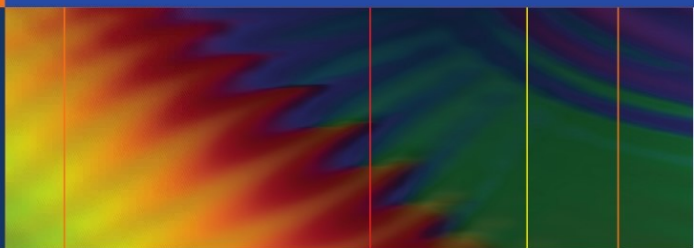


Gary W. Gill



Cytopreparation

Principles & Practice

Essentials in Cytopathology

Series Editor

Dorothy Rosenthal



Springer

Cytopreparation

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Cytopreparation

Principles & Practice

 Springer

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ISSN 1574-9053 ISSN 1574-9061 (electronic)
ISBN 978-1-4614-4932-4 ISBN 978-1-4614-4933-1 (eBook)
DOI 10.1007/978-1-4614-4933-1
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2012947399

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Dedicated to Doris and Buddy, my late parents; they gave me life.

Dedicated to my family: Marianne, stepson BJ, David, Megan, Michael, daughter-in-law Kristen, and grandchildren Jackson Thomas and Mariah MacKenzie; they are my life.

Foreword

At last! A textbook with the accumulated knowledge of Gary Gill on that most tangled web of complexity, cytopreparation. Don't be deceived by the title. This is not a textbook solely for cytotechnologists, cytopreparatory technicians, and educators; it should become every pathologist's companion. Anyone who uses a microscope to study tissue is cognizant of the importance of perfect tissue preparation and stain and its impact on reaching an accurate diagnosis. Staining principles apply to both cytology and histology. However, this textbook explores much more than cytopreparation. It provides useful advice for improving processes that extend beyond cytopathology, highlighted with unexpected tints of humor that will make you laugh out loud. Gary Gill has long been an advocate of optimizing cytopathology for the benefit of the patient, whether in specimen submission, preparation, staining, screening, or reporting. This textbook fills a long-vacant knowledge gap and provides a succinct explanation of the chemical processes involved in staining and processing in a format that is familiar to all laboratories: the principles and practices of standard operating procedures.

Nearly everyone in pathology is familiar with the ubiquitous "Gill hematoxylin," the formulation for which he is famous. From his observations and experience as a newly minted cytotechnologist graduating from The Johns Hopkins Hospital's School of Cytotechnology, Gary Gill concluded that the Papanicolaou stain suffered from a serious lack of standardization and began his investigations on the optimal stain by researching hematoxylin

preparations. He discovered a method of progressive staining that did not require differentiation (the extraction of stain using weak acid rinses), thereby preventing overstaining of cellular chromatin. His progressive hematoxylin has been universally embraced by both histologists and cytologists and has replaced almost all other hematoxylin formulations in most laboratories. He continued his journey by examining all of the chemical reagents and reactions in staining and eventually streamlined Papanicolaou staining to an environmental-friendly processing line that he coined “Enviro-Pap.” His career culminated as the corporate compliance officer for a large cytology laboratory in Indiana, where he ensured excellence and adherence to regulatory standards. His career has touched nearly every aspect of cytopathology. You can read more about his illustrious career in Appendix J.

The cytopathology community knows Gary Gill as its foremost authority on cytology specimen processing, preparation, staining, and screening. In fact, several years ago, he presented “Managing Cytology Information Overload: a Glimpse into Gary Gill’s Brain,” an invited lecture at a Program Faculty Seminar during the American Society of Cytopathology’s Annual Scientific Meeting in 2005. The lecture was intended to answer the question: how do you keep track of your extensive cytological files? He has been nicknamed the “cytogoogler” of the cytopathology community. Just ask Gary, and he will know the answer. When I first met Gary at a national meeting, I was appropriately in awe of this icon, but was immediately placed at ease by his down-to-earth, self-effacing, and approachable personality. Since then, I have not ceased needling him to compile his knowledge into one definitive text, and he hasn’t let me down.

His 1 TB of electronic information and warehouse of paper information have only now made their way into print. It is an opportunity too good to pass up, an endeavor long urged by all his friends and colleagues, and possibly the only time the medical community has been able to rein him in from his personal intellectual pursuits long enough to leave a professional legacy.

If you, too, want to get inside Gary Gill’s brain, then do not skip the appendices—for here lies a true treasure trove of ideas and explanations. My favorite is Appendix I, “Screening and

CPR.” All of those who have ever screened cytology slides and have had a dog will appreciate the analogy and the problems encountered as elucidated in this section.

Bethesda, MD, USA

Barbara A. Crothers

Foreword

In my view, the most important aspect of any book on cytopreparation is that it has practical application to the cytopathology laboratory. In that sense, this book delivers! It has just the right mix of practical application with sound scientific principles. The reader is not only given instructions on what to do, but also explanation as to why they are doing it. This book has everything for the individual thirsting for the best information concerning cytopreparation and does not distract with unneeded embellishments. The author's desire to inspire us to a greater awareness of the importance of excellent cytopreparatory technique and its direct relationship to good patient care is evident throughout the book.

Cytopreparation Principles and Practices is the result of the author's exploration of all the ins-and-outs that comprise good cytopreparatory technique. He meticulously walks us through the steps to good specimen preparation and then challenges us to consider what it really means to screen a cytologic sample. Having known Gary for many years, it is not surprising that his book reflects this practical methodology, which is how he approaches life in general. He's a very rational man who makes decisions based upon proven constructs with sound information.

I suspect that over the years, there are many of us, and I would venture to say most of us in cytopathology who have been touched in some way by Gary's expertise in cytopreparation. I initially met Gary in my first year out of Cytotechnology School while attending his Cytopreparation Workshop at an American Society of Cytopathology annual meeting. At the time, I was in charge of the urine processing for our lab, and we were using membrane filters

for all of our urine preparations. I was having some difficulty getting reproducibly good preparations, and the pathologist I worked with suggested I attend Gary's workshop.

My first impression of Gary was that he possessed a serious demeanor which was, initially, a little intimidating. Dressed in his characteristic double-breasted blazer, he appeared a little stiff, but clearly had an intense interest and grasp of all things related to cytopreparation. By the end of the workshop, I got the information I needed for the preparation of exquisite urine samples, and my pathologist and I were very pleased with our investment in Gary's expertise.

Since that first encounter, it has been my distinct pleasure to know Gary, not only as an icon of cytopreparation, but also as a good friend. His quick wit and dry sense of humor are generally not only entertaining but also informative. These characteristics shine through periodically in the writing of this book as well.

Upon sharing with several individuals that Gary was writing a book on cytopreparation, I was amazed often by their reaction, which was usually, "I thought he had already done that."

In fact, it happened so often that it really got my attention. The man whom everyone assumed had written the book on cytopreparation had actually never written it...quite a testimony to his reputation in the field.

It is with much appreciation that we thank Gary for writing this extraordinary work that will allow all who read it to have a part in carrying forward the Gill legacy: to apply due vigilance when considering the best approach in preparing the patient's cytologic sample set before us.

Indianapolis, IN, USA

William N. Crabtree

Series Preface

When Springer asked me to be Editor-in-Chief of Essentials in Cytopathology, the year was 2004. Even though there was already a plethora of adequate texts on cytomorphology, most were hard-bound and weighty. My editorial board agreed with Springer's concept of small format paper backs that were inexpensive to produce and therefore accessible for the prospective buyer. Each volume has concentrated on the cellular patterns from a particular organ site or related complex, emphasizing diagnostic criteria and pitfalls in a simple format style with abundant high-quality color plates and graphic illustrations. The series has been an unqualified success by any measure, already publishing 12 volumes in 7 years, one volume being a second revised edition with 6 more volumes under contract.

This latest volume (number 13) in the Essentials in Cytopathology series is perhaps the most important. It clearly is unique, as it barely has any photographs of cells and does not define cellular criteria. It does, however, instruct the observant laboratorian in how to achieve optimal cellular samples for microscopic interpretation. Not only is it being published in the year of the 60th anniversary meeting of the American Society of Cytopathology and the author's 70th birthday, but also the 25th anniversary year of the Wall Street Journal articles that earned the 1988 Pulitzer Prize in investigative journalism for the author, Walt Bogdanich. The resultant Clinical Laboratory Amendments of 1988 are addressed in this volume as each of the principles is delineated that responds to a regulation.

Regulatory compliance is not the intent of this work, although it is a side benefit. I coerced Gary into writing it for posterity. My bribe was naming The Johns Hopkins Cytopreparatory Laboratory in honor of him. No one knows cytopathology preparatory techniques and their scientific bases better than Gary. In fact, many of the chapters apply to histopathology samples as well. Therefore, anyone in Anatomic Pathology, from Laboratory Directors and Managers, to the preparatory technicians, can benefit from this unique manual.

I urge everyone who reads this seminal work to consider where we've come as a medical specialty in the quarter century following these journalistic exposes of laboratory incompetence. Much time is spent by laboratory managers attending to the "paper work" necessary to prove compliance to laboratory inspectors. But have we actually been able to prevent deaths from cervical cancer by these measures? Quoting Gary, "quality begins here." The final interpretation of a sample is dictated by the quality of the preparation. Until we get that right, we will not reach our goal for cervical cancer nor provide optimal care for all our patients with the other diseases that come to us at the light microscope.

Dorothy L. Rosenthal, M.D., FIAC
Baltimore, MD, USA

Preface

*"I have no special talents. I am only
passionately curious."*

Albert Einstein

Having recently graduated from Western Maryland College with a baccalaureate degree in premed, I was looking for employment. An ad in the Baltimore Sun newspaper caught my eye. Someone was looking for a person with experience in a variety of biological subjects. I wrote to the box number provided, telling the unidentified source that I had coursework in the advertised areas but no job experience. To shorten a long story, the prospective employer turned out to be Dr. John K. Frost in the Division of Cytopathology of The Johns Hopkins Hospital. The advertised position had been filled internally, but he had a School of Cytotechnology, and there were student stipends available that would cover the cost. Would I be interested in enrolling?

That was 1963, and the rest—as is often said—is history. Confucius was right: find a job you love and you'll never work a day in your life. By pure dumb luck, I had stumbled onto a profession and career path that fuelled the passion that resulted in my writing this book. After graduating on October 9, 1964, with a certificate in "Medical Cytotechnology" from The Johns Hopkins Hospital, I remained employed there until January 16, 1987.

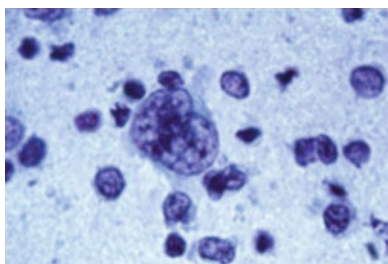
Parenthetically, the formal name of the institution is The Johns Hopkins Hospital. The word "The" is capitalized, and Johns Hopkins is the name of the Quaker philanthropist who donated \$7 million to construct the hospital in 1875 and several other famous

Baltimore-based institutions that bear his name. Johns is a family name; it is not John and is not followed by apostrophes (i.e., not John's or Johns' and not Hopkin's or Hopkins'). He died Christmas Eve 1873 at age 78.

The first research project in which I participated was circulating cancer cells in the blood. Nine years earlier, Engell had published a review about the subject that sparked enormous interest.¹ Note that the year was 1955. We didn't know then what we didn't know.

Our small research team's initial charge was to gather from the published medical literature papers about processing peripheral blood, evaluate each method, identify the most promising one, improve it as needed, and apply it to real-life specimens. One thing above all became abundantly clear: we didn't know what we were doing. Among other things, for example, we couldn't get erythrocytes or leukocytes to stick to glass slides when wet-fixed (i.e., plunged into alcohol). We learned that normal saline—contrary to expectation—destroys cells *in vitro*. We also learned that the Pap stain was not standardized. In short, almost everything we had been taught about cytopreparation was insufficiently reliable to be useful. No one was to blame. After all, it was the 1960s.

Since we were unable to get blood cells to stick to glass slides that were wet-fixed for cytology, instead of having been air-dried for hematology, we began collecting them on Millipore filters. I observed that cells near the boundary of the cell collection area of one preparation in particular were well preserved, while neighboring cells were not. One of our early "successes" is pictured in this photomicrograph of what we believed to be megakaryocyte. Megakaryocytes ordinarily don't circulate in peripheral blood.



That one observation made me think that if we could identify the contributing factors responsible for this isolated success, we could take the guesswork out of making filter preparations of well-preserved cells. Thus began the unending questions and answers that are embodied in this book.

Readers will note that most of the cited references are in journals unrelated to cytology as we know it, and they're *old*. Many were published in the first half of the twentieth century and, occasionally, the seventeenth century. These reflect the fact that I had questions, and they had answers. I had no recourse but to visit the musty dusty stacks of the Welch Medical Library of The Johns Hopkins Medical Institutions. In those days, now nearly 50 years ago, there was no easy way to research topics of interest. PubMed and Google were far into the future. Volumes and volumes of Index Medicus on tables and tables in the library's reading room do not inspire serious scholarship. To facilitate focused searches, I learned that reading the lists of references in published papers that were useful to me often revealed titles of articles of likely interest and the names of journals outside those commonly associated with diagnostic cytopathology. I would often go to the non-air-conditioned stacks, select the last issue of these unfamiliar journals for each year, and read the titles of articles published for the entire year. The library's policy allowed me to check out the journals and copy the articles, which I still have.

This volume can be used to teach cytopreparation and help students:

- *Understand the principles that underlie the various procedures and practices*
- *Appreciate that everything done to a specimen makes a microscopically appreciable difference*
- *Encourage observations that may elicit suggestions for improvements*
- *Discourage potential shortcuts that cost more than they gain*
- *Promote curiosity (e.g, How do you know that? Are you sure? Show me the citation.)*

These lectures are needed because cytopreparation for technicians is not taught anywhere as a formal program. While part of

every cytotechnologist's education, it is a relatively small part and often not taught well. Nationwide, the need for high-quality cytopreparation is great.

This book covers the entire range of processes that contribute to a useful cytologic preparation, from specimen collection through microscopy. Since "the Pap test is cytopathology," I have also included an approach to screening Pap tests and data analysis. I have tried to provide sufficient details throughout the book so that others outside this country may benefit.

I want to acknowledge with gratitude my first teachers in cytopathology: Dr. John K. Frost, Arline K. Howdon, and Sue T. Shutt. Their unbridled enthusiasm was infectious; their encouragement, unflagging. Pre-everything regulatory, nothing slowed my researches or dampened my curiosity. Others at Hopkins I want to acknowledge include the following: Dr. Yener S. Erozan, Dr. Prabodh K. Gupta, Dr. William M. Howdon, and Dr. Norman J. Pressman; cytotechnologists Fran Burroughs, Sue Ermatinger, Gene Ford, Deirdre Kelly, Jack Kirby, Ellen Patz, and Karen Plowden; cytopreparatory technicians Dianna Farrar, Villa Gardner, Darlene Ratajczak, and Linda Reynolds; and Secretary Shirley Long. The named individuals were the core staff during my 23-year tenure. I remember them all fondly.

Lastly, I want to thank Dr. Dorothy Rosenthal, Series Editor of *Essentials in Cytopathology*, for inviting me to write this book. She also spearheaded the November 7, 2011 dedication in my name of the Cytopreparatory Laboratory in the Pathology Building of The Johns Hopkins Hospital. The dedication recognizes the fundamental soundness of my contributions to cytopreparation, which have stood the test of time since my 1987 departure.

Will there always be a place for cytopreparation in a world of molecular medicine? I think so as long as humans are curious to see things otherwise invisible. On the other hand, however, "prediction is very difficult, especially about the future"—Neils Bohr.

In the 1981 movie *On Golden Pond*, Henry Fonda portrays Norman Thayer, an 80-year old curmudgeon who is celebrating his 80th birthday. When presented with a cake ablaze with 80 candles, he says: "I've been trying all day to draw some...

profound conclusions about living fourscore years. Haven't thought of anything. Surprised it got here so fast." It's the latter statement I remember and a sentiment I now understand.

Reference

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