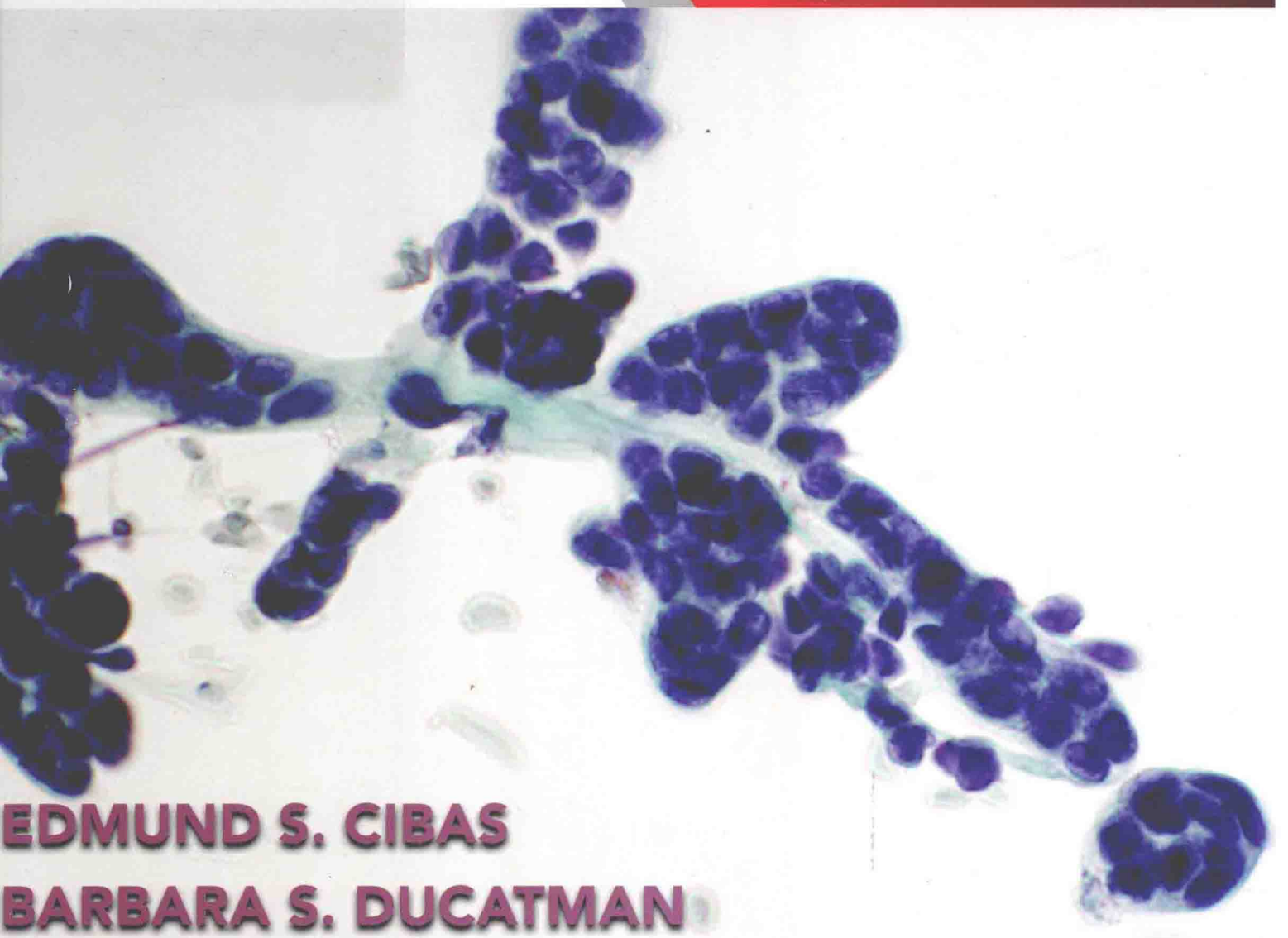

EDMUND S. CIBAS
BARBARA S. DUCATMAN

CYTOLOGY

Diagnostic Principles and Clinical Correlates

Fourth Edition

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CYTOLOGY

Diagnostic Principles and Clinical Correlates

FOURTH EDITION

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CYTOLOGY

Diagnostic Principles and Clinical Correlates

FOURTH EDITION

To Todd Bryant Stewart and Alan M. Ducatman

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PREFACE

We hope this book will serve as a useful guide for the pathologist in practice and for the trainee—resident or fellow—who is looking to obtain expertise in the subspecialty of cytopathology.

It has been four years since the publication of the third edition of *Cytology: Diagnostic Principles and Clinical Correlates*. Since then, cytology has continued to grow and evolve as a discipline devoted to the diagnosis of cellular tissue obtained by minimally invasive methods (e.g., scraping, brushing, aspiration), thus the need for this updated edition. However, we have retained many of the qualities of the prior editions. This edition again aims to be concise yet comprehensive. We have emphasized brevity and clarity. The text is grounded in an understanding of surgical pathology and current diagnostic terminology. Where relevant, we have illustrated the value of established ancillary studies. Although the book is multi-authored, the chapters follow a similar format: indications, sample collection and preparation methods, recommended terminology for reporting results, accuracy (including common pitfalls that lead to false-negative and false-positive diagnoses), a description of normal elements, and, finally, a how-to guide for the diagnosis of benign and malignant lesions with an emphasis on differential diagnosis. We have retained the bulleted "capsule summaries," particularly for summarizing cytomorphologic features and differential diagnoses. We have continued to emphasize clinical correlation (hence the title). For example, Chapter 1 includes the recently revised guidelines of the American Society for Colposcopy and Cervical Pathology for managing women with abnormal cervical cytologic diagnoses. Good cytologists are those who understand the clinical implications of their interpretations.

A major enhancement of this new edition is the inclusion of a dedicated chapter on fine-needle aspiration technique and specimen handling, accompanied by a video demonstration. We hope trainees and even practicing pathologists will find this especially useful.

Once again, we hope we have conveyed the beauty, strength, and challenge of cytology. With this book we have strived to take some of the mystery out of cytology, but mysteries remain, their solutions still obscure. If this text inspires the reader to explore and even solve some of them, we will consider ourselves doubly rewarded.

Edmund S. Cibas, MD
Barbara S. Ducatman, MD
2013

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We express our deep appreciation to Mr. Dennis Padget of DLPadget Enterprises, Inc., for his help with the complexities of billing in Chapter 18. We relied extensively on his *Pathology Service Coding Handbook* for the information set forth in that chapter. Readers who want more information on pathology coding questions can contact Mr. Padget at DennisPadget@EmbarqMail.com (502-693-5462) for information about subscribing to that comprehensive electronic text.

We are indebted to many members of the staff of the Brigham and Women's Hospital and West Virginia University School of Medicine and Hospital—the cytotechnologists, cytopathologists, and trainees—who inspire us with their devotion to cytopathology and who continue to challenge us. In particular, we acknowledge Dorothy Nappi, CT (ASCP), and Grace Goffi, CT, MIAC, who have helped us train so many pathology residents and fellows over the years. Without their help we would not have our extraordinary collections of cytology teaching cases from which so many of the images in this book are derived.

Finally, to our friends, families, and loved ones, especially Todd Stewart and Alan Ducatman, who tolerated the long evening and weekend hours that deprived them (temporarily!) of a large share of our time. This book would not exist without their love and strength.

Edmund S. Cibas

Barbara S. Ducatman

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chapter 1

CERVICAL AND VAGINAL CYTOLOGY

Edmund S. Cibas

History of the Papanicolaou Test and Its Current Practice

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Atypical Endometrial Cells

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Malignant Melanoma
Malignant Lymphoma
Malignant Mixed Mesodermal Tumors
Metastatic Tumors

Endometrial Cells in Women Older than 40 Years of Age

The 20th century witnessed a remarkable decline in the mortality from cervical cancer in many developed countries. This achievement is attributable to the implementation of the Papanicolaou (Pap) test. In the 1930s, before Pap test screening was introduced, cervical cancer was the most common cause of cancer deaths in women in the United States.[1] Today, it is not even in the top 10.[2]

There are approximately 12,000 new cases of cervical cancer in the United States each year, with 4000 deaths.[2] Worldwide, however, the cervical cancer incidence (over 500,000 cases annually) and mortality (275,000 deaths per year) are second only to those for breast cancer.[3] Screening programs, unfortunately, are rudimentary or nonexistent in many parts of the world. Less than 5% of women in developing countries have ever had a Pap test.[4] By contrast, 89% of women in the United States report having had a Pap test in the preceding 3 years.

Around the world, Pap test screening is implemented in two different ways, commonly referred to as

opportunistic versus *organized*.[5] An *organized screening program* is planned at the national or regional level. It specifies a target population and screening intervals and has a mechanism for inviting women to attend screening services, informing them of their result, and referring them for treatment. *Opportunistic screening*, the system in place in the United States, for example, is done independently of an organized or population-based program, on women who are often visiting health services for other reasons. Screening is recommended during a consultation or requested by the woman. Opportunistic screening tends to reach younger, lower-risk women who are attending family planning and antenatal services. It is generally accepted that organized screening is more cost-effective than opportunistic screening, making better use of available resources and ensuring that the greatest number of women benefit.

History of the Papanicolaou Test and Its Current Practice

The Pap test is considered by many to be the most cost-effective cancer reduction program ever devised.[1] Credit for its conception and development goes to George N. Papanicolaou, an anatomist and Greek immigrant to the United States. In 1928 he reported that malignant cells from the cervix can be identified in vaginal smears.[6] Later, in collaboration with the gynecologist Herbert Traut, who provided him with a large number of clinical samples, Papanicolaou published detailed descriptions of preinvasive cervical lesions.[7,8] Pathologists and clinicians initially greeted this technique with skepticism, but by the late 1940s Papanicolaou's observations had been confirmed by others. The Canadian gynecologist J. Ernest Ayre suggested taking samples directly from the cervix with a wooden spatula, rather than from the vagina with a pipette as originally described by Papanicolaou.[9] Eventually, cytologic smears were embraced as an ideal screening test for preinvasive lesions, which, if treated, would be prevented from developing into invasive cancer.

The first cervical cancer screening clinics were established in the 1940s.[10] The Pap test was never evaluated in a controlled, prospective study, but several pieces of evidence link it to the prevention of cervical cancer. First, the mortality rate from cervical cancer fell dramatically after screening was introduced, by 72% in British Columbia[11] and 70% in Kentucky.[12] Second, there was a direct correlation between the intensity of screening and the decrease in mortality. Among Nordic countries, the death rate fell by 80% in Iceland, where screening was greatest; in Norway, where screening was lowest, the death rate fell by only 10%.[13] A similar correlation was observed in high- and low-screening regions of Scotland[14] and Canada.[15] In the United States, the decrease in deaths from cervical cancer was proportional to the screening rates in various states.[16] Finally, women in whom invasive cancer does not develop are more likely to have had a Pap test than women with cancer. In a Canadian study, the relative risk for women who had not had a Pap test for 5 years was 2.7,[17] and screening history was a highly significant risk factor independent of other factors such as age, income, education, sexual history, and smoking. In Denmark, a woman's risk of developing cervical cancer decreased in proportion to the number of negative smears she had had—by 48% with just one negative smear, 69% with two to four negative smears, and 100% with five or more smears.[18]

Screening guidelines differ around the world. In the United States, revised cervical cancer screening recommendations were issued in 2012 by the American College of Obstetricians and Gynecologists (ACOG),[19] the U.S. Preventive Services Task Force (USPSTF),[20] and a consortium of the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology (ACS/ASCCP/ASCP).[21] Their guidelines differ in minor ways, but there is general agreement on the larger points, including longer screening intervals and a later age to start screening (age 21) than had been recommended in the past (Table 1.1). The U.S. Department of Health and Human Services (DHHS) offers a web-based National Guideline Clearinghouse that synthesizes the guidelines of the different organizations.[22] The guidelines address women with an average risk for cervical cancer. Women at higher risk—those with a history of cervical cancer, in utero diethylstilbestrol (DES) exposure, and/or immunocompromise (due to organ transplantation, chemotherapy, chronic corticosteroid treatment, or infection with the human immunodeficiency virus [HIV])—may benefit from more frequent screening. Because women with HIV infection/acquired immune deficiency syndrome (AIDS) have higher rates of cervical cancer than the general population, it is recommended that HIV-seropositive women have a Pap test twice during the first year after diagnosis of HIV infection and, if the results are normal,

TABLE 1.1 CERVICAL CANCER SCREENING GUIDELINES IN THE UNITED STATES (FOR WOMEN AT AVERAGE RISK)

Circumstance	Recommendation
Age to begin screening	Age 21. Women younger than age 21 should not be screened, regardless of the age of sexual initiation
Women aged 21 to 29 years	Every 3 years with cytology (liquid-based or conventional) alone
Women aged 30 to 65 years	Every 3 years with cytology alone, or Every 5 years if cotesting with cytology and human papillomavirus (HPV) assay (preferred by ACOG and ACS/ASCCP/ASCP)
Discontinuation of screening	Age 65 years if adequate prior screening and no history of cervical intraepithelial neoplasia (CIN) 2 or higher*
Screening after total hysterectomy	Not recommended if no history of CIN 2 or higher

ACOG, American College of Obstetrics and Gynecology; *ACS/ASCCP/ASCP*, American Cancer Society/American Society for Colposcopy and Cervical Pathology/American Society for Clinical Pathology; *CIN 2*, cervical intraepithelial lesion grade 2.
*ACOG and ACS/ASCCP/ASCP define "adequate prior screening" as *three consecutive negative cytology results or two consecutive negative co-test results within the previous 10 years, with the most recent test performed within the past 5 years*. "No history of CIN 2 or higher" is defined by ACS/ASCCP/ASCP as *within the last 20 years*.