

THE CLINICIAN'S GUIDE TO DIAGNOSTIC CYTOLOGY

G. BERRY SCHUMANN / V. FRANKLIN COLÓN

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*To those physicians
who strive for clinical excellence
while demonstrating humane concern
for their patients.*

Foreword

NEARLY 40 YEARS have elapsed since publication of the book *The Diagnosis of Uterine Cancer by the Vaginal Smear* by Papanicolaou and Traut, which ushered in the present era of diagnostic cytology. Yet, except for the cervical smear, commonly referred to as “Pap smear,” the majority of practicing physicians and surgeons have remained oblivious to the vast scope of diagnostic possibilities that contemporary cytologic techniques can provide for their patients.

Clinical cytology, as currently conceived, includes a broad spectrum of diagnostic options, encompassing virtually every organ system and every space-occupying lesion, whether identified by palpation, roentgenologic techniques, or ultrasound. The concept of exfoliative cytology has been vastly expanded with the use of fiberoptic instruments and thin-needle aspiration biopsies to obtain cell samples. These procedures, which are generally safe for the patient, provide, in many cases, a simple, rapid, accurate, and inexpensive alternative to tissue biopsy. I am convinced that cytologic sampling will play an ever-increasing role in morphologic diagnosis of cancer and other disorders.

The optimal utilization of clinical cytology rests on two essential elements: the sampling technique and the interpretation of the sample. It is clear that inadequate or poorly prepared specimens cannot be correctly interpreted. It is also clear that the pathologist, who is the customary recipient of the sample, must have sufficient background and experience to interpret the material in a competent fashion and to render his verdict in the precise language of surgical pathology, understandable to the clinician. Thus, Papanicolaou’s “classes” have no further place in diagnostic interpretation, since they do not provide a diagnostic statement on which further evaluation or treatment can be based.

This book, written jointly by an expert cytopathologist and a clinician, provides the much-needed *vade mecum* for clinical cytology and tells simply and concisely “how to do it” and what can be achieved and expected. While this book is primarily addressed to clinicians, it may also stimulate

practicing pathologists to familiarize themselves further with the important developments in the realm of cytologic diagnosis of human disease.

I am particularly pleased to see Dr. G. Berry Schumann in the forefront of this effort, as I have known him since his medical school days, and hope that this now remote association may have had some influence upon his brilliant career.

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Preface

DIAGNOSTIC CYTOLOGY is not new; it is just unfamiliar to most clinicians. In its various technical forms, such as exfoliative and aspiration cytology, it has been a part of the practice of medicine for many years. Currently, there are several illustrated textbooks on clinical or diagnostic cytology that emphasize the morphologic correlation between anatomy, histopathology and cytopathology. Unfortunately, clinical cytology still remains underutilized by many medical practitioners simply because the subject has not been well disseminated in most medical school curricula or to practitioners.

This handbook of clinical cytology is a result of the collaboration between a cytopathologist and a clinician. The collaboration culminated in a series of six articles published in *The American Family Physician* from 1978 to 1980. Those articles were so well received by the clinicians who read them that we decided to write a more complete series of articles in the form of a monograph. It was our common point of view that, in order for this very effective diagnostic technique to be promoted among clinicians, a practical and uncomplicated approach to the issues needed to be made. This book is the result of many hours of conversation in which the practical aspects of cytology for clinicians were explored. It has not been our plan that this book should be a comprehensive text. Common cytologic techniques that can be performed with a limited amount of preparation and minimal equipment have been emphasized. Some of the more complex cytologic procedures have been mentioned to make clinicians aware that such procedures are available and to aid the physician in describing them to his patients. Our primary emphasis is on the clinical use of cytology in the ambulatory setting.

Although cytopathologist and clinician have slightly different approaches to the science of cytology, the goal of both is to provide excellent care to patients. We recognize that among the problems encountered in disseminating cytologic information is that of demonstrating the value of this technique in view of the number of competing diagnostic tests that have been developed in recent years. The technical aspects of cytology have been

well communicated to laboratory personnel in many excellent presentations, books, and articles. On the other hand, clear-cut, practical guidelines for clinicians have not been provided or distributed, nor has the information been simply presented. It became our goal to prepare a format for teaching the practical aspects of diagnostic cytology to those who will find the techniques of greatest clinical value.

We have made every effort to answer the clinician's questions as to (1) who should be selected for cytology, (2) what procedure should be followed and what materials used, (3) where the procedure is most appropriately performed, (4) when the procedure is most likely to yield results, (5) why a particular patient or group of patients should be evaluated, and (6) how best results may be obtained. In every way possible, we have tried to be concise and specific. The chapters are arranged according to the probable relative importance to the clinician of the cytologic data presented. The figures, tables and photomicrographs are all intended to simplify the presentation for the reader and to encourage the utilization of cytology in circumstances that the physician may not have considered in the past. The clinician will find that there are many ways in which cytology can be used in everyday practice, thus expanding his diagnostic resources. As he familiarizes himself with and utilizes these techniques, he will find it easier and more appropriate to include cytology in his practice.

We hope that this handbook will help medical students and practicing physicians to appreciate the valuable techniques of this science and apply them to their practice of medicine. In the long run, the physician will gain diagnostic capabilities and his patients will gain through the quality of care rendered to them.

Acknowledgments

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We are also deeply grateful to Verna Papania and Marie Marley of the Department of Family Medicine, University of Cincinnati, and to Mona Chhatpar and the entire secretarial staff of the document processing area, Department of Pathology, University of Utah School of Medicine, for their extreme patience and understanding while typing this manuscript. Many thanks go to Marjorie Colón for her long hours of proofreading and for clarifying many of the authors' thoughts.

Naturally, there are several other contributors whose names are not mentioned in this limited space, but the authors wish to thank them for their sincere efforts in making this handbook possible. Last, we wish to thank Year Book Medical Publishers and Nancy Chorprenning for their guidance and continual support in the preparation of this book.

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1

Introduction

CYTOPATHOLOGY IS A DIAGNOSTIC method whose time has finally arrived.^{1, 9, 11, 12, 14} Many of its basic tenets have been known for more than 100 years,⁵ but in 1928, George N. Papanicolaou, an anatomist, introduced the concept that one could diagnose malignancy by the microscopic interpretation of cellular materials that had been properly collected and spread on glass slides.^{3, 6, 10, 17} This concept was not readily accepted by pathologists, who had long based the diagnosis of malignancy on microscopic parameters such as growth patterns and cellular arrangements seen in tissue sections. Cytology is the study of directly obtained and/or exfoliated cells collected using several techniques that are relatively easy to learn and use. It depends on the ability of the clinician and cytologist to cooperate in collecting, concentrating, preparing, and staining the cellular elements and subsequently identifying the specific cell type(s). Once a cytotechnologist and/or a cytopathologist microscopically identifies the normal constituents of a properly obtained specimen from a specific anatomical region, identification of abnormal cellular elements is the next diagnostic step.

Because all epithelial surfaces continually exfoliate cellular material, microscopic examination of the freed or shed cells frequently provides morphologic information regarding the status of an organ or structure not amenable to direct observation or examination.^{1, 8, 14, 16, 19} Although tissue has been obtained for diagnostic study, for many years, by various methods (surgical, open, excisional, or cutting needle biopsy), in many medical institutions the technique of examination of directly obtained exfoliated cells has not had the wide use that it merits. To obtain representative tissue specimens for diagnosis, invasive methods for tissue section study have too often been exclusively relied upon. Figure 1-1 demonstrates various sizes of aspirating and cutting biopsy needles. Figure 1-2 compares the diameters of various biopsy needles and demonstrates the physical advantage of fine-needle aspiration.

In 1943, following the landmark work describing specimen preparation and staining by George N. Papanicolaou, diagnostic cytology was finally

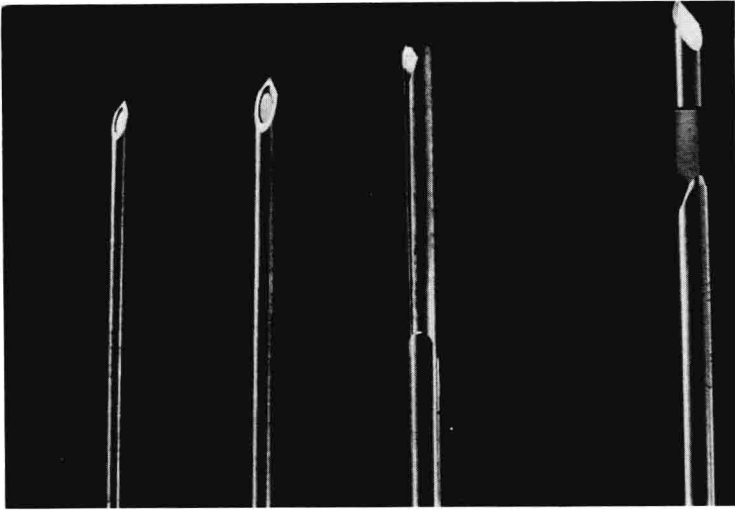


Fig 1-1.—Commonly used aspiration and cutting needles for removal and examination of tissue cells or fluids. Shown from left to right are (1) 21-gauge spinal needle, (2) 18-gauge spinal needle, (3) Franklin-Silverman cutting needle, and (4) Travenol cutting needle. (Courtesy of Dr. John D. Armstrong, Utah Medical Center.

accepted as a clinical tool.⁶ It should be pointed out that, although there is general agreement that Dr. Papanicolaou is considered the founder of the cytologic technique for female genital tract cancer detection, a Rumanian author, Dr. Babes, was the first to publish works on gynecologic cytology. The monumental work of Leopold G. Koss¹² in documenting the histopathologic basis of cytology has allowed diagnostic cytology to become more prominent in the past three decades. The current increase in U.S. interest in this laboratory procedure is, in part, the result of the successful use of fine-needle aspiration cytology performed routinely in Europe, particularly by the Scandinavians, and in a few institutions in this country.

Since the mid-1950s, physicians and a large portion of the lay population have understood the medical implications of the routine gynecologic "Pap smear." What has not been widely appreciated in clinical medicine is that Papanicolaou's efforts can be extended well beyond the realm of gynecologic cytology to a large number of anatomical areas. Common uses of cytologic diagnoses are as follows:

1. Evaluation of inflammatory conditions (e.g., acute, chronic, granulomatous).
2. Identification of microbiologic organisms (e.g., bacteria, parasites, virally infected cells, fungi).

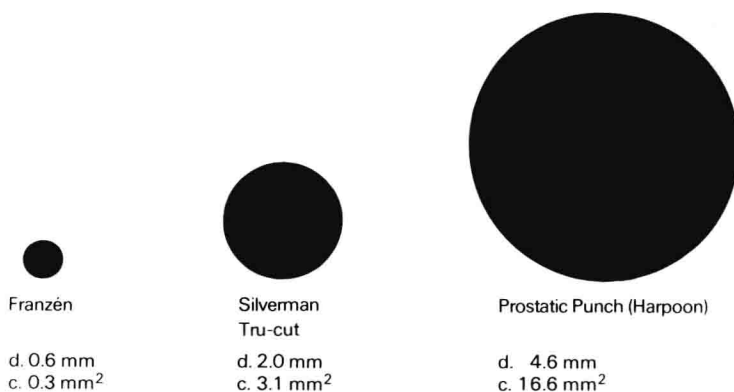


Fig 1-2.—Commonly used biopsy needles in cross section (d, diameter; c, cross-sectioned surface). (From Schattauer, F.K.: *Color Atlas of Cytopathology of the Prostate*, Stuttgart, Verlag, 1975. Used by permission.)

3. Evaluation of cytohormonal effects.
4. Evaluation of benign cellular changes.
5. Detection of unsuspected cancer.
6. Confirmation of suspected cancer.
7. Detection of extent of cancer (metastases).
8. Evaluation and follow up of therapy—radiation, surgery, chemotherapy.
9. Preliminary genetic studies—marginal chromatin (Barr) body.
10. Evaluation of degenerative or toxic cellular changes.

The cause of the inadequate use of cytology as a means of screening and diagnosis lies in the poor dissemination of information about clinical cytology. There is a widespread lack of knowledge regarding the acquisition, preparation, and yield of clinical information from cytologic specimens. Although there is high diagnostic correlation between cytology and direct histologic methods, lack of clarity among clinicians regarding ways to make optimal use of the results has impaired the development of this excellent clinical modality. Table 1-1 lists the diagnostic advantages and disadvantages of cytopathology compared to histopathology.¹⁶

Diagnostic cytology has a number of characteristics that will strongly recommend it to clinicians. The most attractive characteristic is that it is generally noninvasive. Body secretions are the major source of exfoliative cytologic information. Occasionally minimally invasive thin-needle aspiration of cystic or solid structures and of lesions from multiple anatomical sites is required, but the record of safety associated with this procedure further emphasizes its usefulness. Furthermore, cytology is primarily an ambula-

TABLE 1-1.—DIAGNOSTIC ADVANTAGES AND DISADVANTAGES OF CYTOPATHOLOGY COMPARED TO HISTOPATHOLOGY

ADVANTAGES	DISADVANTAGES
1. Rapid, inexpensive, often painless means of diagnosis. May offer a supplementary or replacement alternative for frozen sections or core biopsy.	1. Cytologic diagnosis may be presumptive. Some lesions must be confirmed by histology.
2. Minimal injury to tissue. Allows frequent repetition of cellular samples. Important in evaluation of progression or of posttreatment regression of lesion.	2. Exact location of lesion cannot be pinpointed with exfoliative cytology.
3. Wider area can be sampled than with biopsy. Random areas may be simultaneously evaluated.	3. Time-consuming screening of smears; often not as obvious as histopathology of tissue pattern.
4. Cells can be obtained from areas inaccessible to biopsy (bottom of a crypt, renal pelvis, bottom of diverticulum).	4. Size and depth of lesion cannot be approximated by cytology.
5. Three-dimensional evaluation of cellular structures for identification of such entities as small glands, ducts.	5. Interrelation and arrangement of cells may not be established. Histopathology may be necessary to describe neighboring cells, stromal characteristics, blood vessel, or lymphatic invasion.
6. Better evaluation for nature of such pathologic conditions as inflammation, infection, irradiation.	6. Exfoliated cells may not represent the true nature of entire lesion (e.g., poorly differentiated carcinoma with mixed components).

Note: Cytopathology should not compete with histopathology but rather should complement it. Abnormal cells seen in a smear should be explained by study of histologic sections when possible.

tory procedure and thus can considerably decrease both the cost of making a diagnosis and the time lost by patients.

Certainly diagnostic cytology is an extremely useful and attractive tool.^{1, 9, 12, 14, 16} In the hands of an informed clinician, it is an excellent primary screening method and can be further used as a method of follow-up in patients being observed for a suspected disease process or who have received various types of therapy. In conjunction with other medical procedures, cytology adds a great deal of breadth to the clinician's diagnostic armamentarium.

This handbook is by no means the ultimate tome on the subject of clinical cytology. It is intended to be a straightforward guide for clinicians who wish to acquire basic knowledge of the types of specimens that should be obtained—from whom, when, where, how, and why. We have strived to provide a concise and logical approach to all of these questions in each anatomical area covered. With the information contained in this handbook,

the clinician will be able to educate himself, his staff, and the patient regarding the methods involved and the clinical value of the cytologic procedures. Illustrations, tables, and photomicrographs should assist the clinician to organize his resources to successfully perform the cytologic study selected.

Several steps in each procedure are of extreme importance in successfully completing a study, but none is more important than the preliminary step of becoming acquainted with a well-qualified cytopathologist and an accredited cytology laboratory.^{2, 4} The cytopathologist will frequently be a member of the American or International Society of Cytology and have certification in anatomical and/or clinical pathology.^{7, 13, 15} He will be of great value not only in interpreting cell preparations but in advising the clinician as to how special techniques and procedures may be performed.¹⁸ The cytopathologist will also provide and insure adequate materials for cytologic preparations and transportation.

As this novel handbook is studied, the reader should be aware that only the most common and practical approaches to clinical problems are discussed. There are, for instance, special biliary tract cytologic procedures that we have not considered, or that have been only briefly mentioned, very simply because the medical equipment and diagnostic expertise necessary to perform those procedures is not widely available. The principal areas covered herein pertain to readily accessible sources of cellular materials utilizing minimal equipment and supplies that should be available in most medical institutions and office settings.

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