



## Preface

# Gynecologic cytopathology



David C. Wilbur, MD  
*Guest Editor*

It was the best of times, it was the worst of times.

—Charles Dickens

This opening line to *A Tale of Two Cities* described the times of the French Revolution. Currently we are experiencing another revolution of sorts and, as before, it is the best of times: fine needle aspiration biopsy clinics are flourishing, new imaging techniques allow radiologists to obtain more cellular material from many more places, and even gastroenterologists are getting into the act with a growing number of aspiration procedures being performed with the endoscope. As the ability to image and sample improves, the need to make diagnoses on ever-smaller amounts of cellular material from nonsurgical procedures is rapidly increasing. Fueled by a need for rapid turnaround times, productivity, and cost saving, the sky is the limit for the cytologic method.

On the gynecologic cytology side, the largest cytology-related clinical trial has just been completed, providing a wealth of information regarding patient management. The science of molecular biology is redefining our thought processes about the biology of cervical neoplasia. A recently convened consensus conference brought together an international audience to deliberate about evidence-based terminology and management. In all, the

circles of the science and art related to cervical carcinogenesis—as well as its diagnosis and management—are rapidly merging. New technologies are positively affecting our practice. New devices that improve both accuracy and productivity are ready, or nearly so, to be adopted in our laboratories. New methods of specimen preparation, computer screening of slides, and molecular detection methods are already in use and will become more widely used in the near future.

However, just as in the Dickens novel, a close observer also may see the worst of times ahead. The cervical screening program is the most effective cancer reduction program in history; however, the system is in danger. Our cytotechnology workforce is aging and diminishing in numbers. Schools of Allied Health are closing training programs with ever-increasing regularity because of the high cost of the hands-on training and low faculty-to-student ratios necessary to teach this discipline effectively. Students are becoming more difficult to recruit, perhaps because of the perception that vaccines against the human papillomavirus (HPV) will eradicate cervical cancer and hence render the field of cervical cytology obsolete. Indeed, new methods of screening have already been proposed, and new “markers” for cervical neoplasia are being developed and reported rapidly. Will one of these markers be the magic bullet? At this point, the uncertainty makes it difficult to plan and to therefore move forward. All this and still most laboratories find that the reimbursement for the Papanicolaou smear is at or below cost, and the threat of medico-legal proceedings against the inevitable false negative case weighs heavily on the strained profession.

With both good and bad as the backdrop, the field of gynecologic cytology is an incredibly dynamic one. Revolutions do that to a field. Therefore, the time is ripe for a compilation of all that is going on; this issue of the *Clinics in Laboratory Medicine* reports the very exciting developments that we are enjoying and facing.

To begin, Mark Stoler, a member of the ASCUS-LSIL Triage Study (ALTS) team reports the final results of that very exciting and comprehensive trial. The results of the ALTS formed the basis for the deliberation and changes in terminology that have been developed for the 2001 edition of the Bethesda System for the reporting of cervical cytology interpretations. Mike Henry, a moderator in the proceedings, provides an excellent overview of the new terminology and the rationale for the changes. Moving into the mainstay of cytologic morphology, Ritu Nayar and Sana Tabbara provide an update on all fronts in the controversial area of atypical squamous cells. This topic has garnered as much interest as any subject over the past 10 years, and their review provides readers with the state-of-the-art. David Chhieng and Joan Cangiarella do the same for the “other atypia,” that being the less common, but just as vexing condition of atypical glandular cells. Substantial changes were made to this category in Bethesda 2001, and the authors bring us up to date on this topic of growing importance in cervical cytology. The final morphologic topic falls in an area that most

cytologists admit is very difficult. In the modern world of hormone use and liquid-based preparation methods, the many variants of the nonestrogenized (or atrophic) specimen have become a major differential diagnostic quandary. Rosemary Tambouret and I have found that by studying this area we get better at making proper interpretations; together we describe the problems and hopefully provide a few caveats.

Shifting gears, the topics turn to administrative and technology orientations. Andy Renshaw delves into a topic that most of us would rather not take on: quality control in gynecologic cytology. The system is flawed from both technical and regulatory standpoints. His insightful article explains why things work, why they don't, and what we might (or might not) expect in the future. With competition fierce between the manufacturers of cervical cytology equipment and methods, the laboratory director may be faced with a difficult decision when choosing from various alternatives. Steve Black-Schaffer has been there. He evaluated the methods, took the heat, and made the decisions. His article on choosing between technologies is a story of actual events and processes that took place in his practice. It makes for very interesting reading! Molecular biology, most notably of HPV, forms the cornerstone of the future of cervical cytology. Soner Altioek has provided a comprehensive review of "what every cytologist needs to know about HPV (and then some)." In addition, he reviews testing methodology and the next generation of molecular markers that extend from HPV biology. Ben Davidson and his colleagues at the Radium Hospital in Oslo detail their landmark work in the "other gynecologic cytology specimen," that being the serous body cavity fluid involved by ovarian carcinoma. Their groundbreaking work in discovering the biological differences between primary and disseminated tumors will almost certainly have a profound effect on our understanding of this deadly disease and guide our management options in the future. Finally, I have been personally involved with the development, testing, and use of cytology automation and preparation devices for many years. My update details the process that has gone before, hopefully bringing us to what is presently available and, as much as space permits, details on how the various devices actually work.

Whether you consider the times in gynecologic cytology good or bad, they are certainly interesting. I would like to take this opportunity to thank the authors, all of whom took significant time out of their incredibly busy schedules to contribute these reviews. This issue is a tribute to their hard work and profound understanding of their respective areas. In addition, because the focus of this issue is gynecologic cytology, I would also like to dedicate it to my mentor and friend, the late Stanley F. Patten, Jr., one of the true giants in our field. I find more and more as I progress through my career that I can hear Stan's voice in the back of my head. It is his teaching that guides me in my review of clinical cases. It is his teaching that guides me in my own humble attempts at relaying cytologic principles to our residents and fellows. Finally, it is his teaching that guides me in my approach

to all aspects of investigation. He trained an entire generation of cytopathologists; I am truly proud to have been one of them.

David C. Wilbur, MD  
*Department of Pathology  
Massachusetts General Hospital  
Harvard Medical School  
55 Fruit Street Warren 120  
Boston, MA 02114, USA*

*E-mail address:* [dwilbur@partners.org](mailto:dwilbur@partners.org)