Transbronchial Biopsy in Diffuse Lung Disease

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As an initial diagnostic procedure in diffuse and localized lung disease, transbronchial lung biopsy (TBB) offers an attractive alternative to open lung biopsy. In the past, TBB was carried out by inserting a flexible forceps through a rigid, open-tube bronchoscope or a catheter.1-5 More recently, this technique has been popularized by passing the forceps through the channel of a flexible fiberoptic bronchoscope.6-18

Improvement in design of the fiberoptic bronchoscope has greatly facilitated the technique of TBB. Previously, the small biopsy channel severely limited the size of the forceps and, hence, the size of the biopsy specimen. Now the Machida FBS-6TL, Olympus BF-1T, and Pentax FB-19A all have a biopsy channel 2.6 mm in diameter which permits passage of a large “cup” or “crocodile” forceps. Since the biopsy channel of the bronchoscopy also serves as a route for suction, the effective aspiration of blood, purulent material and secretions is more readily accomplished with the newer fiberoptic instruments.

In diffuse disease, either the rigid or fiberoptic bronchoscope can be utilized to obtain biopsy specimens from the periphery of basal lung segments, but if the infiltrates are localized in upper lobe segments, then only the flexible bronchoscopy has the capability of positioning the forceps “on target.” Because of the ease in performing the procedure, comfort to the patient, good diagnostic yield, and a low incidence of complications, all of the TBB procedures at the University of Iowa are being done through a flexible fiberoptic bronchoscope. When evaluating results of fiberoptic TBB, the standard for comparison is TBB via the rigid bronchoscope where the diagnostic accuracy is 84 percent. We found that bleeding occurs in 1 percent and pneumothorax occurs in 10 to 14 percent.2 The purpose of this article is to: (1) present a useful fiberoptic bronchoscopy form; (2) discuss some of the important technical aspects of the procedure pertaining to the biopsy itself; (3) re-examine the wedge technique in greater detail; (4) emphasize the value of using fluoroscopy; (5) review the high-risk patients; (6) discuss complications with regard to prophylaxis and therapy; (7) provide a list of precautions; and (8) give the results one can reasonably expect from forceps TBB via the bronchoscope.

Bronchoscopy Form

A well designed operative report can be extremely helpful and save time for the bronchoscopist. Figure 1 shows the fiberoptic bronchoscopy form currently in use at the University of Iowa. The first portion of the report provides pertinent information pertaining to the patient’s status, which also may effectively serve as a “check list” for screening the patient. The second half of the report deals with the findings of the bronchoscopist, what was done to the patient and how the biopsy samples were handled.

Technical Aspects of TBB

Following screening of the patient, routine premedication with morphine (7.5-15 mg) and atropine (0.8-1.0 mg) IM, administration of local anesthesia with lidocaine, and insertion of an 8.5 mm oral endotracheal tube, the TBB is carried out by passing the closed forceps peripherally under fluoroscopic guidance to the area of involvement whereupon the biopsy is taken.10,15-16 The exact maneuvers and commands given by the operator during a TBB are as follows (in chronologic order):

1. The pre-selected segmental bronchus, through which the forceps is to be passed, is identified by the operator and a 5 ml bolus of epinephrine 1:20,000 strength is injected into this airway. The local drug effect is that of vasoconstriction and bronchodilatation. My opinion is that hemorrhage is reduced. In diffuse lung disease, basal segments B8 (right anterior; left anteromedial), B9 (lateral), and B10 (posterior) are routinely entered for biopsy. In a training situation, I like to start the operator out on the B8* or B9* segment since it is easier to tell fluoroscopically when the forceps is at the periphery of the lung without having to rotate the patient.
Because of the potential danger of a bilateral pneumothorax, biopsies are taken on one side only. When the pulmonary infiltrates are located in regions other than the lower lobes, the appropriate segmental bronchus is entered with the forceps.

2. As soon as the forceps disappears from endoscopic view, the operator then utilizes fluoroscopic control to pass the biopsy tool to the desired area.

3. In diffuse disease, a peripheral biopsy always is taken. The bronchial arteries are smaller at the periphery of the lung; therefore, the danger of significant bleeding is less. One should keep in mind, however, that the risk of bleeding from pulmonary arterioles and capillaries may be increased by pulmonary hypertension. Care is taken to see that the forceps does not penetrate the visceral pleura. If the patient experiences pain during insertion of the forceps, the biopsy instrument is withdrawn immediately and repositioned. Upon arrival at the periphery, the forceps is retracted 1-2 cm and the following commands are given in fairly rapid order:

(1) To the Patient: "Take a deep breath."
(2) To the Assistant: "Open the forceps."
(3) To the Patient: "Let your air all out."

At this point, during expiration, the bronchoscopist gently advances the forceps forward 1 cm, thus entrapping a small portion of the bronchial wall (Fig 2).

(4) To the Assistant: "Close the forceps."

4. This last command, "Close the forceps," is given at the end of expiration whereupon the endoscopist completely withdraws the forceps, leaving the tip of the bronchofiberscope wedged into the bronchial segment to tamponade any possible bleeding. While retracting the biopsy, pulling of the lung tissue can be felt by the operator and also can be seen on the fluoroscopy monitor.

5. The biopsy forceps, upon its removal through the fiberoptic bronchoscope, is inserted into a sterile tube or Petri dish filled with saline or Ringer's solu-
tion. While opening and closing the forceps, the assistant taps on the distal end of the flexible shaft to dislodge the biopsy material. The tissue rarely has to be teased from the jaws of forceps with a needle. Fluffy, floating tissue is indicative of lung, whereas bronchial tissue is dense and sinks.

6. Routinely, four to five specimens (occasionally as many as eight) are taken. Since the introduction of the crocodile forceps (Fig 3), which requires a 2.6 mm channel bronchoscope for insertion, the number of biopsy samples taken in our unit has been reduced to only two or three at most. This is because the "crocodile" specimens are much larger in size, which in our experience have been obtained with no increased incidence of serious bleeding.

7. The biopsy specimens are transferred by syringe from the solution to a glass slide where a few drops of fresh or reconstituted, freeze-dried human plasma, and tissue thromboplastin, are added to form a fibrin clot around the specimen. This technique consolidates the small pieces of tissue into a single specimen which is then immersed in 10 percent formalin solution and sent to the histopathology laboratory for processing. The reduction of crush artifact has been a notable feature.

Wedge Technique

Currently, all of our transbronchial biopsy procedures are being done by the wedge method to control hemorrhage. The procedure consists of securely lodging the tip of the fiberoptic bronchoscope into the selected distal bronchus before, during and after TBB. Following biopsy, the forceps is withdrawn through the channel and suction is applied, but the fiberoptic bronchoscope is left firmly in place to prevent blood from flooding the tracheobronchial tree. If within a minute no red wall of blood is seen at the tip of the bronchoscope, the instrument is withdrawn, and other areas are chosen for additional biopsies. If hemorrhage occurs, the bronchoscope is kept in the wedge position for four or five minutes to allow time for a clot to form. It is not unusual for the suction channel to become filled with blood, and occasionally a clotted-blood cast of the segmental airway is retrieved. Unfortunately, the wedge technique cannot be used to tamponade severe bleeding if the fiberoptic bronchoscope already has been removed from the patient. Vision is obscured by blood flooding the airway, which precludes re-inserting and positioning the fiberoptic instrument.

It is important to note that when obtaining a TBB...
from the upper lobe, the distal end of the fiberoptic bronchoscope is bent at an acute angle. Therefore, to prevent damage to the instrument, the tight wedge must be broken momentarily, the bronchoscope pulled back a short distance, and the tip straightened before retracting the biopsy forceps. This technical problem has been greatly resolved by some of the new fiberoptic instruments, eg, with the Pentax fiberoptic bronchoscope one can safely insert and remove a flexible biopsy forceps while the distal tip is bent up to $90^\circ$.

Since utilizing the wedge technique, preceded by a 5 ml bolus of 1:20,000 epinephrine injected into the selected segmental bronchus, the amount of blood spilling into the tracheobronchial tree in our last 154 TBB has been reduced to zero! Based on this experience, it seems reasonable to state that hemorrhage as a result of TBB can be entirely confined to the segmental bronchus.

**Fluoroscopy**

Physical limitations at many institutions make the routine use of fluoroscopic techniques difficult. Unfortunately, many transbronchial biopsies are done without fluoroscopic guidance; yet it is much safer and more accurate to perform forceps TBBs under fluoroscopic control. When the forceps is inserted through the long restricting channel of a fiberoptic bronchoscope, tactile sensation is greatly reduced, especially when the distal tip of the fiberoptic instrument is flexed. For this reason, I prefer to rely upon fluoroscopic control to position the forceps at the lung periphery or into a localized infiltrate.

We employ a Siemens C-arm fluoroscope (Siremobil) and an image intensifier for TV fluoroscopy (Fig 4). There are three major advantages to having equipment of this type: (1) the C-arm can be rotated around the patient for oblique and lateral views rather than having to turn the patient, (2) the unit includes an image store and disc recorder for registering a visual record of the position of the biopsy tool (Fig 5), and (3) the amount of radiation time can be reduced.

It is vital for any physician operating a fluoroscope to be thoroughly indoctrinated in its proper usage. In our diagnostic unit, which is a teaching situation, the bronchoscopist and/or his staff instructor perform the fluoroscopic examination. With good training, fluoroscopic time can be kept to a minimum. This means that the operator "does not have a heavy foot on the switch," ie, the fluoroscope should never be in operation unless the image being received on the TV screen is helping the bronchoscopist to do something that he otherwise could not do with safety and accuracy. Furthermore, protective lead aprons and dosimeter badges must be worn by all personnel; otherwise they must leave the room during fluoroscopic procedures.

Localization of the biopsy tool can be verified fluoroscopically by (1) rotating the patient (or the

![Figure 4](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21007/)
C-arm) while checking for coordinated movement of the forceps and lesion, (2) having the patient perform respiratory maneuvers and noting if the lesion and forceps move together, and (3) observing movement of the lesion while engaging it with the forceps or brush.

**HIGH-RISK PATIENTS**

Patients with a history of hemoptysis are more likely to have bleeding after bronchoscopy, uremic patients are in great danger of severe post-TBB hemorrhage, asthmatic patients are highly prone to develop increased airways obstruction, patients with cardiovascular disease (especially ischemic heart disease) more commonly have rhythm disturbances, elderly patients poorly tolerate excessive premedication, and immunocompetent patients are at risk to bleed or to develop infection. The immunocompromised host with advancing pulmonary infiltrates presents a special diagnostic problem requiring an exact diagnosis without delay. Otherwise, random treatment with toxic drugs is the only alternative for a wide spectrum of diseases. These disease states include: *Pneumocystis carinii* pneumonitis, cytomegalic inclusion disease, tuberculosis, nocardiosis, fungal infections (aspergillosis, histoplasmosis, cryptococcosis, toxoplasmosis, etc) or the basic disease itself such as leukemia, malignancy, lymphoma (non-Hodgkin’s), Hodgkin’s disease or collagen vascular disease.

Our present diagnostic approach is fairly aggressive. If the benefits of the procedure are felt to outweigh the risks involved, then a TBB (with concomitant brush biopsy) is carried out with proper precautions on all patients in the above high risk group with notable exception of those with uremia. Any biopsy procedure is avoided, if at all possible, on a uremic patient because of hemorrhage.

**COMPLICATIONS**

The incidence of complications of fiberoptic bronchoscopy have been studied retrospectively and prospectively. The report of an overall complication rate of 8.1 percent and a death rate of 0.1 percent is probably close to the real picture. Thus, although bronchofiberscopy is generally safe, serious complications can and do occur. The potentially serious complications are listed in Table 1.

The prevention of trouble is the key message. Careful screening, proper preparation of the patient, and skillful biopsy techniques will obviate most complications. If a complication inadvertently occurs in spite of good methodology, one should be prepared to handle the problem. It is far better to be prepared than to wish you had been prepared!

With good procedural techniques, a reaction to lidocaine, laryngeal trauma from faulty endotracheal tube insertion, and postbronchoscopic laryngospasm are virtually non-existent. “Caution” is the password when dealing with asthmatic patients. In such patients, fiberoptic bronchoscopy may precipitate increased airways resistance with resulting hypoxemia, hypercapnia, and even death. Trouble can be circumvented by the judicious use of bronchodilators. Our protocol includes the use of atropine 1.0 mg IM one-half hour prior to bronchoscopy; *Solu-Medrol* (methylprednisolone) 125 mg IV 2-6 hours earlier; *aminophylline* 250 mg IV just before bronchoscopy (providing the patient is not already receiving therapeutic doses of theophylline) followed by a slow infusion of 5 percent dextrose in water (500 ml) containing 250 mg of aminophylline; and the injection of a 5 ml bolus of 1:20,000 *epinephrine* into each mainstem bronchus as the bronchoscope is being introduced. Another option is to use *Isuprel* (isoproterenol) or *Bronkosol* (isotharine with phenylephrine) by aerosol in the preparation of the patient.

**Table 1—Potentially Serious Complications**

<table>
<thead>
<tr>
<th>Reaction to the topical anesthetic</th>
<th>Hemorrhage</th>
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<tbody>
<tr>
<td>Trauma secondary to the ET tube</td>
<td>Cardiac arrhythmia</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Bronchoscopy</td>
<td>Flooding the airway from a</td>
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<tr>
<td>Hypoventilation</td>
<td>Ruptured lung abscess</td>
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<tr>
<td>Pneumothorax</td>
<td>Post-bronch. fever/infection</td>
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The most common cause of hypoventilation is excessive premédication. Pneumothorax occurs in approximately 1-5 percent of TBBs. Usually this complication presents no serious threat if recognized early and corrected by insertion of a chest tube with tidal drainage. Generally, a small air leak requires no therapy; nevertheless, the patient should be observed. If the patient is (or becomes) symptomatic or has serious underlying disease, then early recognition and removal of the air from the pleural space is imperative. One should keep in mind that a delayed pneumothorax can occur several hours after biopsy. Fortunately, tension pneumothorax is rare, but this complication can be fatal if not treated immediately!

Pulmonary hemorrhage secondary to biopsy is a matter of concern to many bronchoscopists. In dealing with a wide variety of lung lesions, the procedural incidence of mild to brisk bleeding in TBB has ranged from 5-9 percent. In comparison, immunosuppressed patients have an increased incidence of bleeding, especially those with a blood urea nitrogen greater than 30 mg/dl. In these uremic patients hemorrhagic complications occur three times as frequently (45 percent) as compared to an incidence of 15 percent in nonazotemie, immunosuppressed patients. The problem of serious bronchial bleeding from TBB has now been resolved by utilizing the wedge technique.

The occurrence of cardiac arrhythmias during fiberoptic bronchoscopy is not known. In many medical centers the standard procedure is to monitor electrocardiographically only high-risk patients or those who have a history of cardiovascular disease. In our endoscopy suite, where all patients are monitored, the incidence of premature ventricular contractions (PVCs) is approximately 0.5 percent. Acute myocardial infarctions, ST-T wave changes, or rhythm disturbances other than PVCs have not been observed by us, but are known to occur. A high incidence of cardiac arrhythmias may indicate problems in methods used to prepare the patient for the bronchoscopic procedure.

Occasionally, purulent material from a ruptured abscess can "drown" the patient. The flooding may occur during instrumentation (inserting a biopsy tool into the abscess) or shortly following bronchoscopy. A rigid bronchoscope should be readily available to handle such a situation. Also, any patient with this problem should be kept under close observation after bronchoscopy, preferably in a recovery room.

A notable feature is the absence of bacteremia following fiberoptic bronchoscopy. However, there is a single report of a 53-year-old immunosuppressed patient with lymphoblastic lymphoma and a Pseudomonas bronchitis who developed Pseudomonas septicemia immediately after fiberoptic TBB was performed. Our incidence of post-bronchoscopy pneumonia requiring antibiotic therapy has been low, ie, 1:500 cases. In each instance the patients were elderly and their airways narrowed or obstructed by tumor.

Hypoxemia, secondary to overmedication, to topical anesthesia, to intubation, or to the bronchoscopic procedure itself, is always a potential danger. A fall in the PaO2 is a common occurrence and includes patients without pre-existing lung disease. Thus, one should routinely use oxygen, 5 L/min, by nasal cannula. Note also that many of the items listed (Table 1) may have a common physiologic end result, namely ventilation-perfusion (V/Q) mismatch which may result in lifethreatening hypoxemia.

Precautions

Rather than taking precautions only on high risk patients, I believe it is wise to take the following precautions on all patients: (1) adequate patient screening; (2) perform the bronchoscopy in a well-equipped room; (3) routinely insert an 8.5 mm oral endotracheal tube for passage of the fiberoptic bronchoscope; (4) have good technical assistance; (5) avoid preoperative tranquilizers or barbiturates; (6) routinely use oxygen by nasal cannula; (7) continue nasal oxygen after TBB (often 6-12 hours) for any patient with a borderline or mildly reduced arterial oxygen tension prior to bronchoscopy; (9) monitor the patients on a cardioscope for rate, rhythm, and QRS-T patterns; (10) apply 5 ml boluses of 1:20,000 epinephrine directly onto endoscopically visible tumors prior to biopsy and also into the appropriate segmental bronchus just before each transbronchial biopsy (TBB); (11) utilize the "wedge" technique when performing TBBs to tamponade any bleeding; (12) give an infusion of 6 to 10 platelet packs immediately prior to bronchoscopy in any patient who has a platelet count less than 50,000/cu mm or has abnormally functioning platelets; (13) avoid, if possible, any biopsy procedure (brush or forceps) on uremic patients; (14) have ready access to a rigid bronchoscope; (15) make certain that asthmatic patients are adequately protected with bronchodilator drugs to prevent increased airways obstruction; and (16) utilize postbronchoscopy recovery room.

Results

When discussing the results of fiberoptic TBB in diffuse lung disease, one should keep in mind that
recovery of abnormal lung tissue may yield a specific, etiologic diagnosis or a nonspecific diagnosis. Thus, TBB may be successful in providing the bronchoscopist with a specific diagnosis in a number of diffuse alveolar and parenchymal diseases such as alveolar cell carcinoma; lymphangitic carcinoma; lymphoma (Hodgkin's and non-Hodgkin's type); sarcoidosis; fungal, bacterial and mycobacterial infections; cytomegalic inclusion disease; *Pneumocystis carinii* pneumonitis; pulmonary alveolar proteinosis, etc. In addition, biopsy tissue may show pathologic changes consistent with the diagnosis of silicosis, asbestosis, collagen vascular disease, vasculitis (Wegener's granulomatosis), Goodpasture's syndrome, histiocytosis-X, eosinophilic pneumonia, drug-induced lung disease, etc. Unfortunately, nonspecific inflammation, pneumonitis, or usual interstitial pneumonia (also called diffuse pulmonary fibrosis, classic interstitial pneumonitis-fibrosis, and diffuse fibrosing alveolitis) occurs too often and give the physician no information regarding the cause of the disease process. But in these latter instances, failure to make an exact etiologic diagnosis is not the fault of the biopsy technique.

The diagnostic accuracy in diffuse lung disease has ranged from 62 to 79 percent. In a recent review of fiberoptic TBB in 164 patients, Hanson and colleagues reported diagnostic accuracies of 62, 64, and 67 percent respectively in infectious, interstitial, and malignant lung diseases. In their group with interstitial disease (N = 58), approximately one-third had “usual” interstitial pneumonia and another one-third had granulomatous disease. In the patients with infectious lung disease (N = 37), the largest portion (60 percent) had viral and bacterial pneumonias, including lung abscesses, followed by aspiration pneumonitis (23 percent). In the neoplastic lung disease group (N = 51), bronchogenic carcinoma made up the largest sub-group (60 percent), followed by metastatic cancer, lymphoma and alveolar cell carcinoma. In a separate study, Cunningham and co-workers reviewed a group of 31 immunosuppressed patients and reported a fiberoptic TBB yield of 74 percent with 42 percent classified as etiologic and 32 percent as nonspecific. Both Hanson, Cunningham and their colleagues pointed out that the diagnostic yield was increased in many infectious and some neoplastic diseases by combining bronchial brush biopsy with TBB.

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