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section 18 Respiratory disorders 3992 further refined by assimilating other radiographic abnormalities, such as the presence of pleural disease in the case of asbestosis, or enlarged hilar lymph nodes in the case of sarcoidosis or lymphan- gitis carcinomatosa. Only when the radiographic findings of a patient with diffuse lung disease are taken in conjunction with the clinical features should a working diagnosis be attempted. Many pieces of informa- tion contribute to final diagnosis. In the context of diffuse lung dis- ease, the chest radiograph should be considered as only one part of the clinical jigsaw since a specific diagnosis can rarely be achieved with complete confidence from the radiographic findings alone. In addition to the nonspecific appearances of many diffuse lung dis- eases, the sensitivity of chest radiography is less than ideal, with up to 15% of patients with biopsy-proven diffuse lung disease having a normal chest radiograph. Conversely, a less than ideally exposed chest radiograph, especially of an obese patient, may misleadingly raise the spectre of diffuse lung disease. In the last few decades the development of high-resolution CT has changed the radiological approach to the diagnosis of diffuse lung disease, providing valuable prognostic insights that have substantially aided management of patients with diffuse intersti- tial lung disease. As stated previously, high-resolution CT images of the lung correlate closely with the macroscopic appearances of pathological specimens; can precisely estimate the extent of diffuse lung disease; and are less prone than biopsy to errors of sampling (although open lung biopsy is still required to achieve a definitive histological diagnosis in difficult cases). In addition, when a bi- opsy is indicated, the distribution of disease will indicate whether a transbronchial biopsy or an open lung biopsy is more likely to obtain a representative specimen. Future developments include computer- aided quantification of individual CT patterns to monitor

response to therapy (Fig. 18.3.2.37), which is particularly relevant to the de- velopment of new treatments for fibrosing lung diseases. FURTHER READING Adam A, Dixon AK, Gillard JH, Schaefer-Prokop CM (eds) (2015). Grainger and Allison’s diagnostic imaging, 6th edition. Churchill Livingstone Elsevier, Philadelphia. Bradley YC (2013). PET/CT. Radiologic clinics of North America. Elsevier, Philadelphia. Callister MEJ, et al. (2015). British Thoracic Society guidelines for the investigation and management of pulmonary nodules. Thorax, 70, ii1–54. Desai SR, Copley SJ, Aziz ZA, Hansell DM (2012). Thoracic imaging (Oxford specialist handbooks in radiology). Oxford University Press, Oxford. Goodman LR (2014). Felson’s principles of chest roentgenology, 4th edition. W. B. Saunders, Philadelphia. Hansell DM, et al. (2008). Fleischner Society: glossary of terms for thoracic imaging. Radiology, 246, 697–722. Hansell DM, Lynch DA, McAdams HP, Bankier AA (2010). Imaging of diseases of the chest, 5th edition. Mosby Elsevier, Philadelphia. Heitzmann ER (1988). The mediastinum: radiologic correlations with anatomy and pathology, 2nd edition. Springer-Verlag, Berlin. MacMahon H, et al. (2017). Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. Radiology, 284, 228–43. McLoud T, Boiselle P (2010). Thoracic imaging: the requisites, 2nd edition. Mosby Elsevier, Philadelphia. Naidich DP, et al. (2007). Computed tomography and magnetic res- onance of the thorax, 4th edition. Lippincott Williams & Wilkins, Philadelphia. Proto AV, Speckman, JM (1979). The left lateral radiograph of the chest. Medical radiography and photography. Eastman Kodak Company, Rochester, NY. Raghu G, et al. (2018). Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT Clinical practice guideline. Am J Respir Crit Care Med, 198, e44–e68. Rémy-Jardin M, Rémy J (2010). Integrated cardiothoracic imaging with MDCT. Springer-Verlag, Berlin. The National Lung Cancer Screening Team (2011). Reduced lung- cancer mortality with low-dose computed tomographic screening. N Engl J Med, 365, 395–409. Webb RW, Müller NL, Naidich DP (2014). High-resolution CT of the lung, 5th edition. Wolters Kluwer, Lippincott Williams & Wilkins, Philadelphia. 18.3.3 Bronchoscopy, thoracoscopy, and tissue biopsy Pallav L. Shah ESSENTIALS Bronchoscopy, thoracoscopy, and radiologically guided biopsy techniques provide different methods for visualizing and sam- pling thoracic lesions, the approach chosen in any particular case Fig. 18.3.2.37 Volume rendered 3D image of the lungs in a patient with idiopathic fibrosis. Colour coding has been used to depict the extent of low attenuation, ground glass density, reticular pattern, and honeycombing. Image provided courtesy of Brian Bartholmai MD.

 being based on several factors, including the anatomical loca- tion of abnormal areas, presence of coexisting pulmonary dis- ease, presence of comorbidities, and local expertise. CT is useful in both selection and planning of the most appropriate sampling method. Bronchoscopy Bronchoscopy can be used for sampling central lesions, mediastinal lymph nodes, hilar lymph nodes, and—where magnetic navigation technology or radial ultrasound is available—peripheral nodules. Suspected lung cancer is the commonest indication. Lung cancer—bronchoscopy is an essential tool in diagnosis and staging, when a combination of techniques such as bron- chial washings, brushings, and biopsy improves diagnostic yield, as does review of CT imaging before the procedure. Any abnormal mediastinal lymph nodes should be sampled in the first instance by either transbronchial fine needle aspiration or endobronchial ultrasound-guided fine needle aspiration. In the active palliation of lung cancer in patients with primary tumour or metastases involving the trachea or main bronchi, a variety of bronchoscopic techniques can be used to restore airway patency, including stenting in selected cases. Diffuse lung disease and focal parenchymal infiltrates— bronchoalveolar lavage provides information on cellular processes involved, transbronchial lung biopsy on the pathological

charac- teristics, and segmental lavage is a useful tool in patients with sus- pected respiratory infection. Other indications—the role of therapeutic bronchoscopy is increasing with the development of new endoscopic treatments for respiratory diseases such as emphysema and asthma. Thoracoscopy Thoracoscopy allows visual inspection and direct sampling of pleural abnormalities, the commonest indications being (1) evalu- ation of an exudative pleural effusion when cytological analysis of aspirated fluid does not provide a conclusive diagnosis; and (2) in the treatment of a malignant pleural effusion, when a sclerosing agent such as talc can be evenly applied to the pleural surface, a technique which also has a role in the management of recurrent spontaneous pneumothorax. Percutaneous biopsy The role of ‘blind’ (unguided) pleural biopsy is diminishing as it has been superseded by either thoracoscopic or image-guided biopsy. Radiologically guided percutaneous biopsy is usually considered where cancer is suspected and there is no clear indication to pro- ceed to surgical resection. Introduction Direct visualization of the airways by bronchoscopy has become an important tool in the diagnosis of respiratory disease since its introduction in Japan in 1966. The ability to visualize specific areas significantly improves diagnostic yield in comparison to blind pro- cedures. Similarly, the diagnosis and treatment of pleural disease has improved significantly with the introduction of thoracoscopy, which allows the direct inspection of the pleural cavity. Tissue biopsy has also evolved, with more procedures now being per- formed with some form of image guidance. Bronchoscopy Bronchoscopy is an essential basic investigation for the respira- tory physician. The first bronchoscopes were rigid instruments that were adapted from oesophagoscopes. The development of optical fibres enabled flexible bronchoscopes to be constructed, which significantly improved the utility of bronchoscopy, and today videobronchoscopes that provide high-quality images are used routinely. Flexible bronchoscopy permits the visual inspection of the air- ways from the vocal cords, trachea, and endobronchial tree down to the subsegmental level. It also allows for a variety of samples to be easily obtained from the airways. The procedure is very safe and is performed as a day-case procedure, with local anaesthesia with or without short-acting intravenous sedation. Rigid bronchoscopy is still performed, primarily by thoracic surgeons and by some phys- icians for interventional procedures: the equipment has a greater intraluminal diameter than do flexible bronchoscopes and hence allows easier instrumentation, but at the expense of a more re- stricted field of view, limited manoeuvrability, and the requirement for general anaesthesia. Indications The main indications for flexible bronchoscopy are listed in Table 18.3.3.1: suspected lung cancer is the commonest, followed by the assessment of pulmonary infiltrates for microbiological sampling. The role of therapeutic bronchoscopy is increasing with the development of new endoscopic treatments for respiratory diseases. Contraindications Informed consent from the patient or their representative is a pre- requisite. The main contraindications for bronchoscopy are hypoxia that cannot be adequately corrected by oxygen supplementation, and a bleeding diathesis. However, even in these circumstances firm ‘cut-offs’ cannot be given—the risk-benefit must be evaluated on an individual patient basis. The procedure should only be per- formed by an individual with an appropriate level of experience, or under supervision by an experienced bronchoscopist. Adequate facilities for resuscitation, and the skills and equipment to deal with any potential complication, should be immediately available. Bronchoscopy staff should be trained and competent in dealing with problems such as respiratory failure, cardiac arrhythmias, haemor- rhage, pneumothoraces, and the requirement for intercostal drain insertion. Equipment The flexible bronchoscope is a flexible tube containing bundles of optical fibres that carry light to the distal end to illuminate the airways, and a further bundle to transmit the image back to the eyepiece. The distal end of the bronchoscope can be angled through 160° by a lever at the head of the scope. This, in combin-

ation with rotation of the scope, allows it to be manipulated during the examination of the airways. There is an instrument channel

section 18 Respiratory disorders 3994 that allows procedures such as biopsies to be performed and which also functions as a suction channel. A variety of instruments are available, with the specification of the bronchoscope influencing its use; those with larger instrument channels are more suitable for interventional procedures, whereas smaller instruments allow more distal airways to be examined. The latest generation of video bronchoscopes have improved angulation and also the ability to rotate the distal insertion portion of the bronchoscope through 150°, facilitating improved access for diagnostic and therapeutic purposes. Modern videobronchoscopes have a charge-coupled device (CCD) chip at the distal end, which allows the image to be pro- jected on to a monitor. The latest systems utilize high-definition TV technology and produce high-quality full-screen images, which significantly enhance diagnosis. There are also several hybrid devices that use fibreoptic bundles to carry light down and images back up towards the proximal portion of the bronchoscope. A CCD chip in the head of the scope allows the image to be trans- mitted onto a monitor, the image quality being determined by the number of optical fibres and the size of the CCD chip. These hybrid scopes have the advantage of having either a smaller ex- ternal diameter or a much larger instrument channel than conven- tional videobronchoscopes. The most important development in the last decade has been the development of an integrated bronchoscope with a linear array ultrasound probe at the distal end. This endobronchial ultrasound bronchoscope (EBUS), with real-time transbronchial fine needle as- piration (EBUS-TBNA), has transformed the diagnosis and staging of lung cancer, and its role in other diseases such as sarcoidosis and tuberculosis is also expanding. Disinfection Bronchoscopes are cleaned and disinfected before and after the procedure. Particular care should be taken to clean the in- strument channel and suction ports manually with a brush, as well as flushing the channel with sterile water. The instrument is then placed in a disinfection solution such as 2% alkaline glutaraldehyde (the commonest used), or phenyl or isopropyl al- cohol, and automatic disinfection with 0.2% peracetic acid can also be used. In all cases the instruments should be soaked in the disinfectant solution for at least 20 min. Cross-infection has been observed with organisms such as environmental mycobacteria and pseudomonas species; processes must therefore be in place to document disinfection before use in each patient, and the serial number of the bronchoscope(s) used in individual patients should be recorded for tracing in the event of suspected cross-infection. In most cases of cross-infection, inadequate manual cleaning of bronchoscopes has been a factor. Biopsy forceps and needles are more invasive and hence need to be sterilized rather than simply disinfected. The potential risk of infections with viruses and prions has driven the development of single-use disposable instruments. The development of instruments that can be sterilized rather than dis- infected is an alternative option, but would incur significant capital investment. Because there is a significant time delay for instru- ments that require sterilization (days, rather than the short time required for disinfection), more than 10 bronchoscopes would be required to maintain a clinical service. Patient preparation Patients need to provide informed consent before the procedure and should ideally be provided with written information in advance, with key aspects such as risks of the procedure and alternative ap- proaches discussed prior to giving final consent. Bronchoscopy is usually performed as an outpatient procedure with conscious sed- ation, and patients should be advised not to eat or drink for at least 4 h beforehand. Box 18.3.3.1 provides a simple checklist for patient preparation. All available imaging should be reviewed prior to bronchos- copy. Ideally, a recent CT scan should be available, as there is good evidence that review of such images before flexible bronchoscopy

significantly improves the yield from the procedure. In one study, 171 patients being evaluated for suspected lung cancer were ran- domized: all had a CT scan performed before bronchoscopy, but in one group the scans were reviewed before the procedure, whereas in another (control) group they were not. The diagnostic yield of bronchoscopy was 73% in the former group compared to 54% in the latter and fewer investigations were required in the group where Table 18.3.3.1 Indications for bronchoscopy Investigation
of symptoms Haemoptysis Persistent cough Recurrent infection Suspected neoplasia Unexplained paralysis of vocal cords Stridor Localized monophonic wheeze Segmental or lobar collapse Unexplained paralysis of hemidiaphragm Suspicious sputum cytology Unexplained pleural effusion Mediastinal tissue—diagnosis and staging Assessing suitability for surgery Staging of lung cancer Infection Assessment of pulmonary infiltrates Identification of organisms Evaluation of airways if recurrent or persistent infection Interstitial lung disease Differential cell counts and cytology Transbronchial lung biopsy Transbronchial cryobiopsy Therapeutic Clearance of airway secretions Recurrent plugging of patient on ventilators following lobar collapse Foreign body removal Palliation of neoplasm Endobronchial ablation of tumour Dilatation of bronchial strictures Insertion of stents Bronchoscopic lung volume reduction for Emphysema Insertion of one-way endobronchial valves for bronchopleural fistula Bronchial thermoplasty for asthma

 the CT scans were reviewed before bronchoscopy. This approach is therefore more cost-effective and this author advocates it for all patients undergoing assessment for possible lung cancer. It also al- lows additional staging procedures such as transbronchial needle aspiration to be performed at the same time as the initial diagnostic bronchoscopy. A short-acting intravenous benzodiazepine such as intravenous midazolam or an opiate such as fentanyl or alfentanil may be used for sedation. Midazolam has the advantage of amnesic properties, whereas fentanyl and alfentanil have good antitussive properties. In some institutions a low-dose propofol infusion is used to induce and maintain sedation. Patients who have been given sedation should be advised not to drive or handle any machinery for at least 24 h after the procedure. The procedure can be performed without any sed- ation, which should be considered in some individuals who become aggressive and uncontrollable following intravenous benzodiazep- ines. It is also an option in patients who cannot be accompanied for 24 h after the procedure. Patients are monitored by continuous oximetry throughout the procedure. Those with pre-existing cardiac disease, or where hyp- oxia is not fully controlled by oxygen therapy, should also have elec- trocardiographic (ECG) monitoring and regular blood pressure measurements. Basic procedure Bronchoscopy can be performed with the patient semi-recumbent and approached from the front, or alternatively the patient can be lying flat and approached from behind. The choice is determined by local practice and also the procedure that is being performed. Intubation can be performed through either the nose or the oro- pharynx. Again, local practice seems to influence the approach, but the external diameter of the bronchoscope and the procedure being undertaken should also be taken into account. The oral pharynx is first anaesthetized with 4% lignocaine (lido- caine) for all procedures. The nasal passage is then anaesthetized with 2% lignocaine gel if a transnasal approach is used. With the nasal route, the bronchoscope is passed through the nares and naso- pharynx under direct vision until the epiglottis is visualized. With the oral route, the patient is asked to gently bite onto a mouthguard and the bronchoscope is then placed through this mouthguard into the oropharynx to the level of the epiglottis. The vocal cords should be visible from this level and their move- ment assessed, after which they are anaesthetized with 2 ml aliquots of 2% lignocaine. When any coughing subsides, the scope is ad- vanced through the widest

part of the glottis, with care taken not to touch the vocal cords. The subglottic area of the trachea is very sen- sitive and patients initially feel as if they are choking. Further 2 ml aliquots of 2% lignocaine are administered in the trachea, carina, right main bronchus, and left main bronchus. The trachea and endobronchial tree can be inspected down to the segmental areas (Fig. 18.3.3.1), the limiting factor being the size of the bronchoscope. The average bronchoscope with a 5 mm external diameter can reach the second or third generation subsegments. The following can be assessed at bronchoscopy: • Dynamic and fixed changes in airway calibre, including areas of ex- trinsic compression from enlarged lymph nodes or extrabronchial tumour masses • Distortion of the airways due to traction from fibrotic or collapsed areas of lung • The general appearance of the mucosa, with changes ranging from subtle abnormalities such as increased vascularity (Fig. 18.3.3.1d) and oedema through to gross tumour infiltration Polypoid tumours involving the first or second generation subseg ments should be easily identified at bronchoscopy (Fig. 18.3.3.1c). However, submucosal disease can be easily missed, and can range from subtle thickening of the airways through to small pearly nodules (may be present in tuberculosis or sarcoidosis). Small ulcers are also occasionally seen with tuberculosis or Wegener's granulomatosis. In Kaposi's sarcoma, cherry-red-like lesions are visible. Basic techniques and sampling Bronchial washings Obtaining bronchial washings involves the instillation of 10–20 ml aliquots of 0.9% saline into a subsegment, as close as possible to the site of abnormality. The sensitivity is variable, being 48% (range 21– 76%) in a recent review that evaluated 30 studies where the yield from the different bronchoscopic techniques was evaluated in at least 50 patients with suspected lung cancer. Bronchial biopsies Biopsy forceps can be inserted through the instrument channel of the bronchoscope and pinch biopsies obtained under direct vision, with several biopsies obtained to ensure that adequate tissue has been obtained for diagnosis. A higher yield can be obtained from endobronchial biopsies, with an overall sensitivity for lung cancer of 74% (range 48–97%), but where an exophytic tumour is visible the diagnostic yield should be at least 90%. The technique is generally very safe and the main complication is that of bleeding, particularly where vascular lesions are sampled, but this is rarely significant and can usually be controlled with conservative measures. Bronchial brushings A cytology brush can be used to scrape cells from the surface of any abnormal areas seen at bronchoscopy. These can then be either smeared onto a slide or rinsed in saline, according to local prefer- ence. In the meta-analysis described in the previously section, the yield from bronchial brushings was 59% (range 23–93%). The main Box 18.3.3.1 Preparation for bronchoscopy • Patient information—verbal and written information • Informed consent • Full blood count and clotting prior to transbronchial lung biopsy • Baseline ECG if history of cardiac disease • Spirometry if arterial oxygen saturation is less than 95% • Arterial blood gases if oxygen saturation is less than 92% • If the patient is to have any sedation, ensure that someone is going to accompany them home after the procedure • Remind the patient that if they are sedated they will be unable to drive or operate machinery for at least 24 h • Intravenous access • Consider bronchodilators if evidence of bronchospasm • Prophylactic antibiotics if asplenia, mechanical heart valve prosthesis, or history of endocarditis

 complication is minor bleeding, but there is a risk of a pneumo- thorax where a brush is advanced blindly beyond a subsegmental bronchus. Transbronchial fine needle aspiration In this technique a transbronchial fine needle is inserted through the mucosa and into a submucosal lesion beyond the endobronchial surface and a few cells are aspirated for cytological analysis. It has a sensitivity of around 56% (range 23–90%). Transbronchial fine needle aspiration can also be used to sample lymph nodes and is particularly

useful in the diagnosis and sta- ging of lung cancer, with a recent CT scan of the thorax required for planning of the procedure. The needle is inserted through the instrument channel of the bronchoscope and then through the tra- cheal or bronchial surface at the position determined, as perpen- dicularly as possible (at least 45° angle) to the airway wall, with a jabbing motion, and with suction applied with a 20 ml syringe at the other end. The cells that are aspirated are sent off for cytological ana- lysis. Occasionally a small piece of tissue is also obtained with this technique. The sensitivity of this technique in lung cancer is around 68% (range 45–85%). It provides both diagnostic and staging infor- mation, and is often the sole mode of diagnosis (25% of patients). The availability of rapid on-site cytological analysis significantly improves the diagnostic yield. However, a negative result does not Fig. 18.3.3.1 The videobronchoscopic appearance of (a) the trachea and main bronchi; (b) segmental bronchi in the right lower lobe; (c) polypoid tumour arising from a bronchial segment; and (d) submucosal disease.

18.3.3 Bronchoscopy, thoracoscopy, and tissue biopsy 3997 exclude neoplastic disease and should be followed up by further in- vestigations such as mediastinoscopy in appropriate cases. Although it is possible to diagnose lymphoma with transbronchial fine needle aspiration, the samples obtained are predominantly cyto- logical and do not provide the architectural information required to classify lymphomas. It is also a useful technique in the diagnosis of nonmalignant disease such as sarcoidosis and tuberculosis, but the sensitivity is lower. Overall, transbronchial fine needle aspiration is a very safe and effective technique: complications are rare, consisting of pneumo- thorax, pneumomediastinum, and bleeding (<0.01%). However, the growth and development of endobronchial ultrasound-guided transbronchial fine needle aspiration has almost completely dis- placed blind TBNA, except where local submucosal disease is found. Bronchoalveolar lavage Bronchoalveolar lavage is a useful diagnostic test in the assessment of parenchymal lung disease. It enables sampling of the distal air- ways and alveolar spaces, and is particularly useful in the assessment of (1) diffuse drug-induced interstitial lung disease, (2) parenchymal infiltrates, (3) pulmonary infiltrates in immunocompromised pa- tients, and (4) assessment of occupational dust exposure. The samples obtained provide information on the cellular com- position of pulmonary infiltrates, types of infective organisms, and presence of particulate and acellular matter in the alveolar spaces (Table 18.3.3.2). Identification of specific bacteria, fungi, and acid-fast bacilli are diagnostic. Malignant cells may be identified in the lavage in patients with bronchoalveolar cell cancer, lymphangitis carcinomatosus, or diffuse metastatic disease. A milky lavage laden with amorphous periodic acid–Schiff positive staining cellular debris is diagnostic of pulmonary alveolar prognosis. Bronchoalveolar lavage is performed by wedging the broncho- scope in the desired subsegment. In diffuse lung disease, the right mid-lobe is the segment of choice as it drains well and hence pro- vides the best yield; otherwise the optimal segment is selected on the basis of radiological findings. Once the bronchoscope is wedged, 30- to 60-ml aliquots of normal saline are instilled and aspirated back into a collecting bottle, either by gentle hand suction or with low- pressure suction. The total fluid instilled ranges from 100 to 250 ml, depending on the exact indication and local circumstances. The main adverse effects of bronchoalveolar lavage are usually dyspnoea, wheezing, and transient fever. Many patients are hypoxic due to their underlying condition, and installation of significant volumes of saline can precipitate hypoxia and, in some cases, pul- monary oedema. Transbronchial lung biopsy Transbronchial lung biopsy is invaluable in the assessment of diffuse lung disease and in patients where there is localized parenchymal shadowing (at least of segmental distribution). It has a high diag- nostic yield (>80%) in bronchocentric conditions such as sarcoid- osis and has an important role in the diagnosis of

lymphangitis carcinomatosis, disseminated malignancy, interstitial pneumonitis, and extrinsic allergic alveolitis. The two main complications of transbronchial lung biopsy are haemorrhage and pneumothorax. The risk of the latter is 5–10%, but a clinically significant pneumothorax requiring intervention occurs in about 1% of cases. The degree of bleeding is very variable, but blood loss of more than 250 ml is infrequent, and usually managed with aggressive suctioning of any blood combined with instillation of ice-cold saline and dilute adrenaline (1:100 000). Blocking bal- loons that occlude a lobar bronchus may be used to tamponade the bleeding, and blood transfusion may be required on rare occasions. Fluorescence bronchoscopy Fluorescence bronchoscopy, currently a research tool, is directed to the early detection of lung cancer. It utilizes the finding that normal tissue emits a green fluorescence when illuminated by a light of blue wavelength, whereas dysplastic or cancerous tissue absorbs this fluorescence and appears reddish brown in colour. These changes are not visible to the unaided eye, but can be visualized with the use of appropriate filters and image enhancement. Fluorescence bron- choscopy is significantly more sensitive at detecting severe dysplasia and carcinoma in situ than conventional white light bronchoscopy, but inflammatory lesions and metaplastic changes also appear ab- normal; hence specificity is low and false-positive results are a limiting factor. Narrow band imaging The new video bronchoscopes have a mode that accentuates the signal from blood vessels and highlights the superficial micro-vascular pattern. Patterns of neovascularization are associated with neoplasia, early changes of increased vessel growth, and networks of tortuous vessels progressing to small spiral or cork screw type vessels in microinvasive carcinoma. Combination of conventional Table 18.3.3.2 Cellular composition of bronchoalveolar lavage according to disease aetiology Lymphocytic cell composition Sarcoidosis Extrinsic allergic alveolitis Hypersensitivity pneumonitis Connective tissue disease Tuberculosis Viral pneumonia Neutrophilic cell composition Idiopathic pulmonary fibrosis/usual interstitial pneumonia Desquamative interstitial pneumonitis Acute interstitial pneumonitis Acute respiratory distress syndrome Pneumonia Connective tissue disease Wegener’s granulomatosis Cryptogenic organizing pneumonia/obliterative bronchiolitis Eosinophilic cell infiltrate Eosinophilic pneumonia Churg–Strauss syndrome Allergic bronchopulmonary aspergillosis Drug-induced pneumonitis Mixed picture Cryptogenic organizing/obliterative bronchiolitis Connective tissue disease Nonspecific interstitial pneumonitis

 video bronchoscopy and narrow band imaging has a greater sensi- tivity for the detection of early neoplasia Endobronchial ultrasound-guided transbronchial needle aspiration The development of a linear array ultrasound probe integrated into a videobronchoscope, which allows simultaneous ultrasound and conventional bronchoscopic imaging, has significantly im- proved the utility of ultrasound in bronchoscopy (Fig. 18.3.3.2). Endobronchial ultrasound mediastinoscopy has transformed the diagnosis and staging of suspected lung cancer. The linear probe can be applied against the tracheal wall and the mediastinum assessed for abnormal lymph nodes or any adjacent masses, which are vis- ible as hypoechoic lesions. Blood vessels can be identified as very hypoechoic structures, with identification enhanced by the use of the Doppler mode. A dedicated needle can be inserted through the instrument channel of the bronchoscope and transbronchial needle aspiration performed with real-time ultrasound imaging (Fig. 18.3.3.2). Abnormal lymph nodes as small as 5 mm in diam- eter can be sampled. This elegant technique, which allows sampling of lymph nodes and masses adjacent to the airway, has a diagnostic yield of 85–90% and has superseded mediastinoscopy as the first- line investigation for staging the mediastinum in lung cancer. It also has an important role in the diagnosis of other metastatic disease, as well as in sarcoidosis and tuberculosis. Radial ultrasound

Endobronchial ultrasound was originally performed using a 20 MHz radial vascular mini-ultrasound probe enclosed in a water-filled balloon sheath. These ultrasound probes produce ex- cellent images of the mediastinum and hilar structures, and can provide information on vascular invasion. They are able to identify the different bronchial layers from submucosa to adventitia, and have the potential of determining if the mucosa has been breached by cancer and hence distinguish between carcinoma in situ and invasive carcinoma. The procedure has been adapted by the use of a guide sheath which facilitates sampling of peripheral nodules. The yield is improved in conjunction with fluoroscopy, when the radial ultrasound probe is inserted with a guide sheath through the instrument channel of a video bronchoscope and directed into the appropriate segment. When the radial probe approaches the peripheral mass, the ultrasound signal changes to reveal an ir- regular mass. The guide sheath is secured in this position and the radial probe exchanged for sampling tools such as biopsy forceps, cytology brushes, and peripheral fine needle. Multiple samples should be obtained with fluoroscopic guidance to ensure that the guide sheath has not moved. Magnetic navigation Magnetic positional tip technology can be integrated with CT scan- ning data to create a virtual CT scanner in the bronchoscopy suite. A spiral CT with reconstructions of 1 mm slices is required, the data from which is used to create a virtual bronchoscopy model. Specific landmarks such as the primary and lobar carina are marked. At bronchoscopy, a catheter with a magnetic tracking device is inserted through the instrument channel and the catheter tip is positioned and calibrated with the CT data by systematically examining the bronchial segments. The system then integrates the CT data with the bronchoscopy data and can be used to guide the catheter with the magnetic tracking device to the target lesion (Fig. 18.3.3.3). Once the target is reached, the tracking device is removed, the biopsy for- ceps or needle is inserted through the catheter, and appropriate sam- ples are obtained for diagnosis. The main benefit from this system is that it facilitates the biopsy of peripheral pulmonary lesions which measure more than 20 mm in size. The bronchoscopic route tends to be safer, with a lower in- cidence of complications such as pneumothoraces than percutan- eous approaches. It may also improve the accuracy of transbronchial needle aspiration of mediastinal lymph nodes. Diagnostic role of bronchoscopy in lung diseases Lung cancer Suspected lung cancer is one of the main indications for bronchos- copy, the value of which in the diagnosis of central lesions is self- evident. Although the diagnostic rate is much lower in peripheral lesions, a variety of techniques such as bronchoalveolar lavage, fluoroscopic biopsy, radial ultrasound, and magnetic navigation- guided biopsy can improve this. Where there is mediastinal adenopathy, consideration should be given to sampling of these lymph nodes by transbronchial needle aspiration, ideally with endo- scopic ultrasound guidance (EBUS-TBNA) Diagnosis and staging should be evaluated simultaneously, with every effort made to sample mediastinal lymph nodes where they are enlarged (>10 mm in short axis on CT) or where there is increased uptake on a 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) scan. Diffuse lung disease Bronchoalveolar lavage and transbronchial lung biopsies in conjunc- tion with high-resolution CT form the basis of diagnosis for diffuse lung disease. The cell morphology of the lavage fluid is useful in the diagnosis of specific conditions (see Table 18.3.3.2): in sarcoidosis Fig. 18.3.3.2 An ultrasound image demonstrating a needle in a hypolucent ovoid lymph node during endobronchial ultrasound-guided transbronchial fine needle aspiration.

 there is a lymphocytic infiltrate which may demonstrate a high CD4/ CD8 ratio; a mixed lymphocytosis with CD8 predominance in the presence of foamy macrophages and plasma cells is suggestive of extrinsic allergic alveolitis; haemosiderin-laden macrophages are found in alveolar haemorrhage. A novel technique of

cryobiopsy is currently being evaluated for the diagnosis of interstitial lung disease. A cryoprobe is inserted through the instrument under fluoroscopic guidance. The probe is directed to the area of interest and, following a freeze cycle of about 6–8 seconds, the probe and bronchoscope are both removed as one unit. Tissue adherent to the probe is then thawed and sent for histology. This technique provides relatively large biopsy specimens without crush artefact (as is seen with forceps biopsy) for the diag- nosis and characterization of diffuse lung disease. Respiratory infection Bronchial lavage is useful in the diagnosis of respiratory infection when sputum cannot be obtained. It is usually reserved for patients who are failing to respond to empirical treatment, but has a vital role in the diagnosis of pulmonary infiltrates in those who are immuno- compromised. Bronchial lavage allows optimal specimens to be col- lected for microscopy and culture before starting antituberculous Fig. 18.3.3.3 Magnetic navigation-guided bronchoscopy: (a) screen shot during planning stage with virtual bronchoscopy and CT images; (b) screen shot of procedure stage which demonstrates the location of the magnetic tracker in relation to the target lesion.

 chemotherapy in patients with suspected tuberculosis who are not smear positive on sputum samples. Therapeutic role of bronchoscopy in lung diseases Lung cancer About 30% of patients with lung cancer present with advanced disease that involves the trachea or main bronchi. They develop symptoms such as breathlessness, cough, and haemoptysis, and are prone to recurrent pneumonia. Progressive symptoms of respiratory failure and recurrent endobronchial sepsis lead to death. Endobronchial metastases from other tumour sites have a similar effect. Bronchoscopy can have an important palliative role in the treat- ment of tumours that are accessible via the bronchoscope. Several techniques allow tumour debulking and restoration of airway patency, but these are generally underutilized and most patients only receive external beam radiation or chemotherapy. Tumours can be debulked by flexible bronchoscopy using electrocautery, argon plasma coagulation, neodymium yttrium aluminium garnet (YAG) laser, photodynamic therapy, and cryotherapy, most of which can be performed on a day-case basis in the endoscopy suite under conscious sedation. Improving access to these tech- niques in the palliation of endobronchial malignancy should im- prove survival. In selected patients debulking may need to be combined with the insertion of self-expanding metal stents, the key indication being where there is significant airway narrowing due to extrinsic com- pression by tumour, or where the airway structure has been des- troyed by the cancer. In both situations a stent attempts to improve airway patency by exerting an outward radial force. Covered stents can also be used to seal off airway fistulas and also prevent tumour ingress into the airway. However, the use of airway stents is asso- ciated with important complications including displacement and endoluminal wall damage, mucus impaction, granuloma formation, reobstruction, infection, halitosis due to biofouling, haemoptysis, pain, cough, and stent fracture. Emphysema Dynamic airway collapse in emphysema in conjunction with bullous lung disease leads to significant air trapping, flattened diaphragms, impaired respiratory muscle dynamics, and breath- lessness. Lung volume reduction surgery has been shown to be effective in patients with upper lobe emphysema and poor base- line exercise tolerance. In selected patients bronchoscopic lung volume reduction can be performed with much lower morbidity and mortality than are associated with open surgical procedures. Two main devices are available: one is a valve that is placed in a segmental bronchus and allows air and secretions to drain, but pre- vents air from entering into that lung segment, thus causing lobar atelectasis (Fig. 18.3.3.4b); the other is an umbrella-like device (intrabronchial valve) that acts in a similar manner by blocking air from entering and allowing the drainage of secretions. Clinical trials have demonstrated that patients with heterogenous emphy- sema (greater damage in one lobe

with better lung tissue in the ipsilateral lobe) and intact fissures, or those where the absence of collateral ventilation is proven, derive the greatest benefits. In this selected group improvements in exercise capacity and quality of life are observed in over two-thirds, but there is a greater risk of pneumothoraces in this population (20%). Other techniques that show promise in clinical trials are endobronchial coils, which restore the elastic recoil of the lung. Approximately 10 coils are inserted by bronchoscopy with fluoro- scopic guidance into one of the lobes in each lung, a therapy which suitable for patients with both heterogenous and homogenous em- physema, irrespective of the presence of collateral ventilation, but not in those with severe bullous disease. Experience thus far dem- onstrates appreciable improvements in quality of life, walking dis- tances, and pulmonary function. Thermal ablation with vapour, which causes fibrosis and contracture in the treated area of the lung, Fig. 18.3.3.4 (a) A catheter delivering thermal energy during bronchoscopy in an asthmatic patient; (b) image of a valve in situ in a patient undergoing bronchoscopic lung volume reduction.

 and a biofilm sealant, which induces localized inflammation and fi- brosis, are also under clinical investigation. A different approach, in which artificial airways are created be- tween pockets of trapped gas and the segmental airways, has been developed for patients with homogenous emphysema. The tech- nique identifies avascular areas in the airway with the use of Doppler ultrasound and employs a needle to create a hole measuring up to 5 mm in diameter, which is then maintained with a drug-eluting stent. These new airway passages allow trapped gas to escape and hence reduce lung volume. Preliminary reports suggest physio- logical improvements in lung volumes, exercise capacity, and quality of life. Although proof of principle of efficacy has been established, the airways occlude over time and the benefit diminishes. Asthma Bronchial thermoplasty is a promising bronchoscopic treatment for asthma (Fig. 18.3.3.4a). The technique involves the application of thermal energy under direct vision to the wall of airways more than 3 mm in size, leading to a reduction in smooth muscle. Randomized control trials have demonstrated improvements in asthma-related quality of life measures, and reductions in exacerbations, hospital- ization rates, and days lost due to ill health. Thoracoscopy Thoracoscopy is a simple invasive procedure which can safely be performed under local anaesthesia, with or without conscious sed- ation. It provides excellent direct visualization of the pleural cavity. Indications The commonest indication for medical thoracoscopy is evaluation of an exudative pleural effusion when cytological analysis of aspir- ated fluid does not provide a conclusive diagnosis. It allows direct visualization of the pleura and targeted biopsies of any abnormal areas, and in experienced hands has a diagnostic sensitivity of 90– 95%. It is also a key investigation in the assessment of patients with repeated pneumothoraces or a persistent air leak, and it is also used in some centres for the assessment of interstitial lung disease. Contraindications The main contraindication to thoracoscopy is absence of an ad- equate pleural space due to adhesions or previous surgery. Relative contraindications are a bleeding diathesis (INR >1.4), pulmonary hypertension, severe cardiac disease, or hypoxia. An uncontrolled cough or inability to lie still makes the procedure difficult and is an- other relative contraindication. However, as with bronchoscopy, the risk and benefits of the procedure should be evaluated for the indi- vidual patient. Equipment The basic equipment comprises of a rigid thoracoscope with a 9 or 11 mm diameter. These instruments have a variety of optics that allow straight and angled examination, and there are also integrated biopsy forceps with optics that allow accurate biopsy under direct vision. Other essential pieces of equipment include special nee- dles (Verres or Deneke) for inducing an artificial pneumothorax in the absence of a pleural effusion. A gas insufflator is used to

fill the pleural space with carbon dioxide or another gas to create a large enough space to facilitate inspection of the pleural cavity. The key precaution is to avoid inducing an artificial tension pneumothorax. Sterilization As thoracoscopy is an invasive procedure, it is not adequate to simply disinfect equipment as in bronchoscopy—all of the equipment used has to be sterilized by autoclaving. Patient preparation and basic procedure Patient preparation is as for flexible bronchoscopy. The procedure can be performed with local anaesthesia, with or without con- scious sedation. Patients are fasted for at least 4–6 h beforehand, and oxygen saturation, ECG, and blood pressure are monitored during thoracoscopy. Aseptic conditions are required: operators should wash their hands thoroughly and use sterile gloves and gowns. The patient is usually placed in the lateral decubitus position and the entry site is cleaned with chlorohexidine, with appropriate sterile drapes placed around. The access site is usually the fourth or fifth intercostal space in the midaxillary line, the exact entry port being influenced by the indi- cation for the procedure and also guided by imaging such as CT or ultrasonography. The pleura is visualized and appears as a delicate, transparent, light-reflecting surface with a fine network of blood vessels within it. Any changes in its surface are recorded, varying from areas of increased vascularity or localized thickening to diffuse changes, and there may be obvious nodules or tumour deposits. An angle telescope is often used to inspect the far reaches of the thoracic cavity such as the apex, interlobar space, paravertebral gutter, and mediastinal surfaces. Any fluid present can be sampled and sent for appropriate investi- gations, including cytology, and any areas of localized diffuse thick- ening may be biopsied. Whatever the visual findings, the parietal pleura should usually be biopsied, with care taken to obtain samples from the upper border of the ribs to avoid the neurovascular bundle that runs along the lower margin. It is possible to obtain visceral pleural biopsies and lung biopsies during thoracoscopy, but they carry a greater risk of bleeding and/or inducing a persistent air leak. The main complications of thoracoscopy are bleeding and pro- longed air leaks. Bleeding can usually be controlled by coagulation with either electrocautery or argon plasma photocoagulation. An intercostal drain should be placed whenever biopsy of the visceral pleura or lung has been performed. Serious but less common com- plications include secondary infection, mediastinal or subcutaneous emphysema, and air embolism. Re-expansion oedema is a theoret- ical risk, particularly in patients with long-standing effusions: this can be minimized with slow intercostal tube drainage and carefully managed re-expansion of the lung. Therapeutic role of thoracoscopy The most common therapeutic indication for thoracoscopy is in the treatment of a malignant pleural effusion. The procedure allows the even application of sclerosing agents such as talc on the pleural surface and is very successful in combination with tube drainage. Thoracoscopy also has a role in the management of spontaneous pneumothorax: small blebs may be identified and obliterated with

section 18 Respiratory disorders 4002 argon plasma photocoagulation or electrocautery, usually combined with pleurodesis. It also has a therapeutic role in empyema and tu- berculous pleuritis, where it can be used to break up adhesions and facilitate drainage of effusion. Video-assisted thoracic surgery Video-assisted thoracic surgery is increasingly used in the manage- ment of patients with pleural disease (see Chapter 18.17) and also allows lung biopsy or resection in some patients in whom an open procedure would be high risk because of poor lung function. Under general anaesthesia the ipsilateral lung is collapsed with the use of a double lumen endotracheal tube, and a stab incision with adjacent instrument ports is made in the sixth or seventh intercostal space in the midaxillary line (Fig. 18.3.3.5). In other respects, the tech- nique is similar to standard thoracoscopy. Pulmonary tube drainage is required after the procedure, but hospital stay is shorter

than after standard surgical thoracotomy. Single port video-assisted thoracic surgery is being utilized increasingly for lobar resections and nodal dissection in patients with lung cancer. Percutaneous biopsy Pleural biopsy The use of ‘blind’ (unguided) pleural biopsy is diminishing: wher- ever possible, pleural biopsies should be performed with image guidance. Traditionally, pleural biopsy was performed using an Abrams needle, which has three components: an outer trochar with a notch on its side near the distal tip, an inner cutting cannula that interlocks with the trochar, and a central stylette. A 5 mm incision is made in the skin surface and the whole unit is inserted carefully through the intercostal space just above a rib. The central stylette is withdrawn and the inner cannula is rotated anticlockwise and withdrawn slightly. Aspiration of pleural fluid confirms position in the pleural space. The Abrams needle is then angulated and slowly withdrawn to catch a small piece of pleura within the notch of the trochar, at which point the inner cannula is rotated and moved forwards to cut off and retain the specimen. There are several variants of the Abrams needle, such as the Cope needle and the Radja needle, but they all obtain a biopsy by tearing or shearing a piece of pleura. The blind nature of the procedure and the shearing technique for obtaining a biopsy specimen result in a variable diagnostic yield and a complication rate of 15%, with more serious consequences in about 0.1% of procedures. These range from haemorrhage and pneumothorax to laceration of adjacent organs such as the liver, spleen, and kidneys. Blind pleural biopsy has largely been superseded by CT or ultrasound-guided procedures, and wherever possible by thoracoscopy. The Tru-cut needle is favoured by many radiologists and comprises an outer cutting column and an inner trochar that has a notch within which the biopsy material is collected. Percutaneous lung biopsy Percutaneous biopsies are primarily performed in the assessment of pulmonary nodules for suspected malignancy. They are a par- ticularly important tool in the assessment of patients who are bor- derline candidates for surgery due to comorbidity or disease extent, but are less appropriate where a patient is operable and the nodule is considered highly likely to be cancer. Large masses may be more safely sampled with bronchoscopic techniques. Sampling of en- larged hilar or mediastinal lymph nodes by endoscopic ultrasound guidance should be considered as alternative sites for tissue biopsy and have the advantage of providing staging as well as diagnostic information. The main contraindications to percutaneous lung biopsy are poor respiratory reserve (FEV1 <1 litre) and bleeding diathesis (INR

> 1.4). Relative contraindications are extensive bullous emphysema, intractable cough, patients who are unable to lie still, pulmonary hypertension, and contralateral pneumonectomy. Fine needle aspirates can be used to diagnose malignancy but are very poor at firmly diagnosing benign conditions. The use of cut- ting needles, which obtain a core of tissue, provides greater diag- nostic confidence. Under CT guidance, the needle is placed so that when the needle tip is fired its distal position remains within the mass being sampled (Fig. 18.3.3.6), care being taken to avoid blood vessels, pulmonary fissures, bullae, and adjacent organs. The outer sheath is held in position after initial biopsy so that the procedure can be repeated and further samples obtained without the need to perform repeated needle punctures. Pneumothoraces and haemorrhage are the two main compli- cations of percutaneous biopsy, the frequency of which is influ- enced by the size, depth, and position of the mass. The presence of

> parenchymal lung disease, particularly emphysema, also influ- ences the incidence of pneumothoraces. Air embolism is a rare but serious complication and can occur if the needle lies within the pulmonary vein. Retractor Camera Grasper 180° 0° Fig. 18.3.3.5 The arrangement of ports for video-assisted thoracic surgery. The principal access is in the midaxillary line.

18.3.3 Bronchoscopy, thoracoscopy, and tissue biopsy 4003 FURTHER READING Annema JT, et al. (2010). Mediastinoscopy vs endosonography for mediastinal nodal staging of lung cancer: a randomized trial. JAMA, 304, 2245–52. Baaklini WA, et al. (2000). Diagnostic yield of fiberoptic bron- choscopy in evaluating solitary pulmonary nodules. Chest, 117, 1049–54. Castro M, et al. (2010). Effectiveness and safety of bronchial thermoplasty in the treatment of severe asthma. A multicentre, ran- domized, double blind, sham controlled clinical trial. Am J Respir Crit Care Med, 181 Suppl 1, 116–24. Davey C, et al. (2015). Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (The BeLieVeR-HiFi study): a random- ised controlled study. Lancet, 386, 1066–73. Du Rand IA, et al. (2011). BTS Interventional Bronchoscopy Guideline Group. British Thoracic Society Guidelines for advanced diagnostic and therapeutic flexible bronchoscopy in adults. Thorax, 66, iii1–iii21. Du Rand IA, et al. (2013). British Thoracic Society Bronchoscopy Guideline Group. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults: accredited by NICE. Thorax, 68 Suppl 1, i1–i44. Hartman JE, et al. (2019). Endobronchial valves for severe emphysema. Eur Resp Rev, 28(152), pii: 180121. doi: 10.1183/16000617.0121-2018. Herth FJ, Eberhardt R, Ernst A (2006). The future of bronchoscopy in diagnosing, staging and treatment of lung cancer. Respiration, 73, 399–409. Kurimoto N, et al. (2004). Endobronchial ultrasonography using a guide sheath increases the ability to diagnose peripheral pulmonary lesions endoscopically. Chest, 126, 959–65. Lam S, et al. (1998). Localization of bronchial intraepithelial neoplastic lesions by fluorescence bronchoscopy. Chest, 113, 696–702. Lam WK, et al. (1983). Fibreoptic bronchoscopy in the diagnosis of bronchial cancer: comparison of washings, brushings and biopsies in central and peripheral tumours. Clin Oncol, 9, 35–42. Laroche C, et al. (2000). Role of computed tomographic scanning of the thorax prior to bronchoscopy in the investigation of suspected lung cancer. Thorax, 55, 359–63. Manhire A, et al. (2003). Guidelines for radiologically guided lung bi- opsy. Thorax, 58, 920–36. Prakash UB, Offord KP, Stubbs SE (1991). Bronchoscopy in North America: the ACCP Survey. Chest, 100, 1668–75. Reichenberger F, et al. (1999). The value of transbronchial needle as- piration in the diagnosis of peripheral pulmonary lesions. Chest, 116, 704–8. Schreiber G, McCrory DC (2003). Performance characteristics of dif- ferent modalities for diagnosis of suspected lung cancer: summary of published evidence. Chest, 123 Suppl 1, 115S–128S. Shah PL (2011). Atlas of bronchoscopy. Hodder Arnold, London. Shah PL, et al. (2011). Bronchoscopic lung volume reduction with ex- hale airway stents for emphysema (EASE trial): randomized, sham- controlled multicentre trial. Lancet, 378, 997–1005. Shah PL, et al. (2013). Endobronchial coils for the treatment of severe emphysema with hyperinflation (RESET): a randomised controlled trial. Lancet Respir Med, 1, 233–40. Tassi GF, Davies RJ, Noppen M (2006). Advanced techniques in med- ical thoracoscopy. Eur Respir J, 28, 1051–9. Vergnon JM, Huber RM, Moghissi K (2006). Place of cryotherapy, brachytherapy and photodynamic therapy in therapeutic bronchos- copy of lung cancers. Eur Respir J, 28, 200–18. von Bartheld MB, et al. (2013). Endosonography vs. conventional bronchoscopy for the diagnosis of sarcoidosis: the GRANULOMA randomized clinical trial. JAMA, 309, 2457–64. Fig. 18.3.3.6 CT-guided Tru-cut needle biopsy of a left upper lobe mass.

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