anatomy, including vascular structures and lymph nodes, is clearly imaged with endobronchial ultrasonography and USTBNA decreases the number of aspirates required for paratracheal lymph node sampling.

VIRTUAL BRONCHOSCOPY

Advances in computer technology have permitted development of virtual reality images of the tracheobronchial tree using data sets derived from helical CT of the chest. The dynamic images thus obtained represent virtual bronchoscopy. Comparison of "virtual bronchoscopy" images with videotaped bronchoscopy images have shown that virtual bronchoscopy simulations accurately demonstrate endobronchial obstructions by tumor, airway distortion and/or ectasia, and extraluminal lesions (lymph nodes). This technique may have a role in prebronchoscopy planning, endoscopy training, and/or endobronchial therapy, and merits further study. The major advantage of this technique is its ability to identify and map extrabronchial anatomy, namely the relationship of the tracheobronchial tree to the surrounding structures including blood vessels and lymph nodes. This can be very valuable in the staging of lung cancer and helping the bronchoscopist in planning appropriate procedure such as bronchoscopic needle aspiration. The improving technology will further refine this technique and thus define a role for virtual bronchoscopy in pre-bronchoscopy planning of diagnostic and therapeutic procedures, endoscopy training, and staging of tumors. The most important aspect of this is that while virtual bronchoscopy may reveal the endoluminal and extraluminal lesions, bronchoscopic procedures are required to obtain tissue diagnosis.

LASER BRONCHOSCOPY

The initial enthusiasm for laser bronchoscopy has waned somewhat. The reasons for this include the high cost of

equipment, lack of proper training, need for rigid bronchoscopy in most cases, prolonged duration of the procedure, no improvement in mortality (quality of life is improved), and insufficient number of cases at many centers. However, laser bronchoscopy remains an important adjuvant in the treatment of large airway lesions and in dilatation prior to placement of stents. Majority of bronchoscopic laser therapies utilize Nd:YAG laser. In a series of 1,585 patients who underwent 2,253 Nd:YAG laser therapies over a 11-year period, 78% had non-small cell lung cancer, 6% had small cell lung cancer, 7% had metastatic tumors, and 5% had unclassifiable tumors. Almost all cases were performed under general anesthesia utilizing rigid bronchoscopy. More than 93 percent showed immediate good results. Complications included 18 hemorrhages, 6 pneumothoraces, and 10 deaths. Laryngeal and subglottic lesions can be treated using CO_2 laser.

BRONCHOSCOPIC CRYOTHERAPY

The technique of applying extreme hypothermia to endobronchial tumors in an effort to destroy malignant cells has shown a recent comeback. Using either a FFB or a RB (usually the latter), liquid nitrogen or nitrous is oxide circulated through a catheter probe (passed through bronchoscopic channel) that freezes the tumor on contact. The contact with the tumor is maintained for several minutes or until the formation of "frost" around the tumor. The tumor undergoes cold-necrosis over the next 48-72 hours. The necrotic tumor is expectorated by patients. Objective improvement has been reported in 50-70% of patients. Bronchoscopic cryotherapy has also been applied to treat benign airway strictures. Rigid cryoprobes of 3 mm diameter, for use through the rigid bronchoscopes, and flexible cryoprobes of 2-3 mm diameter for use through FFB are available. Bronchoscopic cryotherapy may become a less expensive alternative to laser therapy for treatment of tracheobronchial neoplasms.

BRONCHOSCOPIC DIATHERMY (CAUTERY)

Bronchoscopic electrocautery is an alternative to laser and cryotherapy for the treatment of both benign and malignant tracheobronchial lesions. The Instruments available are easier to use in combination with the rigid bronchoscope, although electrocautery probes are also available for larger FFB. Diathermy can also be used for coagulation of bronchoscopically visible bleeding lesions. Electrocautery is an available economical tool which has potential value in the diagnosis and therapy of tracheobronchial tumors. The major disadvantage of cauterizing via the bronchoscope is the fact that the coagulation effect stops completely if carbonized tissue covers the surface of the electrode. Repetitive cleaning of the electrode is required, making it a time-consuming procedure. The risk of formation of tracheobronchial stricture secondary to electrocautery therapy itself is a potential complication.

BRACHYTHERAPY

Another method in the adjuvant treatment of endobronchial malignancy. Involves bronchoscopic (FFB) placement of radiation source within the bronchial tree so that the tumor is irradiated from within the bronchial lumen. Many use laser therapy or bronchoscopic debulking before placing radiation seeds. More recently, high-dose brachytherapy has been used to treat endobronchial tumors. The major advantage is the relative rapidity with which the treatment can be completed (often on out-patient basis). Some studies have reported increased risk of significant, occasionally massive, hemoptysis as a complication of high-dose brachytherapy. Severe radiation bronchitis is another complication reported. However, reduction in hemoptysis in 60% and increase in airway diameter in 85% of patients have been described. In some series, patients with submucosal or peribronchial tumors that would not usually be amenable to laser therapy seemed to benefit from high-dose brachytherapy. Low-dose brachytherapy is slightly prolonged (24-48 hours) and requires hospitalization. The choice to use high versus low-dose therapy remains controversial.

BRONCHOSCOPIC PHOTOTHERAPY

Fluorescent compounds such as hematoporphyrin derivative (HpD), and dihematoporphyrin ether (DHE), are well known to function as canter "tags". When administered to patients, these chemicals are retained in malignant tissue at higher concentrations than normal tissue, and emit a characteristic salmon red fluorescence when exposed to light of the proper wavelength. Even though the fluorescent property of HpD and DHE has been used to detect cancers located in the tracheobronchial mucosa, particularly squamous cell carcinoma, the same properties have been used to treat bronchogenic cancers in patients who are surgically unresectable. HpD and DHE also mediate photodynamic chemical reactions which lead to cellular death through the production of

toxic radicals including singlet oxygen and the hydroxyl ion. Experimental studies have shown that the photodynamic effect of these compounds may be useful in the treatment of small superficial cancers. Approximately 300 patients have been treated with photodynamic therapy worldwide; nearly a 50 percent complete response has been observed in tumors that measured <3 cm2 in largest surface area. Many patients have received multiple therapies for recurrence or persistence of cancer. Complications include sunburn (if patients are expose to sunlight after administration of HpD or DHE), cough productive of blood and necrotic tumor debris, and formation of thick necrotic debris following treatment . The latter may require therapeutic bronchoscopy to remove the thick necrotic debris.

TRACHEOBRONCHIAL PROSTHESIS (STENT)

Tracheobronchial stenosis has garnered much interest from bronchoscopists in recent years because of the availability of various techniques available to treat this problem. Bronchoscopic dilatation of tracheobronchial stenosis can be accomplished by balloon dilatation, stent placement, and laser therapy. Rigid bronchoscope itself can be used to dilate many strictures. Balloon dilatation can be performed through FFB with a larger working channel. Dilatation balloons designed for esophageal dilatation can be used to dilate airway stenosis. Esophageal bougies can be used through rigid bronchoscope to dilate tight strictures.

Tracheobronchial stents are being used more frequently to treat both benign and malignant strictures of airways. The market has been flooded with various types of stents for use with rigid bronchoscopy as well as FFB. Several generalizations can be made regarding these. Rigid bronchoscopy is the preferred choice of instrument to insert these. General anesthesia is required for most stent placements. Special expertise is needed to insert these prostheses. Those inserted via FFB are almost always very difficult to remove with FFB. Frequent bronchoscopy and adjustment of the placement may be necessary. Tumor growth can occur through mesh stents. Retained secretions and obstruction by inspissated mucus is a frequent problem. Most strictures require dilatation of some sort before stent can be placed. Placement of stents beyond the origin of lobar bronchus is usually not possible and even if it is accomplished, may not provide much benefit. Most studies have reported that silicone stents are much better tolerated by patients and that they can be easily inserted and removed with the aid of the rigid bronchoscope. Several types of stents can be introduced through the FFB. Removal, however, with FFB is very difficult if not impossible. In contrast to metal stents, the silicone stents are more likely to migrate. No long-term studies are available to evaluate the side effects and complications. Prospective studies are needed to assess the value of these devices.

FIBRIN GLUE

Fibrin glue and other types of "adhesives" or chemical and organic "plugs" have been used to achieve bronchoscopic closure of bronchopleural fistula and persistent pneumothorax by occluding the bronchus. The success of this treatment requires precise identification of the bronchial or segmental location of the air leak. This can be accomplished by injections of small boluses of 133Xenon into a number of segmental bronchi through a FFB and identifying the increase in radioactivity in the intercostal drainage tube. Less expensive method is to use a Fogarty balloon to occlude the bronchus in question and observe for the stoppage of air-leak. A FFB is used in most cases. A double lumen catheter can be inserted into the bronchus to be blocked. These can be obtained from commercial vendors or a triple-lumen pulmonary artery floatation catheter can be modified for this purpose. Injecting the chemicals through the FFB itself may clog the bronchoscopic channel. Equal amounts of cryoprecipitate and tissue thrombin are injected through the catheter to build layer after layer of fibrin glue. Repeated applications may be necessary to achieve good closure. There are several problems with the technique. The technique is time consuming and it is not easy to identify the bronchus leading to the fistula or pneumothorax. Fibrin glue is frequently coughed up or slips out of the bronchus. Repeated application may be necessary. Bronchoscopists should recognize that the technique is time-consuming and the results, not infrequently, disappointing.

BRONCHOSCOPIC DRUGS

Glycopyrrolate (Robinul®) has gradually replaced atropine as the antisialogogue. It is better tolerated, has no or negligible effect on cardiac rhythm, and can be administered IM or IV. Recently, inhaled ipratropium has been used but more studies are needed before it can be recommended as a premedication for bronchoscopy. Midazolam (Versed®) is now the sedative of choice. It can be administered IM or IV. Midazolam is a better amnesic agent than diazepam. Dosage is 0.075 mg/Kg (overall, males require 1.0 mg more than females), but

the dosage should be decreased in the elderly. Hypoventilation is a potential side effect; therefore, dosages have to be titrated. Lacks antitussive activity. With increasing sedation, patients loose inhibition to control cough during the procedure. Sedation reversed by flumazenil 0.4-1.0 mg IV (sse below).

Two narcotic sedatives that have become popular are propofol and fentanyl. Propofol is a lipid soluble phenol derivative available as a white aqueous emulsion (contains soybean oil and egg phosphatide in glycerol). It has a large volume of distribution and is rapidly eliminated by hepatic and extrahepatic metabolism. Its duration of action is short and thus, it is very useful for outpatient general anesthesia. It is an excellent sedative in small doses. May produce hypotension and myocardial/respiratory depression if given with barbiturates, in hypovolemic patients, and elderly. Usual dosage is 50 g/Kg/min IV. Administration of lidocaine 100 mg IV is recommended before propofol because IV propofol is painful. Fentanyl is a synthetic opioid related to phenyl piperidines. Its analgesic potency is 60 times that of morphine. Fentanyl has rapid onset of action (2 min) with limited duration (30 min) of action. In doses of 0.5-2.0 g/Kg, fentanyl is an excellent addition to Midazolam. Vigorous cough can be suppressed by 50-100 g (may cause chest wall rigidity in higher doses). Alfentanyl (less potent) and sufentanyl (more potent) are more expensive.

Flumazenil is a receptor specific benzodiazepine antagonist and is capable of reversing benzodiazepine-induced sedation within 2 min. However, it does not reliably reverse respiratory depression. It is tolerated well in high-risk cardiac patients. Dose 0.4-1.0 mg IV (increments of 0.1-0.4 mg). Naloxone is an opiate antagonist that effectively reverses CNS side effects of all opiates. It reverses opioid-induced respiratory depression without affecting pain relief. Larger doses may terminate analgesia and cause dysrhythmia, hypertension, and pulmonary edema. Dosage - 1-4 g/Kg (use in increments of 25-50 g).

Music has been used to soothe patient's anxiety during bronchoscopy. One study reported that music played to patients through ear phones during bronchoscopy is reported to be a simple and inexpensive nonpharmacologic way to improve patient comfort. Other studies on the role of music as an anxiolytic factor during medical procedures have shown conflicting results. During complicated procedures involving many personnel and when communication among all members of the surgical team is important, a "deafening silence" is preferable to blaring music.

MISCELLANEOUS

Broncholith extraction has been accomplished using bronchoscopic broncholithotripsy. The technique is similar to urolithotripsy. An ultrasonic lithotriptor or pulse-dye laser can be used to pulverize the broncholiths in selected cases. Nd:YAG laser has been used to break broncholiths. Foreign body in pediatric airways has traditionally required rigid bronchoscopic removal. More recently, small-diameter FFB with working channel diameter of 1.0 mm has been used to extract pediatric airway foreign bodies. Urologic instruments (ureteral stone basket and forceps) can be passed easily through the narrow working channel to capture even large foreign bodies. Nevertheless, it is important to recognize that RB remains the instrument of choice for removal of pediatric airway foreign bodies. Even in adults with tracheobronchial foreign bodies, rigid bronchoscopy is preferable. The success rate with RB in adults is >95% where as FFB carries a success rate of about 61% in the removal of adult airway foreign bodies.

Blood clots in the major airways occasionally block the lumen and lead to respiratory distress. Removal of such clots via flexible bronchoscopy is difficult and time-consuming. This is because the clots fragment or the distal ends of the clots are very adherent to the distal bronchial lumen. To overcome this, several bronchoscopists have used intrabronchial instillation of streptokinase to effect endobronchial thrombolysis. Streptokinase has been used in doses of 80,000 to 120,000 U) through the working channel of the flexible bronchoscope. No complications have occurred.

BRONCHOSCOPY IN AIDS

It is well established that bronchoscopy and BAL are invaluable in the diagnosis of infections in patients with AIDS and other (non-AIDS) immunocompromised patients. An interesting finding by the bronchoscopists has been the increasing number of endobronchial lesions observed in patients with AIDS. Tracheobronchial abnormalities in patients with AIDS can be caused by infectious and non-infectious etiologies. In the non-infectious group, endobronchial Kaposi sarcoma is an important entity. Nearly 50 percent of patients with cutaneous Kaposi sarcoma exhibit endobronchial involvement. Larger lesions may cause lobar or segmental atelectasis. The lesions are characterized by bright red or violaceous raised mucosal lesions. Airway obstruction is negligible. Hemoptysis and hemorrhage following endobronchial biopsy are unusual. Endobronchial

lymphoma has been described in patients with AIDS. Should one obtain both BAL and BLB to establish the diagnosis of P. carinii infection? One study has shown that BAL is significantly superior to BLB in detecting P. carinii. BLB, on the other hand, is helpful in diagnosing granulomatous inflammation, cytomegalovirus infection, Kaposi's sarcoma, infection caused by acid-fast bacilli, Cryptosporidium, and organizing pneumonitis. An important finding from a large study was that 6% of the BAL specimens were uninterpretable and 8% of BLB specimens were inadequate. The degree of current clinical reliance on these procedures is such that open lung biopsy is only occasionally considered in this special group of patients. A publication(J Bronchol 1996;3:88-95), reported that an additional 8% of PCP diagnoses can be made by BLB and not by BAL alone and that BLBs were much more important to diagnose infections other than PCP (40% of all such diagnoses) and noninfectious disorders of the respiratory system (63% were diagnosed only by BLB). An important role for BLB in HIV-patients and pulmonary infiltrates is in the diagnosis of Kaposi's sarcoma, cytomegalovirus, and other uncommon processes such as lymphoma, etc. Many major medical centers use a staged approach; that is, patients in whom PCP is a major diagnostic consideration but whose sputa are negative for PCP, only a diagnostic BAL is performed initially; BLB is added to the initial BAL if other diagnostic possibilities are considered likely; and if the initial BAL is nondiagnostic despite strong clinical suspicion of PCP, a BLB is performed.

Among the infectious complications of AIDS, several entities produce endobronchial lesions. Infection by Herpes simplex can cause tracheobronchial mucosal vesicles. Infection caused by M. avium complex can produce endobronchial nodules and segmental or lobar atelectasis. The endobronchial lesions appear pale white or pink and firm to biopsy. Biopsy specimens show typical tubercle granulomas. Patients with AIDS who develop endobronchial lesions secondary to M. kansasii are also described. Cases of Endobronchial mass from P. carinii has been described in patients with AIDS. Tracheobronchial invasive aspergillosis with formation of necrotic membrane in the tracheobronchial tree is also seen in patients with AIDS. Actinomycosis has been reported to produce a white-yellow exophytic mass partially obstructing the left main stem bronchus, with accompanying mucosal erythema and edema. Biopsies of the mass showed necrotic material and the cytologic studies identified actinomycotic granules. Repeat bronchoscopy within a 30-day period in patients with AIDS and pulmonary process is unlikely to provide a newer diagnosis. Many medical centers do not use the bronchoscopes used in patients with AIDS in non-AIDS patients. There is no scientific basis for this philosophy. Appropriate sterilization procedure should virtually eliminate the risk of transmission of HIV through the bronchoscope.

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