Afterword: The Paris System for Reporting Urinary Cytology

Dorothy L. Rosenthal, Eva M. Wojcik, and Daniel F.I. Kurtycz

The primary goal of The Paris System Working Group was standardizing the terminology for reporting urinary cytology based upon histopathology and clinical outcomes. Soon after the initiation of this project, we realized that much of our knowledge base was anecdotal, poorly defined, inadequately studied, or uninvestigated. Therefore, the Working Group depended not only upon the extant medical literature but also considered the data from newly initiated and completed studies that were needed to reach the goal.

From the initial meeting in Paris, we have agreed that detection of High Grade Urothelial Carcinoma is the ultimate goal of urine cytology. Therefore, the entire system was built based on this principle. As a consequence, one of our goals has been to define the risk of HGUC for each diagnostic category based upon tissue confirmation and clinical outcome. This goal, however, can only be accomplished if the standardized terminology is used for defining risk related to the initial diagnostic categories. As such, prospective studies will have to be done to define those risks.

The decision to emphasize HGUC was based most importantly on clinical significance but also on pathogenetic bases of urothelial carcinoma. Although we have presented these pathways in a very simplistic way, we understand that a significant body of work has yet to be done to confirm that low-grade urothelial neoplasms are not carcinomas. As a remedy for this general ignorance, we decided to divide our knowledge of the pathogenesis of Bladder Cancer into two major categories: those causes of cellular neoplastic changes that have been verified by molecular and genetic tests, and those that are still theories or totally unexplored.

This First Edition of The Paris System for Reporting Urinary Cytology (2015) has covered the morphology of cytologic changes from benign to malignant, and has modestly stated what we believe to be generally accepted causes of these changes. Many of the ancillary tests are still in the investigative phase of their development (see Chap. 9) and are in serious need of large clinical trials to validate their clinical reliability and reproducibility among individuals and laboratories.

D.L. Rosenthal et al. (eds.), *The Paris System for Reporting Urinary Cytology*,
DOI 10.1007/978-3-319-22864-8

In anticipation of The Second Edition, the editors, DR, EW, and DK, have asked the Corresponding Authors of the Working Groups to provide us with a Wish List, i.e., those aspects relative to the topic of their chapter that are in immediate need of investigation. The major purpose of this list, summarized as an appendix to this Afterword, is to stimulate seminal research by medical scientists. We also hope that funding agencies, whether governmental, philanthropic or private industry, will step forward and turn this Grass Roots effort into a major force in combatting Bladder Cancer. As the world's population ages, bladder cancer will become more of a financial burden than it already is, worthy of effective methods of prevention, and early noninvasive detection methods resulting in minimal procedures for effective cures.

Future Clinical and Research Needs for All Diagnostic Categories of The Paris System for Reporting Urinary Cytology

General essentials to assure the longevity of The Paris System

1. Determine the reporting rates of all categories after proper usage of the criteria has occurred for a significant period of time.
2. Perform outcome and interobserver reproducibility studies with the updated criteria.
3. Relate risk for the development of HGUC to the cytologic categories.
4. Establish clear-cut management guidelines based upon outcomes and with input from Urologic Surgeons and acceptance of patients.
5. Consider whether subsequent urothelial tumors are a recurrence of the initial tumor or a new lesion.

Chapter 1: Pathogenesis

1. Conduct further molecular studies to confirm or disprove that hyperplastic and dysplastic pathways are separate in the pathogenesis of urothelial neoplasms.
2. Further evaluate the concept that low grade urothelial neoplasms (LGUNs) are not "carcinomas".

Chapter 2: Specimen Adequacy

1. Define essential variables, e.g., optimal minimum and maximum volume of voided urines, cellularity necessary for diagnosis of HGUC, preservation of cellular integrity dependent upon length of time between collection and processing.
2. Establish when the term "inadequate" is appropriate, and the clinical implications.

Chapter 3: Negative for HGUC (NHGUC)

1. Catalogue outcomes of all entities included within the NHGUC category.
2. Explore whether any of the "benign" entities, especially Polyoma virus and calculi, have a causal relationship with urothelial cancers.

Chapter 4: Atypical Urothelial Cells (AUC)

1. Construct studies to refine criteria and meaningfully reduce the size of the AUC category.
2. Compare use of the category among laboratories of various sizes and risk levels of patients.

Chapter 5: Suspicious for HGUC (SHGUC)

1. Define the cytological categories of "suspicious for HGUC" and "positive for HGUC" in terms of their association with subsequent histological HGUC diagnoses to determine whether they should remain separate categories.
2. Establish management guidelines for a "suspicious" diagnosis based on the results of future large studies.

Chapter 6: HGUC

1. Define the specificity and sensitivity of HGUC cytology for detecting HGUC on biopsy, depending upon the type of cytologic sample obtained.
2. Design large prospective studies to establish risk of recurrence and invasion based upon grade predicted by cytologic diagnosis.

Chapter 7: LGUN

1. Construct studies that are adequately powered to achieve statistical significance in order to establish the clinical utility of the LGUN category.
2. Decide whether any lesions within the LGUN category are truly carcinomas, i.e., capable of invading and metastasizing, and whether these lesions can progress from LGUC to HGUC.

Chapter 8: Non-urothelial

1. Evaluate clinical data from major academic centers to assess the success of morphology and immunohistochemistry for cytological detection of non-urothelial malignancies of the urinary tract.
2. Investigate application of innovative molecular and genetic tests to aid in the identification of sources of non-urothelial cancers of the urinary tract as well as determine the cell of origin in primary non-urothelial tumors.

Chapter 9: Ancillary Tests

1. Prospectively compare the performance of novel tests on the sensitivity and negative predictive value of AUC and SHGUC categories.
2. Determine whether surveillance guidelines can be changed using currently approved ancillary tests (e.g., U-FISH and uCyt) for patients with urothelial carcinoma depending on individual risk factors.
3. Establish the cost-effectiveness of ancillary testing across different countries and health care systems.

Chapter 10: Preparation

1. Determine whether time, temperature, and chemical composition of urine impact collection and processing.
2. Establish evidence-based recommendations for collecting urine specimens (e.g., voided early a.m. vs. discard-hydrate-void; voided vs. catheterized vs. washing).

Chapter 11: Clinical Management

1. Explore new technologies to improve the accuracy of cystoscopy, such as fluorescence-assisted cystoscopy, narrow band imaging, among others, that have been introduced or will be coming down the pipeline.
2. Perform prospective clinical trials to see how these tests can be integrated with cytology to enhance its performance.

Index

D.L. Rosenthal et al. (eds.), *The Paris System for Reporting Urinary Cytology*,
DOI 10.1007/978-3-319-22864-8