# Percutaneous Needle Biopsy

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Jesus Zornoza, M.D.

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**Jesus Zornoza, M.D.**

Associate Radiologist and
Associate Professor of Radiology
Department of Diagnostic Radiology
The University of Texas System Cancer Center
M. D. Anderson Hospital and Tumor Institute
Houston, Texas


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**A mis padres and to**
**Jeanne, Andy and Anne**

# FOREWORD

There have been many major advances in diagnostic radiology during the past twenty-five years, but probably none have had a more profound effect upon the conduct of the specialty than the development of image intensification. Thirty-two years ago, when I began my residency, there was little actual involvement of the radiologist in the performance of examinations requiring minor surgical procedures. Neurologists and neurosurgeons performed myelograms, cerebral arteriograms and pneumograms, and the few vascular procedures relating to other parts of the body were in the province of the surgeon. Percutaneous biopsy techniques under radiographic control were largely unknown and, indeed, in some departments of radiology, house staff or referring physicians were summoned to inject contrast material for intraveneous pyelography. Now all of this has changed. The production of a clear fluoroscopic image, in a moderately lighted room at a reasonable level of radiation, has led to the development of sophisticated "special procedures" which have significantly altered the relationships of radiologists to their patients and colleagues. The ability of radiologists to utilize their knowledge of equipment and radiographic anatomy in the performance of invasive procedures has resulted in virtually all of these examinations falling within their purview. One of the significant developments of this trend has been the increased use of the percutaneous biopsy. The fluoroscopic identification of pertinent anatomic structures has resulted in a precision which was not previously possible and diagnostic problems which, in the past, required surgical exploration are now often resolved within the space of a few moments in the Departments of Radiology and Pathology.

The value of a percutaneous biopsy is, of course, directly dependent upon the cooperation of the pathologist and his familiarity with cytologic techniques. His is probably the more difficult role, but competence in both the radiologic and cytologic aspects is not difficult to achieve and the savings to the patient in time, expense and morbidity are difficult to overstate. Dr. Zornoza and his contributors are to be congratulated on the compilation of a volume which will unquestionably influence the handling of patients at many levels of care.

**Gerald D. Dodd, M. D.**
**Professor and Chairman, Department of Diagnostic Radiology**
**The University of Texas System Cancer Center**
**Houston, Texas**

# PREFACE

Historically, the radiologist has employed the least invasive technique available to make a diagnosis. Recently, such radiological techniques as computed axial tomography, ultrasonography, and subselective angiography have changed diagnostic radiology. In addition to these remarkable advances in imaging techniques, radiology has expanded to include interventionist services such as percutaneous needle biopsies, drainage procedures, selective embolization procedures, and percutaneous intra-arterial dilatation. With the advent of these new radiological procedures, the present-day radiologist can no longer confine his knowledge to radiological techniques; instead, he must also acquaint himself with the clinical and laboratory status of the patient upon whom he will shortly apply his skills.

With the use of percutaneous needle biopsy, an accurate pathological diagnosis can be made in selected patients without the need for surgery. Consequently, the patient can be spared the risk and expense of the surgical procedure. The latter is important in view of the rising cost of medical care. Percutaneous needle biopsy has been successfully employed to establish the diagnoses of lesions of the lung, bone, kidney, thyroid, breast, and other organs. Although cytological methods will never eliminate the need for histological diagnosis, clinical experience over the past decade has shown that percutaneous biopsy has a definite place in the management of neoplastic disorders.

The purpose of this monograph is to describe the different biopsy techniques currently practiced, along with their indications, contraindications, results, and complications. Also, the case material presented demonstrates the incorporation of these procedures into the everyday clinical practice of radiology.

**JESUS ZORNOZA, M.D.**

# CONTRIBUTORS

**Luis Alonso deSantos, M.D.**
Department of Radiology, Plaza del Oro Hospital, Houston, Texas. Former Clinical Assistant Radiologist, The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute, Houston, Texas

**Philip J. Dubois, M.B.B.S., F.R.C.R.**
Assistant Professor of Radiology, Imaging Division, Department of Radiology, Duke University Medical Center, Durham, North Carolina

**Moshe Friedman, M.D.**
Associate Chief, Department of Radiation Medicine, Roswell Park Memorial Institute, Buffalo, New York

**John S. Kennerdell, M.D.**
Associate Professor of Ophthalmology, Department of Ophthalmology and Neurology, University of Pittsburgh School of Medicine, The Ear and Eye Hospital, Pittsburgh, Pennsylvania

**John M. Lukeman, M.D.**
Pathologist and Professor of Pathology, Director of Cytology Section, Department of Pathology, The University of Texas System Cancer Center M. D. Anderson Hospital and Tumor Institute, Houston, Texas

**Christopher J. Moran, M.D.**
Assistant Professor of Radiology, Section of Neuroradiology, Mallinckrodt Institute of Radiology, St. Louis, Missouri

**Thomas P. Naidich, M.D.**
Associate Professor of Radiology, Section of Neuroradiology, Mallinckrodt Institute of Radiology, St. Louis, Missouri

**Björn Nordenström, M.D.**
Professor and Chairman, Department of Radiology, Karolinska Hospital, Stockholm, Sweden

**Nelson G. Ordoñez, M.D.**
Assistant Pathologist and Assistant Professor of Pathology, Department of Pathology, The University of Texas System Cancer Center, M. D. Anderson Hospital and Tumor Institute, Houston, Texas

**Robert M. Quencer, M.D.**
Associate Professor of Radiology and Neurological Surgery, Department of Radiology, University of Miami, Jackson Memorial Medical Center, Miami, Florida

**Håkan Rydèn, M.Sc.**
Project Manager Biomedical Engineering, Tekniska Rontgencentralen AB, Fack, Stockholm, Sweden

**Katsutaro Shimaoka, M.D.**
Associate Chief, Department of Clinical Pharmacology and Therapeutics, Roswell Park Memorial Hospital, Buffalo, New York

**Gunilla Svane, M.D.**
Resident, Department of Radiology, Karolinska Hospital, Stockholm, Sweden

**Jesus Zornoza, M.D.**
Associate Radiologist and Associate Professor of Radiology, Department of Diagnostic Radiology, The University of Texas System Cancer Center, M. D. Anderson Hospital and Tumor Institute, Houston, Texas

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# CONTENTS

# Chapter 1 Cytological Diagnosis and Techniques

JOHN M. LUKEMAN, M.D.

The burgeoning use of diagnostic cytology as an accepted procedure in our medical armamentarium has brought aspiration cytology into the spotlight (3). For the past four decades, aspiration biopsy of the prostate gland, breast, lymph nodes, bone, and cysts has been used frequently throughout the world, but especially in Europe. Although used as a diagnostic procedure since the 1930's (5), it has been used very sparingly in the United States (4) because the open biopsy has been so easily accomplished. However, it may ideally shorten the interval between the time of diagnosis and the institution of therapy. Currently it is being used with increasing enthusiasm in many medical centers, but not in smaller hospitals because of an insufficient number of trained cytopathologists and some hesitancy on the part of the clinicians and radiologists to attempt aspiration biopsy. The extremely high cost of medical care and hospitalization have focused the physician's attention on the amount of time and expense that may be saved by this simple and rapid diagnostic procedure. The fine needle aspiration biopsy is comparable to, and the cytological equivalent of, the 1-ml tissue biopsy sampled by the endoscopist. However, it may be more diagnostic because both distortion and artifact can be eliminated if the procedure is performed properly. The diagnosis is often accepted as the equivalent of a surgical pathology report and must be meaningful and accurate.

The quality of the biopsy and the experience of the cytopathologist are of great importance. The cytopathologist must have a broad knowledge of the normal histology and an intimate knowledge of the cytology of the various organ systems and of the benign and the malignant pathological processes that involve those systems. To render a proper assessment of a biopsy, he should be informed of the suspected clinical diagnosis, physical findings on the patient, and the site from which the biopsy was taken. A "blind" biopsy unaccompanied by supportive clinical data may lead to misinterpretation of the specimen by an unwary, busy cytopathologist.

It is not always possible to obtain a diagnostic specimen. The inexperienced physician will need to perform several biopsies until the technique is mastered. Familiarity with factors such as the differentiation between tumor tissue and debris, the importance of needle rotation, and the texture and resistance of the tissue requires experience. Too frequently, the physician who is unskilled in aspiration techniques unknowingly collects necrotic debris, fibrin, or blood. He subsequently receives a report that declares the absence of tumor cells in an obviously existent mass, and becomes disenchanted with the procedure. In some instances, the aspirate contains only a few degenerating diagnostic neoplastic cells or none at all. This must not deter the physician from attempting additional biopsies.

It should be mentioned that aspirates of epithelial tumors that show little cellular cohesiveness, e.g., melanomas, adenocarcinomas, and squamous cell carcinomas, usually contain adequate cellular material. Aspirates of the solid mesodermal tumors,

such as fibrosarcomas, chondrosarcomas, etc., may not yield good cellular samples. In such cases, use of a 19- or 20-gauge needle may be required. A question frequently asked of pathologists is: "What is the possibility that there may be implantation of tumor cells along the needle tract?" This has been mentioned by several authors (5). However, this complication occurs so very rarely that the possibility of its occurrence is of little practical significance. A positive diagnosis is followed by surgical resection, a more extensive surgical procedure, or irradiation with or without chemotherapy. Therefore, it is exceedingly unlikely that recurrence in the needle tract will result in regrowth or seeding of the tumor. No examples of such seeding have been encountered at our institution.

There are pitfalls to aspiration cytology. A good clinical history and the differential diagnosis must be available. The precise location of the lesion aspirated, the age and sex of the patient as well as the radiographic findings are of major importance in the evaluation of a tumor. When aspirated cancer cells show diagnostic features such as keratinization, acinar formation, or melanin pigment, a definitive diagnosis can be made. The diagnosis of undifferentiated small (oat) cell carcinoma can usually be made without difficulty. When the cells examined are poorly differentiated, it is rarely possible to say more than that they are poorly differentiated neoplastic cells. Similarly, it is not possible to determine the site of the primary lesion from a few malignant cells aspirated from an enlarged lymph node containing metastatic carcinoma unless they show unique and specific characteristics. A mucin-producing adenocarcinoma metastatic to the lung is cytologically indistinguishable from a primary mucinous adenocarcinoma of the lung.

M.D. Anderson Hospital is a categorical institution committed to the therapy and management of cancer patients. Its major emphasis, therefore, lies in the earliest possible detection of primary or recurrent cancers and in the immediate institution of therapy for possible cure or control of the disease.

Experience with aspiration biopsies at our institution has been gained predominantly in the lung, abdominal viscera, retroperitoneum, lymph nodes, and bone.

## PREPARATORY TECHNIQUES

Methods of processing the aspirated specimen vary with different institutions. Some cytopathologists brought up in the tradition of hematologists prefer air dried smears to wet fixation in 95% ethanol. With the air dried smears, the Wright-Giemsa, or May-Grunwald stain are used. Most American cytopathologists prefer wet fixation with 95% ethanol and use the Papanicolaou stain. Some pathologists process the smears or embed the aspirates in paraffin as surgical pathology specimens. They are then processed in the Autotechnicon and stained with hematoxylin and eosin. At our institution, wet fixation and Papanicolaou stain are preferred and used routinely. Rapid wet fixation penetrates the cytoplasm and nucleus quickly; it preserves the entire cell and prevents distortion, shrinkage, and swelling. Elimination of these factors results in improved nuclear detail and, consequently, in greater accuracy of diagnosis. It must be acknowledged that cells on the smear represent a "manipulated" population because they have been forcefully extracted from their environment. With the architectural pattern and cell relationships modified, the importance of maximal cell preservation and optimal staining to enhance nuclear detail cannot be overemphasized. Poor technique may result in the failure to detect, identify, or classify malignant cells properly. The well-differentiated neoplasms are diagnosed with ease. When the aspirate contains only poorly differentiated cells, minute nuclear detail may represent the difference between an accurate positive diagnosis and an inconclusive one. Experience has shown that multiple small oval nucleoli are seldom encountered in squamous carcinoma; irregular chromatin clumps or large single nucleoli are usually found. Prominent or large nucleoli occur in adenocarcinoma, melanoma, and histiocytic lymphoma, but are rarely, if ever, encountered in the undifferentiated small (oat) cell carcinoma. It is our opinion that most of the cases diagnosed improperly

are the result of inadequate sampling, processing, and staining. The general pathologist performing aspiration cytopathology must address these problems.

There is no better example to demonstrate the distortion that occurs in biopsies than the forceps biopsy taken through the fiberoptic bronchoscope. The "crush" artifact (Fig. 1.1), regardless of how well the tissue is processed and stained, makes it extremely difficult in many cases, if not impossible, to determine whether the small hyperchromatic, distorted, and compressed cells represent a malignant lymphoma, an undifferentiated small (oat) cell carcinoma, or a poorly differentiated squamous cell or adenocarcinoma. The same problems occur when an attempt is made to apply a definitive diagnosis to aspiration biopsies if adequate processing and staining are not utilized.

Immediately upon withdrawal of the aspirate, the specimen is expelled into Mucolexx, a mucolytic preservative fluid that produces little or no distortion. The specimen is promptly sent to the cytopreparatory laboratory where it is centrifuged for 10 min at 3500 rpm. After centrifugation, the number of smears to be prepared is determined by visual estimation of the cell volume below the supernatant fluid. The cytotechnologist determines the optimal number of smears to be made depending upon the cell concentration. It has been our experience that the variable cellularity of the specimen, its contamination by blood, inflammatory cells, and necrotic debris, make it more desirable that an experienced cytotechnologist prepare the smears from a liquid specimen rather than that the radiologist or other physician prepare them directly from the specimen upon its removal from the patient. Often the physician's technique is not of consistently high quality and the smears are thick, bloody, and uneven, and show considerable distortion.

Usually there are three options available to the cytotechnologist.

1. If the sediment is of poor cellularity, then a sufficient portion of the supernatant is removed so the entire remaining specimen is 1 to 2 ml in volume. The specimen is agitated and transferred to two cytocentrifuge chambers. The cytocentrifuge preparations are made on completely frosted slides. They are placed immediately in Carnoy's solution if the material is hemorrhagic; if not, then they are fixed at once in 95% ethanol and stained by the Papanicolaou technique. The smears are frequently deceiving in red blood cell content, and Carnoy's solution is used almost routinely. Unstained smears may appear to contain very few erythrocytes, but more may be present than suspected.

2a. If the cell sediment appears adequate, then the supernatant is removed by bulb pipette and placed in a properly labeled test tube. With the pipette a small amount of the sediment is placed on a completely frosted glass slide. A single thin smear is made of the sediment by even and careful distribution of the material on the slide with the tip of the pipette. If there is blood on the slide, then the smear is immediately immersed in Carnoy's solution for 15 to 30 min unless the specimen is STAT from the operating room or an outpatient clinic. In such cases, the time in Carnoy's solution is shortened to approximately 10 min by manual agitation of the smears in several consecutive Copeland jars. Only after red cell lysis appears complete is processing continued.

2b. Two cytocentrifuge specimens are made in a manner identical to that described in option 1.

3a. Should small tissue fragments be found in the specimen, they are either treated as a small biopsy and submitted for a cell block preparation in 10% formalin, or crushed between two completely frosted slides and treated as pipetted smears with 95% alcohol fixation.

3b. With an excellent yield of cells without tissue fragments, two smears are prepared by pipette technique and two cytocentrifuge preparations are made precisely as described above but only after dilution of 2 drops of thick sediment with 5 to 10 ml of Mucolexx.

A. If, however, the cell population of the cytocentrifuge smears appear thick or crowded, then the cytocentrifuge preparations are treated as hematology smears, i.e., each preparation is covered with a frosted slide, pressed lightly together for even spread, and pulled apart. These are treated as pipetted smears.

B. The original specimen is now further diluted with Mucolexx as necessary to insure that the 6-mm space on the frosted cytocentrifuge slide is not again covered with too many cells.

All residual and unused material is resuspended in fresh Mucolexx, refrigerated, and held in reserve until the final report has been completed. If it is learned from the radiologist, clinician, or the accompanying registration slip, that a poorly differentiated malignant neoplasm has been found previously, then a portion of the concentrated sediment is placed in 2% gluteraldehyde and submitted to the electron microscopy laboratory for evaluation and possibly a more definitive diagnosis (see Chapter 11). Smears for special stains are similarly prepared for identification of mucin, glycogen, fungi, pneumocystis, melanin, etc., when indicated. When leukemia or lymphoma are clinically suspected and so indicated on the requisition slip, several nonfrosted glass slides are also smeared so that they may be stained with Wright's or Wright-Giemsa stain. These stains are especially valuable in the diagnosis of granulocytic leukemia, for demonstrating cytoplasmic granules and Auer rods. They also may be useful in the diagnosis of lymphoma.

## LUNG

Large caliber needle aspiration biopsy of the lung was first used early in this century for the diagnosis of pneumonia, carcinoma, and other lesions of the thorax, including pleurisy. Unfortunately, the trocar and cutting needles produced hemorrhage, air embolism, a high incidence of pneumothorax and other complications. The procedure fell into disrepute and was used infrequently until 1955, when Grunze (2) suggested that the large bore needles and cutting edge needles were probably responsible for these and other complications. He recommended the use of small caliber needles without a cutting edge for aspiration of the lung. Although interest was somewhat rekindled, the persistently high incidence of pneumothorax reported (25 to 35%) did not inspire confidence, and aspiration biopsies were used sporadically until the late 1960's. The rising incidence of patients with advanced lung cancer and the number of individuals with lung masses complicated by cardiac problems, emphysema, and chronic obstructive pulmonary disease, made it mandatory to establish a diagnosis in many of these patients without resorting to thoracotomy. Benign and malignant tumors of all types are capable of diagnosis by aspiration biopsy provided an adequate number of cells are removed and processed properly.

A simplified cytological classification is used. It is less extensive than the histological classification recommended by the World Health Organization. It must be remembered that an aspiration biopsy represents only a minute sample of the tumor and that it may not be completely representative of all areas of the tumor. Only when multiple samples from different areas of a tumor are examined is it possible to establish a definitive diagnosis.

The cytological classification follows: *1*) Squamous cell carcinoma: well differentiated; moderately differentiated; poorly differentiated. *2*) Undifferentiated small (oat) cell carcinoma: lymphocyte-like oat cell; intermediate-fusiform oat cell. *3*) Adenocarcinoma: well differentiated; moderately differentiated; poorly differentiated; bronciolo-alveolar. *4*) Undifferentiated (anaplastic) large cell carcinoma giant cell. *5*) Bi- or multicomponent tumors. *6*) Carcinoid: benign; atypical. *7*) Sarcoma—typed, if possible. *8*) Malignant lymphoma, non-Hodgkin's, typed. *9*) Hodgkin's disease.

Metastatic carcinoma to the lung from breast, genitourinary tract, skin, bone, gastrointestinal tract, and other organs is readily identified. It is pointless to describe in detail the cytologic appearance of the multiple cells of primary or metastatic carcinoma found in the aspirates (Figs. 1.2 to 1.7). It is quite easy to identify specific cell types when they are well differentiated, but a pertinent clinical history is essential for the diagnosis of metastatic lesions. A squamous cell carcinoma from the tongue, lip, larynx, or cervix will appear identical to a primary squamous cell carcinoma of the bronchus in an aspirated specimen.

## RETROPERITONEAL LYMPH NODES

Lymph nodes of the subcutaneous tissues have been examined by needle aspiration for many years. It is an accepted doctrine that lymph nodes are not partly

resected, but are totally removed so the architectural pattern is preserved and cell relationships are maintained. This is of utmost importance when lymphomas are suspected. Usually, reactive inflammatory processes, malignant lymphoma, or metastatic carcinoma are the lesions to be identified. Enlarged, fixed, firm cervical, supraclavicular or axillary lymph nodes are suspicious for metastatic cancer or lymphoma. The correct diagnosis of lesions involving these nodes can usually be made by aspiration biopsy. However, it is rarely possible to determine the site of the primary neoplasm from an aspiration biopsy or even from histological section of a lymph node harboring a metastatic carcinoma.

Pelvic and paraaortic nodes have been the kind of lymph nodes most often biopsied at our institution. Patients with squamous cell carcinoma or adenocarcinoma of the cervix, carcinoma of the endometrium, or carcinomas of the prostate or testes are followed routinely by lymphangiography. If the findings are suspicious or abnormal, then a direct transabdominal aspiration biopsy is performed. In some aspirated specimens, numerous large, multinucleated histiocytes are found. They are reactive to the opaque dye injected for lymphangiography (Fig. 1.8). When fragments of malignant tissue or cells of metastatic carcinoma are recovered, treatment can be instituted without delay or laparotomy.

The presence of malignant cells of metastatic squamous cell carcinoma of the cervix (Fig. 1.9), adenocarcinoma of the endometrium (Fig. 1.10), adenocarcinoma of the prostate (Fig. 1.11), and melanocytic melanoma are not a diagnostic problem when a representative sample is obtained. However, the poorly differentiated tumors are baffling when few malignant cells are found and there is no evidence of a known primary carcinoma. Similarly, confirmation of some types of lymphoma may be extremely difficult.

Reactive processes such as either infectious mononucleosis with markedly atypical enlarged lymphocytes or chronic nonspecific hyperplastic lymphadenitis may show sufficient pleomorphism to mislead the cytopathologist into suspecting the presence of a malignant lymphoma. Reactive germinal center cells are 3 to 4 times the size of a normal lymphocyte, contain large nucleoli and variable chromatin patterns which are disturbing. Many cells with slight variability of the nuclear chromatin occur in chronic lymphocytic leukemia or its lymphoma counterpart, but similar cells may also occur in reactive lymph nodes. Thus, the diagnosis of chronic lymphocytic leukemia or well-differentiated lymphocytic lymphoma are not easily rendered unless clinical data and other findings are corroborative. Aspiration biopsies may be suggestive but not diagnostic of these entities. When the aspirated cells show marked nuclear variation, and immature (blast) forms, cleaved forms, and stem cells are present, the diagnosis of lymphoma is easily made. Large cell (histiocytic) lymphoma is diagnosed with ease. This lesion is composed predominantly of abnormal pleomorphic mononuclear histiocytic cells, blast and stem cells, and a sprinkling of lymphocytes. The histiocytic cells vary markedly; in some, the nuclear parachromatin is watery; in others, it is finely granular. The nuclei often are lobulated or show nuclear protrusions. A single large nucleolus is characteristic; occasionally, a cell with several smaller nucleoli is found. Hodgkin's disease may be diagnosed only if characteristic Reed-Sternberg cells are detected. Abnormal mononuclear cells identical with those of histiocytic lymphoma occur in the aspirated specimen. The presence of eosinophils is suggestive; however, if Reed-Sternberg cells are not present, then it may be impossible to render the diagnosis. Hodgkin's disease of mixed cellularity may be difficult or impossible to diagnose unless the diagnostic Reed-Sternberg cells are observed. The (malignant) mononuclear cell of Hodgkin's disease should be at least 2 to 4 times the size of the normal lymphocyte and contain finely granular nuclear chromatin and a prominent large irregular nucleolus. Binucleation or cells with multiple nuclei that overlap may be present. Occasionally, the diagnostic binucleated "mirror image" cells with large single nucleoli are found. Often after irradiation therapy has been given, atypical bi- or multinucleated histiocytes are present. These may be found after lymphangiographic examinations and