HANDBOOK OF FINE NEEDLE ASPIRATION BIOPSY CYTOLOGY

Second Edition

Tilde S. Kline

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In memory of my father, Otto Saphir
and, in appreciation,
to my husband, Irwin K. Kline

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Foreword to the Second Edition

Seven years have passed since the first edition of this book was published. It became apparent that a new edition was necessary because of growing confidence and acceptance of aspiration biopsy cytology (ABC) by the clinical community and because of refinements in the interpretation of cytologic material.

Every new or underutilized procedure in medicine has its proponents, but Dr. Kline has been the catalyst that has pushed ABC from obscurity to easy recognition. She has turned skeptical clinicians into enthusiastic believers.

All surgeons at our institution now perform mastectomy or other definitive surgery on the basis of a positive needle aspiration biopsy (NAB) alone without a confirmatory inpatient frozen section or open biopsy done on an outpatient. The economic and psychological advantages of this are obvious. The urologists have found the sampling of prostate nodules by NAB a valuable and dependable office procedure, and pulmonologists and orthopods increasingly utilize this technique. Invasive radiologists have been convinced of its efficiency, and add a cytologic dimension to CT scanning and ultrasonic evaluation of deep-seated lesions.

Dr. Kline was certainly a pioneer in establishing ABC, and her enthusiasm and dedicated teaching created a growing number of enlightened disciples. With this second edition, I hope she will dispel any residual reticence to the usefulness of ABC in the management of human disease.

Hunter S. Neal, M.D.
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Foreword to the First Edition

"The greatest and noblest pleasure which men can have in this world is to discover new truths; and the next is to shake off old prejudices." (Frederick the Great)

Those of us who function as thoughtful clinicians find that we are increasingly dependent on a greater variety of laboratory and radiographic sophistication to reach our diagnostic and therapeutic conclusions. The pathologist and radiologist offer an ever enlarging spectrum of diagnostic studies. Aspiration biopsy cytology (ABC) is a cost-effective clinical tool.

To accept the value of ABC, the clinician must overcome his prejudice — that passing a thin needle into a malignant lesion will surely spread the tumor. This objection has not been substantiated in studies of thousands of cases.

The application of this simple, inexpensive technique has had a profound effect on the profile of surgery in institutions where it is appropriately applied. At Lankenau Hospital in the two years before 1970, when fine needle biopsy was unavailable, only 20% of patients admitted for excisional biopsy of breast tumors with frozen section had a mastectomy for carcinoma. In the two years preceding 1979, when thin needle aspiration was performed, approximately 60% of the patients admitted for breast surgery required mastectomy. Most knew the diagnosis before surgery, and the majority underwent mastectomy without frozen section examination. The economic and emotional advantages of this are obvious.

In the sometimes subtle diagnosis of pancreatic malignancy at laparotomy, aspiration biopsy has been a boon as an accurate tool, having none of the rather significant complications of larger, cutting-needle or wedge biopsies. Our recent experience with thin needle aspiration biopsies in thyroid pathology has paralleled that of Crile, and now is frequently performed on the first office visit, before thyroid scanning. In the matter of the pulmonary nodule, the technique has been very helpful in separating the benign from the malignant lesion and the primary from the metastatic tumor. To date we have had no chest wall seeding.

Another prejudice is that cellular pathology is not accurate enough to justify its widespread application. Yet who would question the diagnostic value of an upper gastrointestinal x-ray film to elucidate the presence of ulcer disease? It is no more accurate than a thin needle biopsy of a malignant tumor and considerably more expensive.

It is hoped that this volume will stimulate widespread acceptance of this technique and help ABC assume the importance it deserves. As a clinical surgeon, I am deeply grateful to Dr. Kline for providing this hospital with this most useful diagnostic procedure.

Hunter S. Neal, M.D.
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Preface to the Second Edition

In the seven years since the publication of the first edition of this volume, aspiration biopsy has been popularized in medical parlance in the United States. Conferences for pathologists are replete with workshops and discussions of various aspects of this fascinating field. Correspondingly, clinical interest has become immense.

While the aim of the first edition was to set the wares temptingly before the public, this second edition is devoted to displaying and categorizing the recently published literature. This wealth of material has permitted the addition of chapters devoted to mediastinum (Dr. Sally Rosen), liver (Dr. Liang-Che Tao), eye (Dr. Misao Takeda), and immunocytochemistry (Dr. Albert A. Keshgegian). The enthusiasm and skill of the many radiologists, who have changed shadows into substance, is exemplified by Drs. Steven Teplick and Pamela Haskin in their chapter on imaging modalities. Additionally, the variety of experts garnering the biopsies has led to a section devoted to technique.

The original chapters have been revised and enlarged, although the format remains the same. Throughout, salient identifying features for pertinent lesions are presented. This is done initially and primarily by pattern recognition and then by study of individual cells. All material is prepared according to the Papanicolaou method. Each presentation includes a brief sketch of the clinical features and histopathology. The chapters are concluded by review of the accuracy of the procedure and diagnostic pitfalls. Finally, there is a comprehensive list of references.

The team approach has proven invaluable. The clinician or radiologist provides the specimen and the pathologist interprets it in light of the clinical setting. For us, this method meets the needs of the clinical community and affords optimum use of the medical specialities for the benefit of the patient.

I have received much help in the preparation of this *Handbook*. My colleagues, Drs. Irwin K. Kline, Ilona R. Ring, Joseph H. Cooper, and Albert K. Keshgegian, have enhanced my understanding in many spheres. I am indebted to my coworker, Dr. Vaidehi Kannan, for her meticulous cytomorphologic observations. I am grateful to the cytotechnologists: Suzanne Kent, Mary Cahalan, Maryann Davis, Linda Muzroll, and Claire Sims, and to Carolyn Lachowicz for her editorial assistance. Marie Norton, our librarian, has provided needed articles, both without and with the use of her new computer. I am especially indebted to Michelle Darby for her indefatigable pursuit of excellence in endless manuscript preparation. Special thanks are in order to Tess Jennifer Kline for her photographic assistance. I would also like to express appreciation for the clerical assistance of Cecilia Gallagher.

Tilde S. Kline, M.D.

Preface to the First Edition

Fine needle biopsy is here to stay. It has emerged slowly since Martin and Ellis conducted their study in 1930 and has been refined by 25 years of use in Scandinavia. It is my aim to assist in adapting this invaluable tool to the practice of medicine in the United States — in medical centers and within offices and clinics. This book is based on 11 years of experience with fine needle biopsy at Lankenau Hospital, a 448-bed general hospital with attached physicians' offices.

The term ABC — aspiration biopsy cytology (as used by Zajicek and Löwhagen) — was selected from a number of synonyms. It was chosen to clearly distinguish aspiration from exfoliative cytology and to emphasize its simplicity.

The optimum success of ABC requires an interdisciplinary approach — a partnership among the clinician, radiologist, and pathologist. It can be serviceable to all clinicians in all specialties. Surgeons have found it particularly advantageous for preliminary examination and as a special biopsy technique in the operating room. Its use among radiologists is burgeoning in conjunction with ultrasonic and computerized tomographic scans. To meet the needs of the clinician and radiologist, the technique, indications, numerous advantages, rare complications, accuracy, and pertinent case reports are stressed in the text. There are also comprehensive bibliographies. As is obvious in any book written by a pathologist, the text is designed for interpretation of cellular material. Within these pages, tissue pathology is integrated with aspiration biopsy cytology. Similarly, most figures include photographs of histologic sections. The newly interested pathologist, resident, and cytotechnologist can garner study sets by application of the fine needle to surgical and autopsy specimens. Each chapter concludes with diagnostic pitfalls. These are of particular importance to the novice but, it is hoped, will also aid the experienced practitioner.

All organs have become targets for aspiration biopsy. In some areas my experience is limited. Chapter 10 is an attempt to explore these new horizons and to present some of the emerging data and a reference bibliography.

Smetana stated that for proper evaluation of aspiration biopsy these questions must be answered: "Do the results justify the means? If there is a choice, is aspiration biopsy the method of choice? Does the simplicity of the technical procedure outweigh the possible danger to the patient?" All of these queries can be answered affirmatively, as the following chapters show.

I want to express my gratitude to my colleagues Drs. Irwin Kline, Ilona Ring, Joseph Cooper, Donald Cook, and Vaidehi Kannan for their help and understanding and to my fellow in cytopathology, Dr. Rajeev Sachdeva, for aid with special stains. My thanks go to the cytotechnologists Karen Biester, Mary Cahalan, Sue Groff, Claire Sims, and Mary Ann Vinitski for their suggestions, and Carolyn Lachowicz for her editorial assistance; to Thea Fischer, our librarian; and to Rosalind Leighton for her advice. For manuscript preparation I am indebted to Delores Pascale and Ruth Nurmi.

I am grateful to Drs. Steven Teplick and Lawrence Goodman for permission to utilize their material and to Dr. Martin Rush for his encouragement. My appreciation goes to the many clinicians who utilized the technique and especially to Dr. Hunter S. Neal for inaugurating and supporting fine needle aspiration biopsy at Lankenau Hospital. Special thanks are owed to Joel Kline for his innumerable hours devoted to photography. And finally, I gratefully acknowledge the debt to my teachers of cytopathology, Drs. James Reagan and Otto Saphir.

Tilde S. Kline, M.D.

The reader is asked to please note that, in this book, "ABC" is an abbreviation for "Aspiration Biopsy Cytology" and "NAB" is an abbreviation for "Needle Aspiration Biopsy."

Contents

Color Plates follow page 296.

1

General Considerations

Fine-needle aspiration biopsy is the study of cells obtained by a small-gauge needle, generally with a vacuum system provided by an air tight syringe. All areas of the body are suitable sites for this procedure. The lesion may be a palpable superficial or deep mass, or it may be one that has been seen or felt at laparotomy. Alternatively, the lesion may be visible only with the use of imaging modalities. The procedure involves penetration of the lesion which is surrounded by a zone of normal tissue, by a fine needle. The specimen thus obtained consists of a minute amount of tissue or evacuated fluid.

Two terms used consistently in this handbook are NAB (needle aspiration biopsy) and ABC (aspiration biopsy cytology). The term NAB was coined by Hunter S. Neal, Chairman of Surgery at Lankenau Hospital, and refers to the actual biopsy procedure. The term ABC was coined by Löwhagen and colleagues[25] and refers to the specimen on the slide.

HISTORY

Many significant observations had been made by morphologists and pathologists interested in normal and morbid cytology and its diagnostic possibilities. Yet this impressive volume of investigative work did not reach a stage of general recognition for many decades until finally its cumulative force, strengthened by the impact of new contributions, caused a break in the dam of inertia and skepticism that had blocked its progressive course.[29]

This statement, expressed by Papanicolaou[29] in 1952, refers to exfoliative cytology but is equally applicable to ABC today.

It is of historical interest that Papanicolaou, the father of exfoliative cytology,[6] and Martin and Ellis[27] and Stewart,[38] the conjoint sires of aspiration biopsy, conducted their cellular investigations in neighboring New York hospitals and published their preliminary findings within a two-year span (1928–1930). Both techniques were virtually neglected for several decades. Then, while exfoliative cytology was adopted in the United States, ABC aroused most interest abroad, particularly in Scandinavia.

In the beginning and even much later, acrimonious words were exchanged regarding the value of aspiration biopsy. Pathologists believed that they could establish satisfactory diagnoses only when plentiful tissue was available with which to evalu-

ate architectural relationships. Clinicians condemned the procedure because of the phantom of tumor activation and transmission of malignant cells through the needle tract.[39]

Gradually, a trickle of articles appeared. A few were authored by the progenitors and a few by physicians and trainees at Memorial Hospital.[1,26,28] Two reports of special consequence were the 1930 study of the prostate by Ferguson[14] and the 1938 study of the lung by Craver and Binkley.[9] By the 1950s, reports in the literature included those by Rosemond and associates[31] on the lung, one by Söderström[37] on the thyroid and salivary glands, one by Cornillot and Verhaeghe[8] on the breast, and general reviews by Smetana,[34] Godwin,[16] and Smith and colleagues.[35] In addition, the Netherlands' pioneer, hematologist Cardozo, published a monograph on clinical cytology.[5] Advances in radiology rekindled enthusiasm for NAB of the lung and led to Dahlgren and Nordenström's treatise in 1966,[10] which was soon followed by the works of Söderström[36] and Paseyro.[30] In 1973, Cardozo[4] published the *Atlas of Clinical Cytology* which included more than 3,000 colored plates. The next year, Zajicek[43] published his classic work reflecting the wealth of material from the Scandinavian experience. At this time, because of the enthusiasm of Hunter S. Neal, we, too, commenced using the procedure.[23,24] A number of other scientists, distinguished in the field of aspiration biopsy, preceded and postdated the famous New York trio. The following chapters are introduced with surveys of their work.

In the United States, although aspiration biopsy had been performed by a small, dedicated band of clinicians and pathologists, widespread interest in the procedure lay dormant until quite recently. In this country, several pathologists have been especially influential in disseminating data. Since his first edition of *Diagnostic Cytology and Its Histologic Bases* was published in 1961,[2] Koss has devoted ever-increasing space to aspiration biopsy in subsequent editions. Wied, editor of *Acta Cytologica*, has for several decades presented the findings of the European pioneers of this procedure, and Frable, author and past president of the American Society of Cytology, has imparted his enthusiasm for the procedure to its members. It is interesting to note that, at the annual meeting of this group a decade ago, mine was the solitary workshop on ABC, whereas currently, 21 of 40 workshops are devoted to all aspects of the procedure. Now, more than half a century after Martin, Ellis, and Stewart first described their 65 cases, ABC has come of age, and its future is limitless.[21]

INDICATIONS AND ADVANTAGES

In 1937, Ferguson,[13] pioneer of prostatic aspirations, wrote: "The only function of aspiration biopsy is to differentiate neoplastic from non-neoplastic tissue." Today, this concept still remains the primary goal. There are, however, a number of additional indications for the procedure. These include identification of the tissue constituting the mass (especially in the neck),[20] recovery of specific organisms, and use in research.

Among the advantages of aspiration biopsy which are numerous and which are, therefore, addressed in detail in later chapters, are the following:

1. It usually is an office procedure, necessitating neither patient preparation nor specialized anesthesia.
2. It eliminates or modifies lengthy periods of "watchful waiting."
3. It is safe and almost painless.
4. Both the procedure and its interpretation may be completed rapidly.
5. Sensitivity and specificity are high.
6. It is cost-effective and ideal for implementation of diagnosis-related groups (DRGs).

NAB should be used as part of the initial examination of the patient and, when indicated, should be equal in priority to a chest radiograph or electrocardiogram.

LIMITATIONS

Specific limitations of NAB, which are discussed in the following chapters, must be understood. Open biopsy must be performed whenever indicated. The two methods are not in opposition to,

and may even complement, each other.[33] Limitations lessen as interpretative expertise rises,[40] but still include

1. An inability to diagnose unusual tumors
2. Difficulty in the classification of neoplasms
3. Inappropriate or insufficient biopsy specimens

These limitations are similar to those encountered with formal biopsy. Sometimes, special studies, such as electron microscopy or immunochemistry, as well as tissue sections, can be used to establish a specific diagnosis on ABC. A problem unique to NAB, however, is the effect of fibrosis on adequate biopsy sampling (see the section on Diagnostic Pitfalls, below).

Pathologists must be able to recognize these limitations and to withstand pressure from their clinical confreres. We all have seen cases in which carcinoma was diagnosed only after two or more tissue biopsies (e.g., in Ch. 11, see the section on Diagnostic Accuracy). In fact, at times, the pathologist's inability to make a definitive diagnosis by ABC is paralleled by diagnostic problems in corresponding tissue sections.[15] Yet the pathologist, particularly during initiation into ABC, may be reluctant to issue an equivocal report. The competent pathologist must be able not only to interpret many lesions definitively, but also to recognize the occasions when the interpretation must read: "insufficient material for diagnosis," or "atypical cells are not conclusive evidence of carcinoma." Finally, "pathologists and clinicians should be aware of the limitations [of ABC] and [must obtain] . . . an open biopsy . . . when clinical suspicion for malignancy is not confirmed by aspiration".[33]

COMPLICATIONS

Few complications result from NAB, and these must be compared with those from incisional or excisional biopsy.[32] Special complications are discussed in the following chapters.

Seeding of tumor cells, the most frequently cited limitation of aspiration biopsy, is almost a myth. A handful of cases have been recorded in the thousands of reports from the world literature. Despite the potential danger of dispersal of tumor cells,[12] long-term studies indicate scant risk. Following NAB, there was no recurrence of tumor along the needle tract during a 10-year study of 157 patients with mixed tumor of the salivary glands or during a 5-year study of 469 patients with prostatic carcinoma treated only with hormones.[11] Moreover, the procedure had no adverse influence on prognosis in a 5-year comparative study of patients with renal carcinoma[42] or in a 15-year study of patients with breast carcinoma.[3]

Morbidity following aspiration biopsy is rare. Martin and Stewart[28] reported no serious complications from 3,500 aspirates, and we have observed none after more than 20,000. Indeed, the safety of aspiration biopsy was proven in the large Scandinavian series.[43]

DIAGNOSTIC CRITERIA

The diagnostician, familiar with exfoliative cytology, requires a bridge for transition to the study of ABC. Exfoliative cytology depends on individual cell recognition, whereas ABC depends on pattern recognition. Diagnosis based on exfoliative cytology is made chiefly by examination of the specimen with a high-power lens. In contrast, diagnosis by ABC often is made by examination with a scanning and low-power lens.

The ABC criteria of malignancy, judiciously applied, are the interpreter's guide to objectivity rather than subjectivity; through experience, these criteria have been developed by us and by numerous other critical students of ABC. We have tabulated these criteria into the maximally utilized major and the less ferquently required minor criteria. The major criteria of malignancy, listed in order of importance, are

1. Cellularity
2. Dyshesion
3. Monomorphism
4. Nuclear membrane irregularity
5. Anisonucleosis
6. Eosinophilic macronucleoli

Minor criteria include

1. Loss of polarity
2. Nuclear crowding and piling

3. Indistinct cell borders
4. Cell enlargement
5. Nuclear/cytoplasmic ratio alteration
6. Clumped chromatin

Both preliminary and final examination of ABC should include a rapid slide review with the scanning lens. The three most important ABC criteria of malignancy—cellularity, dyshesion, and monomorphism—are evaluated easily in contrast to three criteria essential for exfoliated malignant cells: nuclear/cytoplasmic ratio alteration, hyperchromasia, and pleomorphism. Therefore, a microscopic stage should be eliminated for examination of ABC. Pattern recognition results in a much speedier diagnosis for ABC than does the scrutiny of individual cells that is necessary for exfoliative cytology.

Cellularity is a critical feature in determining the nature of an aspirate. It is dependent on biopsy technique and slide preparation, and is only uniform in quantity when NAB is performed by a single unit. Thus, when NAB is performed by many operators, cellularity may be difficult to evaluate until the diagnostician becomes accustomed to the fluctuations. Additionally, an aspirate that is distributed equally between two slides is less cellular than one that is concentrated on a single slide (see Ch. 2).

Dyshesion, according to *Dorland's Illustrated Medical Dictionary*, 26th Edition, is defined as "disordered cell adherence; loss of intercellular cohesion, a characteristic of malignancy, as determined by aspiration biopsy cytology." Coman[7] demonstrated experimentally that the force binding benign cells is much greater than the force binding malignant cells. The ABC from many carcinomas is distinguished by an abundance of dyshesive cells that are either in loose sheets or aggregates, or isolated. The cell groups exhibit loss of polarity with nuclear crowding and piling.

Aspirates from malignant tumors may show monomorphism, or "the quality of existing in only one form" (*Dorland's Illustrated Medical Dictionary*, 26th Edition). The cells all appear to be from the same family. Consequently, a population of malignant cells may appear to be quite uniform and even bland.

Nuclear alterations are diagnostic criteria for ABC as well as for exfoliative cytology. These alterations may include nuclear membrane irregularity, anisonucleosis (unequal-sized nuclei), and eosinophilic macronucleoli (nucleoli $> 1.25\ \mu m$). Binucleation and multinucleation are not unusual, but abnormal mitoses are rare. Neither hyperchromasia nor clumped chromatin are of particular importance in the diagnosis of a number of malignant neoplasms. A diathesis of blood, inflammation, and necrotic debris is more commonly associated with inflammatory conditions than with carcinoma.

The ABC of a benign lesion is evaluated by obverse adherence to the criteria for malignancy. These criteria, in order of importance, include

1. Relative sparsity of cells
2. Cohesion
3. Polymorphism
4. Nuclear membrane regularity
5. Equal-sized nuclei
6. Polarity
7. Distinct cell borders

Benign lesions are characterized by cohesive groups of polarized cells in monolayered sheets or acini. Because of their cohesive properties, these aspirates often are scant. Cellular paucity, however, is a criterion requiring careful evaluation. Is a specimen sparsely cellular because of intercellular binding forces or because of inappropriate technique? Clearly, evaluation of technique is essential for accurate diagnosis (see Ch. 2).

Polymorphism, or "the quality of occurring in several different forms" (*Dorland's Illustrated Medical Dictionary*, 26th Edition), is associated with benign lesions. It is characteristic of the ABC from fibrocystic disease with its variety of ductal, apocrine, and foam cells. The benign cells, which often have distinct boundaries, also have uniform, smooth nuclei.

No single criterion is absolute in the interpretation of ABC. Each criterion of malignancy may be seen, to a limited extent, in benign lesions, and conversely, each criterion of benignity may be seen in malignant lesions. A few cells exhibiting anisonucleosis, anisocytosis, and/or macronucleoli more likely originate from a focally atypical lesion than from a carcinoma. Furthermore, the observed criteria depend, to some extent, on the histology of the aspirated tissue and the morphology of the malignant neoplasm. For example, only a cell-rich specimen is satisfactory from a hyperplastic lymph

node, whereas a cell-poor specimen is associated with infiltrating lobular carcinoma. Anisonucleosis is common to both an aspirate from a benign colloid nodule and from a malignant melanoma. Whereas monomorphism is important for diagnosis of infiltrating ductal carcinoma, polymorphism plays a fundamental role in the interpretation of Hodgkin's disease. Thus, as in exfoliative cytology and histopathology, there is no single criterion that establishes the diagnosis of a malignant neoplasm in any one organ. Systematic use of all criteria of malignancy, however, permits accurate and reproducible diagnostic assessment.

INTERPRETATIVE NOMENCLATURE

The terminology for diagnosis of ABC should be histologic in type. The "I–V" classification system is unacceptable, and "positive" or "negative" categorizations should be used sparingly and with amplification. The terms "suspicious" or "unsatisfactory" require an explanatory sentence and sometimes, direct communication (in Ch. 2, see the section on The Operator).

For meaningful diagnoses of benign lesions, there must be adequate and representative specimens, terms that become delineated with experience. A satisfactory aspirate from a patient with fibrocystic disease of the breast may yield a sparse specimen whereas that from a patient with a hyperplastic lymph node is cellular. In lesions with an inflammatory origin, the causative factor may be determined directly from the Papanicolaou-stained aspirate, after application of special stains, or from culture media. Thus, a report of a benign lesion may be as significant as one of a carcinoma.

Diagnoses of neoplasms are contingent upon the availability of sufficient numbers of well-preserved cells that display most or all of the major criteria of malignancy. Whenever possible, the definitive diagnosis should differentiate between carcinoma, sarcoma, and lymphoma; should classify the lesion; and should delineate its degree of differentiation.

A "suspicious" diagnosis may be indicated, even by the experienced diagnostician. Such a diagnosis is established on the basis of

1. A paucity of abnormal cells
2. ABC with some but not all criteria of malignancy
3. Poorly preserved atypical cells

Although its use in conjunction with image-guided biopsies or intraoperative procedures is inconclusive, in superficial sites, a "suspicious" interpretation often is constructive. Depending upon the clinical impression and the organ involved, it should determine whether NAB should be repeated or whether immediate histologic biopsy should be undertaken.

An "unsatisfactory" report must be issued when the specimen is inadequate for interpretation. This occurs with

1. Insufficient numbers of cells
2. Poorly preserved cells
3. Hemorrhagic diathesis that obscures the underlying cells
4. Considerable inflammation and debris, with clinical evidence of a necrotic neoplasm

Proper usage of the term requires knowledge of NAB technique (in Ch. 2, see the section on The Operator). A sparsely cellular aspirate, when obtained by an inexperienced operator, must be interpreted as an "unsatisfactory" specimen, whereas, an aspirate of the same pattern, obtained by an experienced clinician, sometimes may be considered benign.

Each ABC report must be issued according to the team approach, involving the clinician, cytotechnologist, and pathologist (see Ch. 2). In our laboratory, all aspirates are obtained by the clinicians. They are screened and tentatively interpreted by the cytotechnologists. The pathologist, with knowledge of the spectrum of disease and its cellular reflection, then provides the final diagnosis. In many instances, and always in the case of malignant tumors, the final report is issued only after discussion with the referring clinician.

DIAGNOSTIC PITFALLS

A special feature of this book is its emphasis on interpretative traps. Some of these pitfalls, applicable to all body sites, include

1. Inexperience
2. Inflammation
3. Fibrosis

Today, the chief cause of both false-positive and false-negative diagnoses is still inexperience, not only in interpretation of the ABC but also in biopsy technique and specimen preparation. "Geographic miss" and lack of representative and sufficient specimen material may be the result of inept technique. Cellularity, a major criterion of malignancy, is based on the supposition that adequate samples are procured for interpretation.

Two important diagnostic pitfalls are fibrosis and inflammation. Fibrosis, a component of certain benign and malignant lesions and a tissue reaction to radiation, hinders the release of tumor cells from their matrix. Therefore, the experienced physician may perform NAB and harvest only a scant, tumor-free ABC specimen, even though the needle passes into malignant tumor. Inflammatory lesions may pose diagnostic problems for the surgical pathologist. For the cytopathologist, areas of inflammation can be misleading in exfoliative studies, and are a major cause of misinterpretation of ABC.

In most cases, the team approach ameliorates interpretative traps. The patient's history, the clinician's impression, and the pathologist's findings combine to diminish possible errors (in Ch. 2, see the section on The Operator). In the following chapters, pertinent diagnostic pitfalls are illuminated.

DIAGNOSTIC ACCURACY

Aspiration biopsy adds a significant dimension to the art of diagnosis. When it is used correctly, this procedure has a high specificity and accuracy, with the latter ranging from about 80 to 97 percent. This topic will be discussed in detail in the following chapters. Like all biopsies, however, erroneous diagnoses may ensue.[19] Thus, aspiration biopsy must never be the single standard substituted for clinical judgment, or used to negate the indications for tissue biopsy.

On occasion, NAB may yield a more accurate biopsy than will a core biopsy from a coarse, inflexible instrument or even a specimen wedge procured with a scalpel. I have been consulted on interpretation of an ABC specimen from a breast lesion which had been interpreted as positive although subsequent tissue biopsy was benign; repeat biopsy, however, disclosed a small carcinoma. All who have examined aspirates from the prostate have reported a few cases in which only multiple core biopsies were successful in sampling the carcinoma which had initially been diagnosed by NAB.[22] Innes and Feldman[17] reported seven malignant tumors which had been interpreted accurately by NAB but which remained incorrectly unsubstantiated by core and open biopsy. Because of similar experiences, Tao and associates[41] coined the appropriate nomenclature "false false-positive." In this regard, however, a caveat must be issued. The false false-positive concept should be evoked only after considerable interpretative experience and never by a novice, unfamiliar with the pitfalls of ABC.

COMMENCEMENT

How does the novice inaugurate aspiration biopsy? For this endeavor, two potential obstacles must be surmounted

1. Unfamiliarity with NAB and ABC
2. Reluctant physicians

Both require conscientious tutelage.

Initially, some mastery of the technique and its interpretation is essential. Currently, a plethora of workshops are offered. Yet, the most beneficial teaching modality is situated within the pathology department—surgical and autopsy specimens. Here, clinician and pathologist can perform NAB. Here, the pathologist can study all organs and their lesions by ABC. After this bench experience, samples must then be collected and examined from patients. The clinician should be encouraged to conduct a biopsy duet consisting of a core biopsy preceded by NAB. The pathologist should attempt to interpret the ABC before examining the tissue section. This joint performance involving pathologist and clinician ideally leads to the "team approach." When the technique and interpretation of the specimen become familiar, and are rein-