Guidelines of the Papanicolaou Society of Cytopathology for the Examination of Cytologic Specimens Obtained from the Respiratory Tract

Papanicolaou Society of Cytopathology Task Force on Standards of Practice*

Cytologic examination of specimens obtained from the respiratory tract is a primary and frequently the initial diagnostic technique performed in patients with respiratory symptoms or in those presenting with a pulmonary abnormality. While occasional cytologic specimens are obtained from the upper respiratory tract, the majority of pulmonary diagnostic cytology involves the study of the lower respiratory tract. The guidelines contained within this document will address evaluation of specimens relating to the lower respiratory system (trachea, bronchi, bronchioles, and alveoli).

Due to the complexity of the respiratory tract and the location of various target lesions, a variety of cytologic techniques have been developed for the study of diseases involving the respiratory system. Both exfoliative cytology techniques and fine-needle aspiration (FNA) are used extensively for diagnosis of pulmonary lesions. While respiratory cytology is used predominantly for the study of neoplastic or potentially neoplastic disease, it is also variably useful in the investigation of a variety of benign diseases including opportunistic infections, tuberculosis, sarcoidosis, industrial disease (e.g., asbestosis), and lung transplant rejection.^{1–24}

Safety at Work

Laboratory staff processing pulmonary cytologic materials are at particular risk of exposure to aerosol infections. They must protect themselves from this potential hazard by wearing protective masks and gowns, handling the material within an appropriate cabinet equipped with a laminar flow biohazard containment hood, and following standard laboratory hygienic procedures.

Exfoliative Cytology of the Respiratory Tract

Each of the techniques used for obtaining exfoliative specimens from the respiratory tract has associated limita-

Standards of Practice Task Force members: Kenneth C. Suen, M.D. (chair),¹ Fadi W. Abdul-Karim, M.D.,² David B. Kaminsky, M.D.,³ Lester J. Layfield, M.D.,⁴ Theodore R. Miller, M.D.,⁵ Susan E. Spires, M.D.,⁶ and Donald E. Stanley, D.O.⁷

- Consultant members: Carlos W.M. Bedrossian, M.D.,⁸ Michael B. Cohen, M.D.,⁹ William J. Frable, M.D.,¹⁰ Tilde S. Kline, M.D.,¹¹ Virginia A. LiVolsi, M.D.,¹² G. Khanh Nguyen, M.D.,¹³ Celeste N. Powers, M.D.,¹⁴ Jan F. Silverman, M.D.,¹⁵ Michale W. Stanley, M.D.,¹⁶ and Thomas A. Thomson, M.D.¹⁷
- ¹Department of Pathology, Vancouver Hospital and Health Sciences Centre, Vancouver, British Columbia, Canada

²Institute of Pathology, Case Western Reserve University, Cleveland, Ohio

³Department of Pathology, Eisenhower Medical Center, Rancho Mirage, California

⁴Department of Pathology, University of Utah Health Sciences Center, Salt Lake City, Utah

⁵Department of Pathology, University of California, San Francisco Medical Center, San Francisco, California

⁶Department of Pathology, Saint Joseph Hospital, Lexington, Kentucky

⁷Department of Pathology, Rutland Regional Medical Center, Rutland, Vermont

⁸Department of Cytopathology, Northwestern Memorial Hospital, Chicago, Illinois

⁹Department of Pathology, University of Iowa Hospitals and Clinics, Iowa City, Iowa

¹⁰Department of Pathology, Medical College of Virginia Hospital, Richmond, Virginia

¹¹Main Line Clinical Laboratories, Wynnewood, Pennsylvania

¹²Department of Pathology, University of Pennsylvania, Philadelphia, Pennsylvania

¹³Department of Pathology, University of Alberta Hospitals, Edmonton, Alberta, Canada

¹⁴Department of Pathology, State University of New York, Syracuse, New York

¹⁵Department of Pathology, East Carolina University School of Medicine, Greenville, North Carolina

¹⁶Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas

¹⁷Department of Pathology, British Columbia Cancer Agency, Vancouver, British Columbia, Canada

This article is being simultaneously published in Modern Pathology.

*Correspondence to: Lester J. Layfield, M.D., Department of Pathology, University of Utah Health Sciences Center, 50 North Medical Drive, Salt Lake City, UT 84132.

Received 19 October 1998; Accepted 28 October 1998

tions, advantages, and diagnostic accuracy. Diagnostic accuracy can be optimized by selecting the most appropriate technique for a given clinical situation. Sputum cytology is noninvasive and is the most easily obtainable of the techniques available.

Sputum Cytology

The spontaneous production of significant amounts of sputum often indicates pulmonary disease. Sputum is composed predominantly of mucoid substances, as well as variable numbers of inflammatory and epithelial cells.²⁴ Variations in the numbers of macrophages, neutrophils, and epithelial cells and morphologic alterations in the latter elements can yield significant insight into the underlying pathologic process. Similarly, the level of pigmentation within macrophages and the presence or absence of Curschmann's spirals indicate much about the underlying pulmonary pathophysiology.^{25–28}

Specimen Procurement and Processing

Diagnosis of pulmonary lesions is optimal when the specimen is an early-morning spontaneously produced sputum.^{29,30} When sufficient amounts of spontaneously produced sputum are unobtainable, specimens may be induced by inhalation of a nebulized solution composed of 15% sodium chloride, with or without 20% propylene glycol, or simply 3–8% sodium chloride heated to 115°F.³¹ Fixation is not necessary if specimens can be promptly delivered to the laboratory.³² A variety of techniques have been adopted for the processing of sputum specimens. Predominant among these are "pick and smear," fixation by the Saccomanno blender technique, membrane filtration, and cytocentrifugation.^{33–39}

The most popular techniques are the "pick-and-smear" technique and the Saccomanno methodology.^{40–44} The "pickand-smear" technique avoids the use of carbowax and begins with visual inspection of fresh specimens for strands or flecks of solid or bloody material. Experience is essential to pick out significant areas for processing. These are selected along with random samples, and prepared as direct smears for immediate fixation (95% ethyl alcohol or spray fixation).⁴⁵ If the material is abundant, paraffin-embedded cell blocks may be prepared, sectioned, and stained with hematoxylin-eosin.⁴² This may increase the diagnostic yield but at added expense.

When a significant delay is anticipated between specimen procurement and laboratory processing, prefixation and processing by the Saccomanno method are preferred. Cells are collected in 50% ethanol and 2% polyethylene glycol (carbowax). Upon receipt in the laboratory, a blender is used to emulsify the specimen, which is subsequently centrifuged and prepared as smears.^{43,44} Multiple additional smears can be made from such a specimen if the first several do not demonstrate malignancy but the clinical suspicion is high.

The sensitivity of sputum cytology is optimized when five samples are obtained over 5 consecutive days.^{40,41} Using this methodology, the detection rate for malignancy can approach 90–95%.^{40,41} However, submission of three adequate single specimens has been accepted as the minimum requirement for reasonable sensitivity in sputum cytology.⁴² This number of specimens will identify at least 65% of carcinomas occurring in the lung.

Specimen Adequacy

Adequate sputum samples must contain alveolar macrophages. Absence of such cells indicates the presence of only saliva. No numerical cutpoint for number of macrophages is consistently reported in the literature, but an adequate specimen should have numerous easily identifiable cells of this type. Greenberg stated that the "adequacy of a sputum sample is directly proportional to the number of alveolar macrophages it contains."⁴⁶ In addition, a sputum sample should be large enough to prepare 2-4 slides.⁴⁶ Bardales et al.⁴⁷ showed that the preparation of four smears from a sputum specimen increased the diagnostic yield, but significantly increased the screening and turnaround times and, hence, was not cost-effective. At present, it appears that a sputum specimen should be considered adequate for evaluation if a minimum of two smears can be prepared, and microscopic evaluation reveals numerous alveolar macrophages. In addition, the cytologic material should be wellpreserved and well-stained.

Bronchial Washings and Brushings

Indications

Bronchial brushings and washings are complementary to sputum cytology in the diagnosis of pulmonary lesions. The most common indications for bronchoscopy are persistent cough, radiographic documentation of a new solitary pulmonary nodule, hemoptysis, bronchial obstruction, atelectasis, persistent localized wheezes, and persistent infiltrates on chest X-ray.^{48–50} Bronchoscopy may also be used to confirm an abnormal sputum cytology. Bronchoscopy is of questionable value for nodules occurring within peripheral lung fields. However, bronchial brushing appears to have greater sensitivity than either bronchial washings or sputum cytology for peripheral tumors, necrotic carcinomas, and metastatic cancer.⁵¹

The indications for repeat bronchial cytology specimens are poorly formulated, but include initial negative bronchial cytology associated with positive sputum cytology, and highly suspicious clinical or radiographic findings in the face of negative sputum cytology and a negative first bronchial cytology.^{52–54} Some authorities believe that an unequivocal positive sputum cytology associated with clinical findings of cancer is adequate to proceed directly to treatment. Ng and Horak^{53,54} demonstrated that diagnostic sensitivity increased from 70% to 90% when two bronchial cytologic specimens were obtained instead of one.

Specimen Procurement

Technical aspects of the bronchoscopic procedure are beyond the scope of these guidelines but have been wellsummarized by Walloch.⁵⁵ In general, both washings and brushings are taken of any clinically suspicious areas. Washings are obtained by repetitive instillation of 3–5 ml of a sterile balanced salt solution through the bronchoscope and reaspiration of fluid. Brushings are obtained by the use of a small circular stiff-bristle brush. Brushings must be obtained before "bite" biopsies are performed to avoid excessive and obscuring blood.

Smears are prepared by immediately rolling the end of the brush on a glass slide. The smears are fixed immediately in 95% alcohol. Any delay in fixation will result in severe air-drying artifacts and an uninterpretable specimen. In many institutions, clinicians are discouraged from preparing direct smears from endoscopic samples. The disposable brush is cut off its shaft, placed in a tube containing balanced salt solution or Saccomanno fixative, and transported to the laboratory where more uniform and high-quality preparations can be made. In the laboratory, the brush is rolled between two frosted glass slides. The smears are air-dried to increase cell adhesion and stained by the Papanicolaou technique. The brush is placed back in the tube, the tube with the brush is vortexed, the brush is discarded, and a cytocentrifugation specimen and/or cell block is prepared from the cell-enriched fluid.

The aspirated washing material should be immediately transported to the cytopathology laboratory, where they are centrifuged and smears prepared from the cell buttons. The buttons may also be fixed in 10% neutral-buffered formalin and embedded in paraffin for histologic sectioning. Alternatively, material from the washings can be prepared by cytocentrifuge techniques, membrane filtration preparations, or one of the new monolayer methods. In general, a combination of techniques yields the most satisfactory diagnostic sensitivity.

Specimen Adequacy

A bronchial washing/brushing specimen is considered satisfactory when cells or agents diagnostic of a pathologic process are present, but in the absence of such cells or infectious agents, specimen adequacy is less easily defined. In general, a satisfactory specimen should contain a large number of well-preserved, optimally stained ciliated bronchial epithelial cells and macrophages. Specimens which contain few cells or are heavily contaminated and obscured by large numbers of oral squamous cells or oral saprophytes should be deemed unsatisfactory. Similarly, specimens in which the cellular details are obscured by blood, inflammation, or air-drying artifacts should be considered unsatisfactory for definitive evaluation. The reasons for the inadequacy should be documented in the report. A specimen can be considered less than adequate if there is inadequate clinical information provided.

Diagnostic Accuracy

Bronchoscopic samples can achieve a sensitivity of up to 90% when multiple brushings are performed during one bronchoscopic examination.⁵⁶ Multiple brushings not only increase diagnostic sensitivity but also decrease the need for rebronchoscopy or other invasive procedures, including FNA.⁵⁶ Overall sensitivity depends on a number of factors, including skill of the endoscopist and the location, size, and histologic type of the neoplasm.^{41,53,57,58}

Bronchoalveolar Lavage

Although invasive, bronchoalveolar lavage (BAL) has such low morbidity that it can be safely used in critically ill patients. BAL, along with fine-needle aspiration, represent the only cytologic techniques which can study the contents and composition of the most terminal air spaces. While fine-needle aspiration cytology generally requires a localized and circumscribed target, BAL can successfully investigate diffuse pulmonary disease.

Clinical Applications of BAL

Bronchoalveolar lavage is most widely and effectively used in immunosuppressed patients with pulmonary infiltrates for the diagnosis of opportunistic infections.⁵⁹ Many infectious microorganisms can be diagnosed by cytologic examination of BAL fluid on conventional smears or with the aid of special stains. If indicated, BAL fluid can be submitted for microbiologic cultures. In addition to the identification of microorganisms, BAL shows specific recognizable features in the following conditions: alveolar proteinosis, alveolar microlithiasis, presence of malignant cells, and dust exposure, such as asbestos bodies, and silica and talc particles.⁶⁰

Semiquantitative methods for counting the number of hemosiderin-laden macrophages in BAL have been published.^{61,62} In one study,⁶³ the finding of >20% hemosiderin macrophages in BAL was indicative of significant alveolar hemorrhage. Alveolar hemorrhage has diverse causes, and the physician must therefore interpret this information in the context of clinical or other laboratory findings. Similarly, semiquantitative methods for counting the number of oil red-O-stained lipid-laden macrophages in BAL have been used for the diagnosis of aspiration pneumonia.^{19–23,64}

BAL in most noninfective interstitial lung diseases shows nonspecific changes and its diagnostic value is controversial, but BAL can provide useful prognostic information and monitor disease activity in some selected cases. For example, in the fibrosing alveolitis group, a marked increase in neutrophils and eosinophils has been found to be associated

PAPANICOLAOU SOCIETY

with a high risk of functional deterioration, whereas a high percentage of lymphocytes in BAL correlates with a better outcome.^{60,65,66} In sarcoidosis, a study of the number of T-helper lymphocytes or the ratio of helper lymphocytes to suppressor lymphocytes in BAL fluid can predict clinical activity and response to steroid therapy.⁶⁰ Phenotyping of alveolar lymphocytes can be done by flow cytometry, or immunofluorescent or immunocytochemical techniques.⁶⁷

Specimen Procurement

While techniques of BAL differ,^{67,68} it is usually performed under local anesthesia with a 5-mm bronchoscope. The bronchoscope is advanced into a subsegmental bronchus and wedged into position. In the absence of a localized lesion, the right middle lobe or lingula is usually selected for sampling because of technical convenience and associated high yields of fluid and cells. The lavage is performed with warm saline, using a total volume of 100–300 ml to sample each site. Several sequential fluid instillations are performed with 20–100-ml aliquots. This fluid floods the airspace distal to the bronchoscope and is then reaspirated by the bronchoscopist.

Standardization of the amount of fluid used and the number of aliquots is important because these factors influence cytologic yield.^{61,64} It appears to be preferable to use five 20-ml aliquots, with fractionation for lavage specimens. The first aliquot is usually separated from the subsequent four, which are pooled.⁶⁹ This technique optimizes the separation of bronchial epithelial cells from truly alveolar material. Fractionation decreases the number of unsatisfactory specimens when percentages of bronchial epithelial cells are used as a rejection criterion.

The BAL specimen should be rapidly transported to the cytopathology laboratory, where it may be processed by either a filtration method or cytocentrifugation. Chamberlain et al.⁶⁴ suggested that the filtration technique may be superior to cytocentrifugation because there are fewer unsatisfactory specimens with this technology. If conspicuous amounts of mucus are present, most laboratories begin processing of the specimen with passage through a loose nylon gauze mesh to trap mucous aggregates. Alternatively, the specimen may be treated by sputolysin. Passage through mesh leads to some loss of epithelial cells, but generally to a degree insufficient to affect sample interpretation. Following mesh filtration, the fluid is subjected to low-speed (1,800g)centrifugation to obtain a cell pellet. This is resuspended in balanced salt solution, and aliquots (100,000-200,000 cells are desirable) are used to prepare cytocentrifuge slides or membrane filtrates. For routine evaluation, some slides are stained by the Romanowsky technique, and others by the Papanicolaou method. Some authorities^{63,64} have recommended preparation of hematoxylin-eosin (H&E) eosin stained slides. Additional cytocentrifuge slides should be prepared if special stains (acid fast bacteria, Grocott, methenamine silver) are required for identification of microorganisms. Issues of cytocentrifugation speed and the potential superiority of membrane filtration over cytocentrifugation are discussed in a number of recent publications.^{70–74}

Specimen Adequacy

Bronchoalveolar lavage fluids must be assessed for adequacy. Excessive numbers of ciliated or squamous epithelial cells (greater than 5%) are indicative of contamination by bronchial or oral material, indicating that the specimen may not be representative of the distal portions of the respiratory tract.⁵⁹ Chamberlain et al.⁶⁴ suggested specific criteria for judging specimens as unsatisfactory for evaluation. Criteria for rejection included: 1) paucity of alveolar macrophages on the prepared glass slides (less than 10 alveolar macrophages per 10 high-power fields or less than 25 alveolar macrophages per high-power field in combination with either criterion two or three); 2) excessive numbers of epithelial cells, either showing morphologic degenerative changes or exceeding the number of alveolar macrophages present; 3) a mucopurulent exudate of polymorphonuclear cells; 4) numerous red blood cells in combination with at least one of the other criteria for inadequacy; or 5) degenerative changes or artifacts obscuring cell identity. In addition, a specimen should be considered adequate if it demonstrates a specific pathologic process (viral infection, neoplasia, or fungal or bacterial disease).

Fine-Needle Aspiration

Fine-needle aspiration (FNA) cytology is a widely used technique for the diagnosis of localized pulmonary pathology and is the most effective cytologic technique for establishing a definitive diagnosis of lung carcinoma.⁴⁸ Transthoracic FNA is successful at diagnosing both primary and metastatic disease, and is associated with an overall diagnostic sensitivity between 75–95%.^{75–79} Both transthoracic percutaneous needle aspiration and transbronchial (Wang) needle aspiration biopsy are used for investigation of pulmonary nodules.

Percutaneous Transthoracic Biopsy

Percutaneous transthoracic aspiration biopsy is the more widely used of the two procedures. In many centers, if sputum cytology is negative and the pulmonary lesion is present at the periphery or apex of the lung, transthoracic FNA will be performed without bronchoscopy. In the majority of cases, a 22-gauge Chiba or Greene needle will optimize specimen procurement.

The fine needle is guided to the desired location by fluoroscopy or CT imaging, and once the needle tip is confirmed to be in position, the stylet is removed and a syringe is attached. Suction is applied and the needle moved rapidly forwards and backwards in the lesion. The vacuum is then released, and the needle removed while the patient

holds his breath. A portion of the sample is expelled onto glass slides and smears prepared. Some are allowed to air-dry, while others are fixed in 95% ethanol. The needle may be washed out in either a balanced salt solution or formalin. The air-dried material is stained by the Wright-Giemsa technique (Diff-Quik) and immediately assessed as to specimen adequacy. Alternatively, rapid evaluation can be achieved using smears appropriately fixed and stained by the rapid Papanicolaou stain or a frozen section-type H&E stain. If diagnostic material is not obtained, repeat aspirations are performed until satisfactory material is obtained or the radiologist or patient chooses to end the procedure. Immediate microscopic assessment of material also allows the performance of additional passes when the cytopathologist on immediate review deems special studies, including immunohistochemistry, flow cytometry, electron microscopy, or microbiologic culture, necessary for complete evaluation.^{80, 81} Specimens submitted (other than smears) can be processed by either cytocentrofugation or cell-block techniques. When cytocentrifugation is preferred, the needle should be rinsed in 1-2 ml of balanced salt solution or RPMI medium. Blood clot and visible tissue fragments are best processed as cell-block preparations, and these are obtained by rinsing the needle in 2-3 ml of 10% neutral-buffered formalin. The cell blocks are routinely processed through paraffin, and H&E sections are prepared. In selected cases, immunohistochemistry can be performed on the cell block or cytocentrifuge specimens.⁸¹ Many centers prefer using cell-block material for immunohistochemistry.

Transbronchial (Wang) Needle Biopsy

While transbronchial aspiration biopsy via flexible bronchoscope was originally used to detect metastases within mediastinal lymph nodes, it has become popular with pulmonologists for the workup of lung nodules in or near the major bronchi.82-84 The procedure is used less frequently because it is relatively time-consuming and requires a skilled bronchoscopist. It is, however, a low-risk procedure and may provide diagnostic information when other techniques fail, such as bronchial brushing, washing, and biopsy. It is useful for investigating external bronchial compression or submucosal lesions and for evaluating mediastinal lymph nodes in staging of bronchogenic carcinoma. The addition of transbronchial needle biopsy to bronchoscopy increases the overall sensitivity of that technique to nearly 100% for tumors located in large bronchi.85 Wang needle biopsy should be obtained prior to performing other diagnostic procedures, including bronchial washings, brushings, and grasp biopsy.86,87 Processing and interpretation are performed by a technique identical to that used for percutaneous aspirations. An adequate specimen usually contains many diagnostic cells. Unsatisfactory specimens include samples with much blood, with low cellularity, or with many benign bronchial mucosal cells and macrophages representing contaminants from tracheobronchial secretions on the mucosal surface. A malignant aspirate may be obtained by inadvertent aspiration of endotracheal secretions containing neoplastic cells from the more distal airways. Similarly, in mediastinal staging of pulmonary neoplasms, the aspirate may be contaminated by inadvertent sampling of tumor in the lung parenchyma rather than in the lymph nodes.⁸⁸ In this situation, the cytopathologist should ascertain that the smears contain lymphocytes as evidence of accurate sampling of the peribronchial or tracheal lymph nodes. It seems prudent for the cytopathologist to interpret with caution specimens containing only a few tumor cells, no lymphocytes, and abundant respiratory cells or mucus.⁸⁸

Contraindications for Fine-Needle Aspiration (Percutaneous and Transbronchial)

Relative contraindications for fine-needle aspiration of pulmonary nodules include an uncooperative or unconscious patient, an individual who is unable to control his or her cough reflex, uncorrectable coagulation abnormalities, poor lung function, severe emphysema, marked hypoxemia, pulmonary hypertension, intrapulmonary vascular lesions, and hydatid cyst.^{89–94} While none of these conditions is an absolute contraindication for fine-needle aspiration of a pulmonary lesion, the potential benefits should be substantial before proceeding with the procedure. Because of the potential hazards of transthroacic FNA, it may be best performed in a setting where emergency services are immediately available and where the services of a thoracic surgeon are within reasonable proximity.

Complications associated with percutaneous fine-needle aspiration include pneumothorax,^{95–100} intrathoracic hemorrhage with hemoptysis,^{101,102} and air embolization.^{103–105} Up to one third of patients may develop a clinically significant pneumothorax, but only 5–10% will require treatment.^{95–100} Hemoptysis occurs in between 2–8% of patients but is usually not a significant clinical problem.^{101,102} Air embolism is a very rare complication which may be fatal. Transbronchial needle aspiration of pulmonary lesions is associated with complications similar to those of percutaneous transthoracic fine-needle aspiration, but pneumothorax is less frequent.

Specimen Adequacy

The assessment of specimen adequacy in fine-needle aspirates from pulmonary nodules is a complex issue. The presence of neoplastic cells in a specimen defines it as adequate. However, there are no universally accepted morphologic criteria defining a specimen as adequate in the absence of malignant cells. Demonstration of etiologic agents of infectious disease (e.g., fungal forms or AFB) may also be indicative of the disease process. Other findings, including those of pneumonia, do not necessarily guarantee that the specimen represents the primary pathologic process.

PAPANICOLAOU SOCIETY

Multiple samplings and immediate specimen assessment with repetitive sampling as indicated improve the satisfactory rate. Often factors other than the cytopathologist's opinion of specimen adequacy will determine whether additional passes are attempted:⁸⁸ these include lesional size, location, vascularity, and operator skill.⁸⁰ In general, 2–3 passes optimize the relationship between sample adequacy rates and patient comfort.¹⁰⁵ Williams et al.¹⁰⁵ demonstrated that 80% of pulmonary malignancies were diagnosed within the first two passes, and all malignancies detectable were identified when six separate passes were performed.

Since specific morphologic or numeric criteria for specimen adequacy do not exist for pulmonary fine-needle aspiration cytology, we recommend the terms "adequate" and "nondiagnostic" in the evaluation of pulmonary FNA specimens. When a specimen yields material representative of a specific pathologic entity, the specimen is designated as "adequate." A specimen composed of benign respiratory epithelium, macrophages, and inflammatory cells in the presence of a significant clinical or radiographic lesion is designated as nondiagnostic despite the presence of abundant cellular material. This category implies that clinical follow-up or further investigation should be considered. The assessment of a specimen as adequate or nondiagnostic preferably occurs during the aspiration process and should be reported immediately. Additionally, the assessment of adequacy should be addressed in a comment contained within the final report. This is best done by inclusion of a section which addresses immediate evaluation of adequacy. Such a section has the benefit of documenting the performance of immediate assessment for billing purposes.

Diagnostic Categories for Cytology Specimens

The present guidelines do not attempt to describe the cytologic features related to various lesions occurring within the lung as sampled by multiple techniques. Rather, these guidelines are meant to establish a set of diagnostic categories which succinctly and uniformly transmit pathologic diagnostic information in a standardized format to the clinician. It must be stressed that FNA diagnosis of pulmonary lesions is a clinicopathologic interpretation, and correlation with clinical and radiographic findings is mandatory.

Nondiagnostic Specimens

This category is composed of specimens where no cellular material is obtained, the material is artifactually distorted by blood, poor preservation, or processing artifacts such that a diagnosis cannot be rendered, or a specific clinicopathologic entity cannot be diagnosed. Included in this category are specimens composed of benign cellular elements (respiratory epithelium, macrophages, inflammatory cells) which are insufficient to account for the lesion identified by bronchoscopic or radiographic study. When this diagnostic category is used, a comment should be included explaining the reason the specimen is assigned to this category.

Specific Benign Lesions

This category should include all benign neoplasms, inflammatory processes, and smears in which infectious (fungal, mycobacterial, and bacterial) agents are identified. Within this category each process should be described as specifically as possible. For example, the formulation might read "benign; pulmonary hamartoma" or "benign; granulomatous inflammation consistent with tuberculosis." A comment should be issued when additional information further specifying the nature of the lesion would be helpful to the clinician.

Atypical Cells Present, Probably Benign

This category should be used when an epithelial or mesenchymal component is present with nuclear atypia believed by the cytopathologist to represent a reactive or reparative change. This diagnosis is not a "stand-alone" diagnosis but requires clinicopathologic correlation and additional investigation if clinically indicated.

Atypical, Suspicious for Malignancy

This category includes specimens that show atypical features believed by the cytopathologist to have a significant risk of representing a malignant neoplasm. This category also applies to cases in which severely abnormal cells may be present in numbers too low to permit a definitive diagnosis or the degree of atypia is below the threshold for a definitive diagnosis.

Malignancy Present

This category should contain all specimens in which a definitive diagnosis of malignancy can be made. If a specific histologic type of carcinoma is recognized it should be so diagnosed. Although since definitive pathologic tumor typing is not always possible, an attempt should be made to state whether the malignancy is of epithelial or nonepithelial origin, and if epithelial, whether it represents a small-cell or nonsmall-cell carcinoma or a metastasis. Correlation with clinical history is recommended.

Because some studies¹⁰⁶ have reported only a 75% rate of correctly typing lung carcinomas, it may be prudent to separate lung carcinomas into small- and nonsmall-cell types. This division has clinical support in that most therapeutic decisions require only this level of subclassification. Raab and Silverman¹⁰⁷ reviewed the accuracy and significance of cytologic typing of lung carcinomas.

Reporting of Findings in Cytologic Specimens

The cytologic report should be clear, concise, and clinically relevant, as discussed by Suen et al. in the Guidelines of the Papanicolaou Society of Cytopathology.¹⁰⁸ A statement

regarding the nature of the specimen reviewed should be given to include the number of passes performed and the number of slides received, and it should be documented if materials were received for cytospin or cell-block preparations. Terminology should be consistent, and the cytopathologist should attempt to render as specific a diagnosis as possible. The Papanicolaou class system should not be used, and whenever possible the cytologic diagnosis should closely simulate the corresponding histopathologic diagnosis.

In many cases, a comment should address the adequacy of the specimen, those factors limiting the diagnostic accuracy of the specimen, and the reasons for the categorization of a specimen as nondiagnostic, atypical and probably benign, or atypical and suspicious for malignancy. A recommendation for future action may be included in the report when the cytopathologist feels that it is indicated. In other practice situations, the cytopathologist may wish to report recommendations verbally to the clinician. The recommendation may suggest further diagnostic studies, including bronchial biopsy, mediastinoscopy, or thoracotomy with biopsy. This recommendation need not be part of the report if a definitive diagnosis is rendered. Comments and additional communication are most important when the cytopathologist is unfamiliar with the clinician or clinicians receiving the report.

References

- DeFine LA, Saleba KP, Gibson BB, Wesseler TA, Baughman R. Cytologic evaluation of bronchoalveolar lavage specimens in immunosuppressed patients with suspected opportunistic infections. Acta Cytol 1987;31:235–242.
- Kyriazis AP, Kyriazis AA. Incidence and distribution of opportunistic lung infections in AIDS patients related to intravenous drug use: a study of bronchoalveolar lavage cytology by the Diff-Quik stain. Diagn Cytopathol 1993;9:487–491.
- Miles PR, Baughman RP, Linnemann CC Jr. Cytomegalovirus in the bronchoalveolar lavage fluid of patients with AIDS. Chest 1990;97: 1072–1076.
- Selvaggi SM. Bronchoalveolar lavage in lung transplant patients. Acta Cytol 1992;36:674–679.
- Strigle SM, Gal AA. Review of pulmonary cytopathology in the acquired immunodeficiency syndrome. Diagn Cytopathol 1989;5: 44–54.
- Walts AE, Marchevsky AM, Morgan M. Pulmonary cytology in lung transplant recipients: recent trends in laboratory utilization. Diagn Cytopathol 1991;7:353–358.
- 7. Weiss RL, Snow GW, Schuman GB, Hammond ME. Diagnosis of *Cytomegalovirus pneumonitis* on bronchoalveolar lavage fluid: comparison of cytology, immunofluorescence, and in situ hybridization with viral isolation. Diagn Cytopathol 1991;7:243–247.
- Solans EP, Yong S, Husain AN, Eichorst M, Gattuso P. Bronchoalveolar lavage in the diagnosis of CMV pneumonitis in lung transplant recipients: an immunocytochemical study. Diagn Cytopathol 1997;16: 350–352.
- Kanjanaviro, Kul N, Scripa C, Paupairoj A. Cytologic diagnosis of Cryptococcus neoformans in HIV-positive patients. Acta Cytol 1997; 41:493–496.
- Crystal RG, Bitterman PB, Rennaud I, Hance AJ, Keogh BA. Interstitial lung diseases of unknown cause: disorders characterized by chronic inflammation of the lower respiratory tract. N Engl J Med 1984;310:154–166.

- Crystal RG, Fulmer JD, Roberts WC, Moss ML, Line BR, Reynolds HY. Idiopathic pulmonary fibrosis: clinical, histologic, radiographic, physiologic, scintigraphic, cytologic and biochemical aspects. Ann Intern Med 1976;85:769–788.
- Haslam PL, Turton CWG, Heard B, Lukoszek A, Collins JV, Salsbury AJ, Turner-Warwick M. Bronchoalveolar lavage in pulmonary fibrosis: comparison of cells obtained with lung biopsy and clinical features. Thorax 1980;35:9–18.
- Huang M-S, Colby TV, Goellner JR, Martin WJ Jr. Utility of bronchoalveolar lavage in the diagnosis of drug-induced pulmonary toxicity. Acta Cytol 1989;33:533–538.
- Hunninghake GW, Gadek JE, Kawanami O, Ferrans VJ, Crystal RG. Inflammatory and immune processes in the human lung in health and disease: evaluation by bronchoalveolar lavage. Am J Pathol 1979;97: 149–206.
- Ramirez R-J, Kieffer RF Jr, Ball WC Jr. Bronchopulmonary lavage in man. Ann Intern Med 1965;63:819–828.
- Stoller JK, Rankin JA, Reynolds HY. The impact of bronchoalveolar lavage cell analysis on clinicians' diagnostic reasoning about interstitial lung disease. Chest 1987;92:839–843.
- Studdy PR, Rudd RM, Gellert AR, Uthayakumar S, Sinha G, Geddes DM. Bronchoalveolar lavage in the diagnosis of diffuse pulmonary shadowing. Br J Dis Chest 1984;78:46–54.
- Weinberger SE, Kelman JA, Elson NA, Young RC, Reynolds HY, Fulmer JD, Crystal RG. Bronchoalveolar lavage in interstitial lung disease. Ann Intern Med 1978;89:459–466.
- Merritt TA, Puccia JM, Stuard ID. Cytologic evaluation of pulmonary effluent in neonates with respiratory distress syndrome and bronchopulmonary dysplasia. J Pediatr 1981;98:949–956.
- Silverman JF, Turner BC, West RL, Dillard TA. Bronchoalveolar lavage in the diagnosis of lipoid pneumonia. Diagn Cytopathol 1989;5:3–8.
- Recalde AL, Nickerson BG, Vegas M, Scott CB, Landing BH, Warburton D. Lipid-laden macrophages in tracheal aspirates of newborn infants receiving intravenous lipid infusions: a cytologic study. Pediatr Pathol 1984;2:25–34.
- 22. Nussbaum E, Maggi JC, Mathis R, Galant SP. Association of lipid-laden alveolar macrophages and gastroesophageal reflux in children. J Pediatr 1987;110:190–194.
- Collins Orris KA, Geisinger KR, Block SM, Wagner PH. The cytologic evaluation of lipid-laden alveolar macrophages as an indication of aspiration pneumonia in young children. Acta Cytol 1992;36:598.
- Johnston WW. Cytologic diagnosis of lung cancer: principles and problems. Pathol Res Pract 1986;181:1–36.
- Mylius EA, Gallvas B. Alveolar macrophage count as an indicator of lung reaction to industrial air pollution. Acta Cytol 1986;30:157–162.
- Roby TJ, Swan GE, Sorensen KW, Hubbard GA, Schumann GB. Discriminate analysis of lower respiratory tract components associated with cigarette smoking, based on quantitative sputum cytology. Acta Cytol 1990;34:147–154.
- Swan GE, Schamann LB, Roby TJ, Sorensen KW. Quantitative analysis of sputum cytologic differences between smokers and non-smokers. Diagn Cytopathol 1991;7:569–575.
- Swan GE, Roby TJ, Hodgkin JE, Mittman C, Peters JA, Jacobo A. Relationship of cytomorphology to spirometric findings in cigarette smokers. Acta Cytol 1994;38:547–553.
- Risse EKJ, Vant Hof MA, Vooijs GP. Relationship between patient characteristics and the sputum cytologic diagnosis of lung cancer. Acta Cytol 1987;31:159–165.
- Johnston WW, Frable WJ. The cytopathology of the respiratory tract: a review. Am J Pathol 1976;84:372–414.
- Sproul EE, Huvos A, Britsch C. A two-year follow up study of 261 patients examined by use of superheated aerosol induced sputum. Acta Cytol 1962;6:409–412.
- Johnston WW, Elson CE, Ini Bibbo M. Comprehensive cytopathology, 3rd ed. Philadelphia: W.B. Saunders; 1991. p 320–323.

- Dadgeon LS, Wrigley CH. On the demonstration of particles of malignant growth in the sputum by means of the wet-film method. J Laryngol Otol 1935;50:752–763.
- Hajdu SI. A note on the history of carbowax in cytology. Acta Cytol 1983;27:204–206.
- Saccomanno G, Saunders RP, Ellis H, Archer VE, Wood BG, Beckler PA. Concentration of carcinoma or atypical cells in sputum. Acta Cytol 1963;7:305–310.
- Chang JP, Aken M, Russell WO. Sputum cell concentration by membrane filtration for cancer diagnosis: a preliminary report. Acta Cytol 1961;5:168–172.
- Fields MJ, Martin WF, Young BL, Tweeddale DN. Application of the Nedelkoff-Christopherson Millipore method to sputum cytology. Acta Cytol 1966;10:220–222.
- Suprun H. A comparative filter technique study and the relative efficiency of these sieves as applied in sputum cytology for pulmonary cancer cytodiagnosis. Acta Cytol 1974;18:248–251.
- Fleury-Feith J, Escudier E, Pochelle MJ, Carre C, Bernaudin JF. The effects of cytocentrifugation on differential cell counts in samples obtained by bronchoalveolar lavage. Acta Cytol 1987;31:606–610.
- Erozan YS, Frost JK. Cytopathologic diagnosis of lung cancer. Semin Oncol 1974;1:191–198.
- Koss LG, Melamed MR, Goodner JT. Pulmonary cytology: a brief survey of diagnostic results from July 1st, 1952 until December 31st, 1960. Acta Cytol 1964;8:104–113.
- 42. Bocking A, Biesterfeld S, Chatelain R, Gien-Gerlach G, Esser E. Diagnosis of bronchial carcinoma on sections of paraffin-embedded sputum. Sensitivity and specificity of an alteration to routine cytology. Acta Cytol 1992;36:37–47.
- Perlman EJ, Erozan YS, Howdon A. The role of the Saccomanno technique in sputum cytopathologic diagnosis of lung cancer. Am J Clin Pathol 1989;91:57–60.
- Rizzo T, Schumann GB, Riding JM. Comparison of the pick-andsmear and Saccomanno methods for sputum cytologic analysis. Acta Cytol 1990;34:875–880.
- Chodosh S. Examination of sputum cells. N Engl J Med 1970;282:854– 857.
- Greenberg SD. Recent advances in pulmonary cytopathology. Hum Pathol 1993;14:901–912.
- Bardales RH, Baker SJ, Simpson DD, Schaefer RF, Stanley MW. Sputum cytology: cost effectiveness and diagnostic yield. Acta Cytol 1996;40:1067.
- 48. Johnston WW. Fine needle aspiration biopsy versus sputum and bronchial material in the diagnosis of lung cancer: a comparative study of 168 patients. Acta Cytol 1988;32:641–648.
- 49. Landa JF. Indications for bronchoscopy. Chest 1978;73:686-690.
- Jay SJ, Wehr K, Nicholson DP, Smith AL. Diagnostic sensitivity and specificity of pulmonary cytology: comparison of techniques used in conjunction with flexible fiber optic bronchoscopy. Acta Cytol 1980;24:304–312.
- Truong LD, Underwood RD, Greenberg SD, McLarty JW. Diagnosis and typing of lung carcinomas by cytopathologic methods: a review of 108 cases. Acta Cytol 1985;29:379–384.
- Solomon DA, Solliday NH, Gracey DR. Cytology in fiberoptic bronchoscopy: comparison of bronchial brushing, washing and postbronchoscopy sputum. Chest 1974;65:616–619.
- Ng ABP, Horak GC. Factors significant in the diagnostic accuracy of lung cytology in bronchial washing and sputum: I: Bronchial washings. Acta Cytol 1983;27:391–396.
- Ng ABP, Horak GC. Factors significant in the diagnostic accuracy of lung cytology in bronchial washing and sputum samples: II: Sputum samples. Acta Cytol 1983;27:397–402.
- Walloch J. Pulmonary cytopathology in historical perspective. In: Gruhn JG, Rosen ST, editors. Lung cancer. The evolution of concepts. New York: Field and Wood; 1989. p 509–520.
- Popp W, Merkle M, Schreiber B, Rauscher H, Ritschka L, Zwick H. How much brushing is enough for the diagnosis of lung tumors? Cancer 1992;70:2278–2280.

- Tanaka T, Yamamoto M, Tamura T, Moritani Y, Miyai M, Hiraki S, Ohnoshi T, Kimura I. Cytologic and histologic correlation in primary lung cancer: a study of 154 cases with resectable tumors. Acta Cytol 1985;29:49–56.
- Barbazza R, Toniolo L, Pinnarello A, Scapinello A, Falconieri G, DiBonito L. Accuracy of bronchial aspiration cytology in typing operable (stage I–II) pulmonary carcinomas. Diagn Cytopathol 1992; 8:3–7.
- Stanley MW, Henry-Stanley MJ, Iber C. Bronchoalveolar lavage. Cytology and clinical applications. New York: Igaku-Shion; 1991. p. 10–20.
- Taskinem EI, Tukianinen PS, Alitalo RL, Turunen J. Bronchoalveolar lavage. Am J Pathol 1994;29:121–155.
- Gwebski E, Hess T, Hold G, Speich R, Russi E. Diagnostic value of hemosiderin-containing macrophages in bronchoalveolar lavage. Chest 1992;102:1794–1799.
- Perez-Arellano JL, Garcia JEL, Marcias MCG, Gomez FG, Lopez AJ, de Castro S. Hemosiderin-laden macrophages in bronchoalvoelar lavage fluid. Acta Cytol 1992;36:26–30.
- Drew WL, Finley TN, Golde DW. Diagnostic lavage and occult pulmonary hemorrhage in thrombocytopenic immunocompromised patients. Am Rev Respir Dis 1997;116:215–221.
- Chamberlain DW, Braude AC, Rebuck AS. A critical evaluation of bronchoalveolar lavage. Criteria for identifying unsatisfactory specimens. Acta Cytol 1987;31:599–605.
- 65. Hanninshake GW, Kawanami O, Ferrans VJ, Young RC Jr, Roberts WC, Crystal RG. Characterization of inflammation and immune effector cells in the lung parenchyma of patients with interstitial lung disease. Am Rev Respir Dis 1981;123:407–412.
- 66. Spertini F, Aubert JD, Leimgraber A. The potential of bronchoalveolar lavage in the prognosis and treatment of connective-vascular diseases. Clin Exp Rheumatol 1996;14:681–688.
- Klech H, Pohl W. Technical recommendations and guidelines for bronchoalveolar lavage (BAL). Eur Respir J 1989;2:561–585.
- Ettensohn DB, Jankowski MJ, Duncan PG, Lalor PA. Bronchoalveolar lavage in the normal volunteer subject. I. Technical aspects and inter subject variability. Chest 1988;94:275–280.
- Rennard SI, Ghafouri M, Thompson AB, Linder J, Vaughan W, Jones K, Ertl RF, Christensen K, Prince A, Stahl MG, Robbins RA. Fractional processing of sequential bronchoalveolar lavage to separate bronchial and alveolar samples. Am Rev Respir Dis 1990;141:208–217.
- Willcox M, Kervitsky A, Watters LC, King TJ. Quantification of cells recovered by bronchoalveolar lavage. Comparison of cytocentrifuge preparations with the filter method. Am Rev Respir Dis 1988;138: 74–80.
- Baughman R, Strohofer S, Kim CK. Variation of differential cell counts of bronchoalveolar lavage fluid. Arch Pathol Lab Med 1986;110:341–343.
- Erice A, Hertz MI, Snyder LS, Englund J, Edelman CK, Balfour JH. Evaluation of centrifugation cultures of bronchoalveolar lavage fluid for the diagnosis of *Cytomegalovirus pneumonitis*. Diagn Microbiol Infect Dis 1988;10:205–212.
- Lam S, LeRiche JC, Kijek K. Effect of filtration and concentration on the composition of bronchoalveolar lavage fluid. Chest 1985;87:740– 742.
- Thompson AB, Robbins RA, Ghafouri MA, Linder J, Rennard SI. Bronchoalveolar lavage fluid processing. Effect of membrane filtration preparation on neutrophil recovery. Acta Cytol 1989;33:544–549.
- Alonso P, Sanchez S, Ramirez E, Cicero R. Transthoracic needle biopsy in neoplastic and non-neoplastic pathology: experience in a general hospital. Diagn Cytopathol 1986;2:284–289.
- Bocking A, Close KC, Kyll HJ, Hauptmann S. Cytologic versus histologic evaluation of needle biopsy of the lung, hilum and mediastinum. Acta Cytol 1995;39:463–471.
- 77. Caya JG, Clowry LJ, Wollenberg NJ, Tien TM. Transthoracic fine-needle aspiration cytology: analysis of 82 patients with detailed

verification criteria and evaluation of false-negative cases. Am J Clin Pathol 1984;82:100–103.

- Johnston WW. Percutaneous fine-needle aspiration biopsy of the lung: a study of 1,015 patients. Acta Cytol 1984;28:218–224.
- Zarbo RJ, Fenoglio-Preiser CM. Interstitial data base for comparison of performance in lung fine-needle aspiration cytology: A College of American Pathologists Q-probe study of 5,264 cases with histologic correlation. Arch Pathol Lab Med 1992;116:463–470.
- Layfield LJ, Coogan A, Johnston WW, Patz EF. Transthoracic fine-needle aspiration biopsy: Sensitivity in relation to guidance technique and lesion size and location. Acta Cytol 1996;40:687–690.
- Liu K, Dodge R, Glasgow BJ, Layfield LJ. Fine-needle aspiration: comparison of smear, cytospin, and cell block preparations in diagnostic and cost effectiveness. Diagn Cytopathol 1998;19:70–74.
- Wang KP, Terry P, Marsh B. Bronchoscopic needle aspiration biopsy of paratracheal tumors. Am Rev Respir Dis 1978;118:17–21.
- Wang KP, Brower R, Haponik EF, Siegelman S. Flexible transbronchial needle aspiration for staging of bronchogenic carcinoma. Chest 1983;84:571–576.
- Wang KP, Haponik EF, Britt EJ, Khouri N, Erozan Y. Transbronchial needle aspiration of peripheral pulmonary nodules. Chest 1984;86:819– 823.
- Rosenthal DL, Wallace JM. Fine-needle aspiration of pulmonary lesions via fiberoptic bronchoscopy. Acta Cytol 1984;28:203–210.
- Harrow EM, Oldenburg FA Jr, Lingenfelter MS, Smith AM Jr. Transbronchial needle aspiration in clinical practice: a five-year experience. Chest 1989;96:1268–1272.
- Nguyen G-K, York EL, Jones RL, King EG. Transmucosal needle aspiration biopsy via the fiberoptic bronchoscope: value and limitations in the cytodiagnosis of tumors and tumor-like lesions of the lung. Pathol Annu 1992;27:105–132.
- Suen KC. Adequacy of non-gynecologic cell samples. In: Kline TS, Nguyen GK, editors. Critical issues in cytopathology. New York: Igaku-Shoin; 1996. p 68–82.
- Morkve O, Skaavland E, Myking A, Stangeland L, Gulsvik A. Transthoracic fine-needle aspiration guided by fluoroscopy: validity and complications with 19 operators. Respiration 1988;53:239–245.
- Perlmutt LM, Johnston WW, Dunnick NR. Percutaneous transthoracic needle aspiration: a review. AJR 1989;152:451–455.
- Sanders DE, Thompson DW, Padden BJE. Percutaneous aspiration lung biopsy. Can Med Assoc J 1971;104:139–147.
- Sargent EN, Turner AF, Gordonson J, Schwinn CP, Pashky O. Percutaneous pulmonary needle biopsy: report of 350 patients. AJR 1974;122:758–768.

- Sterrett G, Whitaker D, Glancy J. Fine-needle aspiration of lung, mediastinum, and chest wall: a clinicopathologic exercise. Pathol Annu 1982;17:197–228.
- Tao L-C, Sanders DE, Weisbrod GL, Ho CS, Wilson S. Value and limitations of transthoracic and transabdominal fine-needle aspiration cytology in clinical practice. Diagn Cytopathol 1986;2:271–276.
- Bonfiglio TA. Fine-needle aspiration biopsy of the lung. Pathol Annu 1981;16:159–180.
- Cagle PT, Kovach M, Ramzy I. Causes of false results in transthoracic fine needle lung aspirates. Acta Cytol 1993;37:16–20.
- Cristallini EG, Asceni S, Farabi R, Paganelli C, Peciarolo A, Bolis GB. Fine needle aspiration biopsy in the diagnosis of intrathoracic masses. Acta Cytol 1992;36:416–422.
- Kato H, Konaka C, Kawate N, Yoneyama K, Nishiyama K, Saito M, Sakai H, Kinoshita K, Hayata Y. Percutaneous fine-needle cytology for lung cancer diagnosis. Diagn Cytopathol 1986;2:277–283.
- Saa-Gandi FW, Mearns AJ. Fine needle aspiration biopsy of pulmonary lesions: a 2-year experience in a district general hospital. J R Coll Surg Edinb 1991;36:309–311.
- Stanley JH, Fish GD, Andriole JG, Gobien RP, Betsill WL, Laden SA, Schabel SI. Lung lesions: cytologic diagnosis by fine-needle biopsy. Radiology 1987;162:389–391.
- Sinner WN. Pulmonary neoplasms diagnosed with transthoracic needle biopsy. Cancer 1979;43:1533–1540.
- Westcott JL. Direct percutaneous needle aspiration of localized pulmonary lesions: results in 422 patients. Radiology 1980;137: 31–35.
- Dalquen P, Oberholzen M. Lung biopsy: methods, value, complications, timing and indications. Pathol Res Pract 1979;164:95–103.
- Palmer DL, Davidson M, Lush R. Needle aspiration of the lung in complex pneumonias. Chest 1980;78:16–21.
- 105. Williams AJ, Santiago S, Lohrman S, Popper R. Transcutaneous needle aspiration of solitary pulmonary masses: how many passes? Am Rev Respir Dis 1987;136:452–454.
- Suprun H, Pedio G, Ruttner JR. The diagnostic reliability of cytologic typing in primary lung cancer with a review of the literature. Acta Cytol 1980;24:494–500.
- Raab SS, Silverman J. Clinical utility of cytologic typing of lung tumors. Diagn Cytopathol 1994;10:376–382.
- Papanicolaou Society Task Force on Standards of Practice. Guidelines of the Papanicolaou Society of Cytopathology for the examination of fine-needle aspiration specimens from thyroid nodules. Diagn Cytopathol 1996;15:84–89, Mod Pathol 1996;9:710–715 [simultaneous publication].