

Koss's Cytology of the Urinary Tract
with Histopathologic Correlations

Leopold G. Koss • Rana S. Hoda

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 Springer

Leopold G. Koss, MD, Doct. HC (multiple)
Distinguished Professor University Emeritus
Montefiore Medical Center
Albert Einstein College of Medicine
Bronx, NY USA

Rana S. Hoda, MD, FIAC
Professor of Pathology and Director of
Papanicolaou Cytology Laboratory
Department of Pathology and Laboratory Medicine
New York Presbyterian Hospital
Weill Cornell Medical College
New York, NY USA

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*In Memory of my Parents and Sister who perished
in the Holocaust and for my sons Michael, Andrew
and Richard and their loving families*

Leopold G. Koss, MD

*In Memory of Atiqa and Shafiq Ismail
and for Syed Hoda and Raza Hoda*

Rana S. Hoda, MD

Foreword

“One picture is Worth a Thousand Words (一畫勝千言)” is an ancient Chinese proverb; that captures the essence of this book “Koss’s Cytology of the Urinary Tract with Histopathologic Correlations” by Drs. Leopold Koss and Rana Hoda. I first learned about Leo in the mid-1960s in New Delhi when I was asked to establish a cytopathology laboratory at the All India Institute of Medical Sciences. The late Dr. Ramalingaswami, a friend of Leo’s asked me to look at the “red” book-first edition of his classic “Diagnostic Cytology and Its Histopathologic Basis”, published in 1961 by Lippincott. Being a trained pathologist, I was impressed by his correlative approach to cytopathology, so very critical for morphologic interpretations. His concepts have been embraced, not only by me, but have become the mantra of cytopathology globally. I had the good fortune to meet Leo a few years later in the US, and he continues to be a mentor and a revered friend. Leo has cytopathology in his DNA; his name is synonymous with cytology. He has shaped the practice of cytopathology globally. He continues to be extremely productive. This one book has been coauthored by Dr. Rana Hoda. I have known Rana for a number of years; she worked here at Penn before moving to New York. Dr. Hoda is extremely talented and sharp. It is a testimony to her accomplishments that Dr. Koss invited her to be a coauthor.

This book summarizes the passion of Leo. He started his cytology career looking at the voided urine specimens obtained from factory workers. True to his doctrine, this work represents Leo’s thoughts, concepts, and wisdom in a small colorful crucible of high-quality photomicrographs of cells and their histopathology. One picture is worth a thousand words is evidenced by the use of limited complementary text. Leo is now over 90, I hope and pray that a most enthusiastic reception by the readership of this book shall add many more years to his productive life.

Philadelphia, PA, USA

Prabodh Gupta, MBBS, MD, FIAC

Preface

Technical progress in the identification of cells derived from the urinary bladder and adjacent organs prompted us to restructure an older book “Diagnostic Cytology of The Urinary Tract” published in 1996. This volume is illustrated, for the most part, with photographs of urinary sediment based on current liquid-based techniques.

Besides clinical observations, a fairly large number of laboratory procedures and tests are currently being advocated for detection and follow-up of tumors of the lower urinary tract. The choice of these procedures should be guided by understanding of the principles of the test, always keeping in mind that the specificity and sensitivity of any test are usually reciprocal. A test of great specificity is likely to have low sensitivity and vice versa. The value of the test for an individual patient depends greatly on clinical and pathologic findings, because behavior of urothelial tumors is not always homogeneous or predictable. We hope that this concise volume will be of practical value to cytologists and urologists in the choice of tests, interpretation of results, and hence in the treatment of patients.

Bronx, NY USA
New York, NY, USA

Leopold G. Koss, MD, Doct. HC (multiple)
Rana S. Hoda, MD, FIAC

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Bronx, NY USA
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Leopold G. Koss, MD, Doct. HC (multiple)
Rana S. Hoda, MD, FIAC

Contents

1 Introduction	1
Historical Note	1
Suggested Readings	5
2 Indication, Collection, and Laboratory Processing of Cytologic Samples	7
General	7
Methods of Specimen Collection.....	8
Voided Urine	8
Catheterized Urine	9
Direct Sampling techniques	9
Ileal Bladder Urine.....	10
Laboratory Processing of Urinary Specimens	10
Liquid-Based Processing Techniques	10
SurePath	10
ThinPrep.....	14
Residual LBP Specimen	15
Suggested Readings	15
3 The Cellular and Acellular Components of the Urinary Sediment	17
Normal Lower Urinary Tract	17
Anatomy.....	17
Normal Urothelium (Transitional Epithelium) and Its Cells	18
Histology and Ultrastructure.....	18
Ultrastructure of the Umbrella Cells.....	19
Variants of Normal Urothelium	21
Cells Derived from Normal Urothelium	21
Other Benign Cells.....	28
Squamous Cells.....	28
Blood Cells.....	31
Erythrocytes	31
Noncellular Components of Urinary Sediment.....	32
Crystals	32
Suggested Readings	35

4 The Cytologic Makeup of the Urinary Sediment According to the Collection Technique	37
Introduction.....	37
Cytologic Makeup of the Sediment of Normal Voided Urine	37
Cell Preservation in Voided Urine	40
Cytologic Makeup of Bladder Washings.....	40
Cytologic Makeup of Normal Retrograde Catheterization Specimens.....	42
Cytologic Makeup of Smears Obtained by Brushing	43
Cytologic Makeup of Ileal Bladder Urine	44
Suggested Readings	45
5 Cytologic Manifestations of Benign Disorders Affecting Cells of the Lower Urinary Tract	47
Inflammatory Disorders	47
Bacterial Agents.....	47
Pyelonephritis.....	48
Cystitis	48
Hunner's Ulcer (Interstitial Cystitis).....	49
Inflammatory Pseudopolyp	49
Eosinophilic Cystitis (Eosinophilic Granuloma).....	50
Follicular Cystitis.....	50
Papillary Hyperplasia.....	50
Cystitis Cystica and Cystitis Glandularis.....	51
Nephrogenic Metaplasia (Adenoma).....	52
Actinomyces and Norcardia.....	53
Tuberculosis	53
Fungal Agents.....	54
Viral Infections.....	55
Human Polyomavirus (Decoy Cells)	55
Herpes Simplex Virus	59
Human Papillomavirus.....	60
Cytomegalovirus	60
Cellular Inclusions Not Due to Viral Agents.....	61
Nonspecific Cytoplasmic Eosinophilic Inclusions (Melamed-Wolinska Bodies)	61
Parasites	62
Trematodes: Schistosoma haematobium.....	62
Other Parasites	62
Lithiasis.....	63
Leukoplakia.....	63
Effect of Drugs.....	66
Intravesically Administered Drugs	66
Systemically Administered Drugs	66
Cyclophosphamide (Cytosan, Endoxan).....	66
Busulfan (Myleran).....	68
Effects of Radiotherapy	68
Urinary Cytology in Bone Marrow Transplant Recipients	68
Monitoring of Renal Transplant Patients	68

Rare Benign Conditions.....	69
Malakoplakia.....	69
Benign Giant Cells in Multiple Myeloma.....	70
Suggested Readings.....	70
6 Tumors and Related Conditions of the Bladder and Lower Urinary Tract.....	73
Non-neoplastic Changes.....	73
Urothelial Hyperplasia.....	73
Inverted Papilloma.....	74
Tumors.....	76
Epidemiology.....	76
Histologic Classification of Tumors of the Bladder, Renal Pelves, and Ureters.....	76
Two Pathways of Bladder Tumors.....	77
Low-Grade Papillary Urothelial Tumors with no/Minimal Nuclear Atypia.....	78
Low-Grade Papillary Urothelial Carcinoma.....	78
Cytologic Recognition of Low-Grade Tumors in Urinary Sediment.....	79
High-Grade Urothelial Tumors.....	80
High-Grade Papillary Carcinoma.....	80
Nonpapillary Urothelial Tumors.....	82
Invasive Urothelial Carcinomas.....	85
Histologic Patterns.....	85
Grading.....	85
Staging.....	87
Flat Carcinoma In Situ.....	87
Clinical Presentation.....	88
Histology.....	90
Cytologic Recognition of High-Grade Urothelial Tumors in Urinary Sediment.....	91
Histologic Variants of Urothelial Carcinoma.....	96
Squamous (Keratinizing) Carcinoma.....	96
Adenocarcinoma and Its Variants.....	96
Small Cell (Oat Cell) Carcinomas.....	99
Metastatic Tumors.....	100
Carcinoma and Precancerous States of the Uterine Cervix.....	100
Other Carcinomas of the Female Genital Tract.....	101
Prostatic Carcinoma.....	102
Carcinomas of Colon and Rectum.....	102
Carcinoma of Renal Cell Origin.....	102
Metastatic Carcinomas from Distant Sites.....	103
Other Metastatic Tumors.....	103
Cytologic Monitoring of Patients Treated for Tumors of Lower Urinary Tract.....	104
Reporting of Cytologic Findings.....	105
Suggested Readings.....	106
7 Urine-Based Assays Complementing Cytologic Examination in the Detection of Urothelial Neoplasm.....	109
Introduction.....	109
US FDA-Approved Markers.....	109
Bladder Tumor Antigen (BTA).....	109
Nuclear Matrix Protein 22 (NMP22).....	110
Fibrin–Fibrinogen Degradation Product (FDP).....	111

ImmunoCyt	111
UroVysion.....	112
Potential Markers in Earlier Phases of Clinical Development.....	113
Bladder Cancer Antigen-4 (BLCA-4).....	113
Survivin.....	114
UBC Tests.....	114
CYFRA 21-1.....	114
Hyaluronic Acid (HA)-Hyaluronidase (HAase).....	115
Telomerase.....	115
Quanticyt.....	115
Fibroblast Growth Factor Receptor 3 (FGFR3).....	116
Mucin 7 (MUC7).....	116
VEGF.....	116
Markers Detected by Immunocytochemistry.....	117
CKs.....	117
p53.....	117
Ki-67.....	118
p16.....	118
Epidermal Growth Factor Receptor (EGFR).....	118
E-Cadherin.....	118
Comparison Between Urine Cytology and FDA-Approved Markers.....	119
Conclusion.....	120
References.....	120
Index.....	123

Chapter 1

Introduction

Keywords Urothelium • Hematuria • *Schistosoma hematobium* • Squamous cell carcinoma • Urinalysis • Urine cytology

Historical Note

Examination of urine as a means of diagnosis of human illness has been known since the time of the ancient Egyptians. Badr noted that red urine (hematuria), as evidence of infection with *Schistosoma hematobium* (bilharzia), was recorded in the papyrus of Kahun (1900 B.C.) (Fig. 1.1). The famous Elbers papyrus (1550 B.C.) suggested that hematuria was due to “worms in the belly” (El-Bolkainy). The ancient Egyptians were also aware of the relationship between agricultural activities in the fields irrigated by the river Nile and bloody urine. This relationship was clarified only in 1852 with the discovery of *S. hematobium* by Theodore Bilharz. The relationship of schistosomiasis to bladder cancer was first established by Ferguson in 1911. The mechanism of this association remains unknown.

From the time of Hippocrates into the nineteenth century, the examination of urine was thought to be an important diagnostic procedure. The smell, color, and transparency of the urine and the amount and nature of the sediment, often examined in specially constructed glass containers, was considered to be a guide to diagnosis and treatment of the underlying disorder (Fig. 1.2). There were several sixteenth and seventeenth century paintings of physicians examining urine at the bedside or practicing “uroscopy.” Perhaps the epitome of this “science” was a pamphlet published in London in 1637 by Thomas Brian, Member of Parliament, entitled “*The Pisse-prophet or certaine pisse pot lectures. Wherein are newly discovered the old fallacies, deceit, and juggling of the Pisse-pot Science, used by all those (whether Quacks and Empirics, or other methodicall Physicians) who pretend knowledge of Diseases, by the Urine, in giving judgment of the same.*”



Fig. 1.1 Hematuria, as recorded in the papyrus of Kahun (1900 B.C.), with reference to schistosomiasis (Badr M: Schistosomiasis in Ancient Egypt. In El-Bolkainy, MN and Chu EW Eds: Detection of bladder cancer associated with schistosomiasis. Cairo, Egypt: The National Cancer Institute 1981)

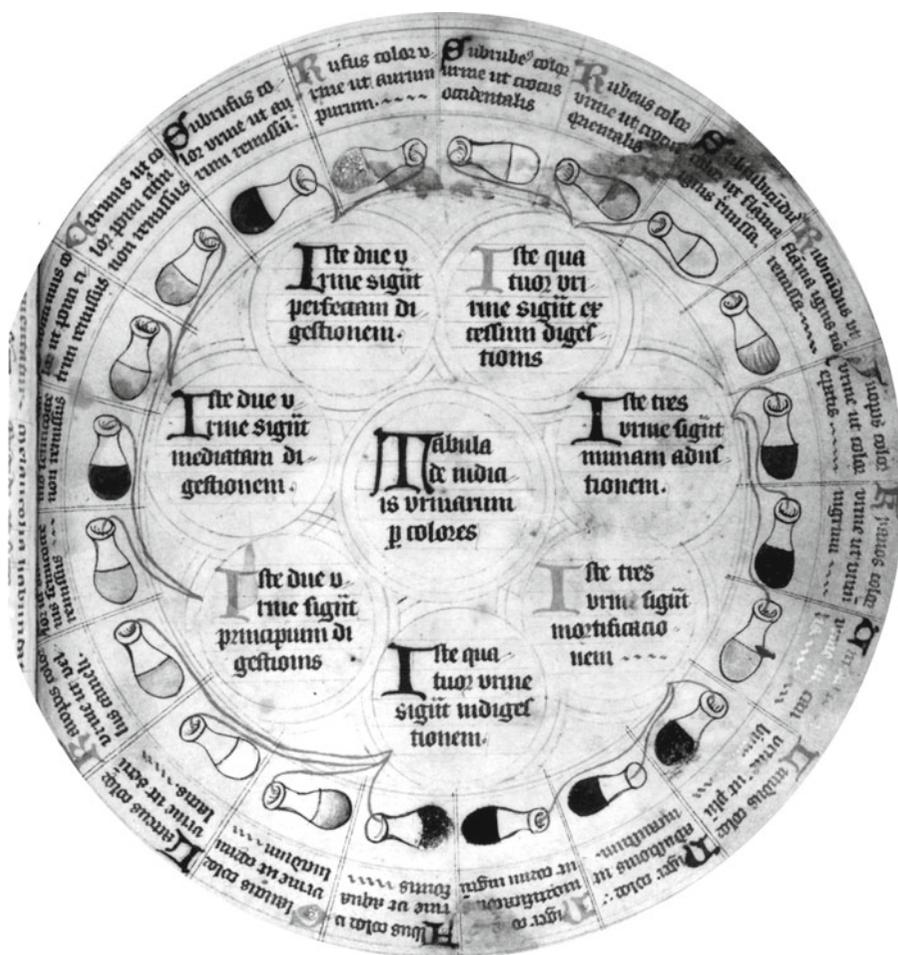


Fig. 1.2 Medieval uroscopy chart used in diagnosis. Note the appearance of glass urinals surrounding the diagnostic options. (Manuscript Ashmole 391 [V], fol. 10r, courtesy of Bodleian Library, Oxford, UK)

In a remarkable article on the subject of uroscopy Fishman (1993) commented on the work of Brian in seventeenth century England. Brian ridiculed the practice of uroscopy, which was often based on examination of urine alone, in the absence of the patient. Samples were often brought to the practitioner's office by servants or family members. Brian's pamphlet describes various ruses used by the seventeenth century physicians to obtain from the messengers helpful information about the patient. It is of interest that the vestiges of these fraudulent practices persisted until the early days of the twentieth century. Fishman cited and illustrated a 1911 advertisement by a company in Grand Rapids, Michigan, to establish a diagnosis and prescribe treatment based on analysis of mailed urine samples.

The nineteenth century brought with it major changes in the examination of urine. Besides the progress in organic chemistry that allowed the study of the major organic constituents of urine and their correlation with disease states, microscopic examination of the urinary sediment slowly entered into the medical armamentarium. The ordinary "urinalysis," persisting until today, calls for a casual microscopic examination of unstained urinary sediment for the presence of erythrocytes, leukocytes, and epithelial cells. Staining of the urinary sediment that would have allowed a more detailed examination of the cells was introduced only in the twentieth century. Today, machines capable of automated image analysis of the urinary sediment have replaced the human eye in many laboratories.

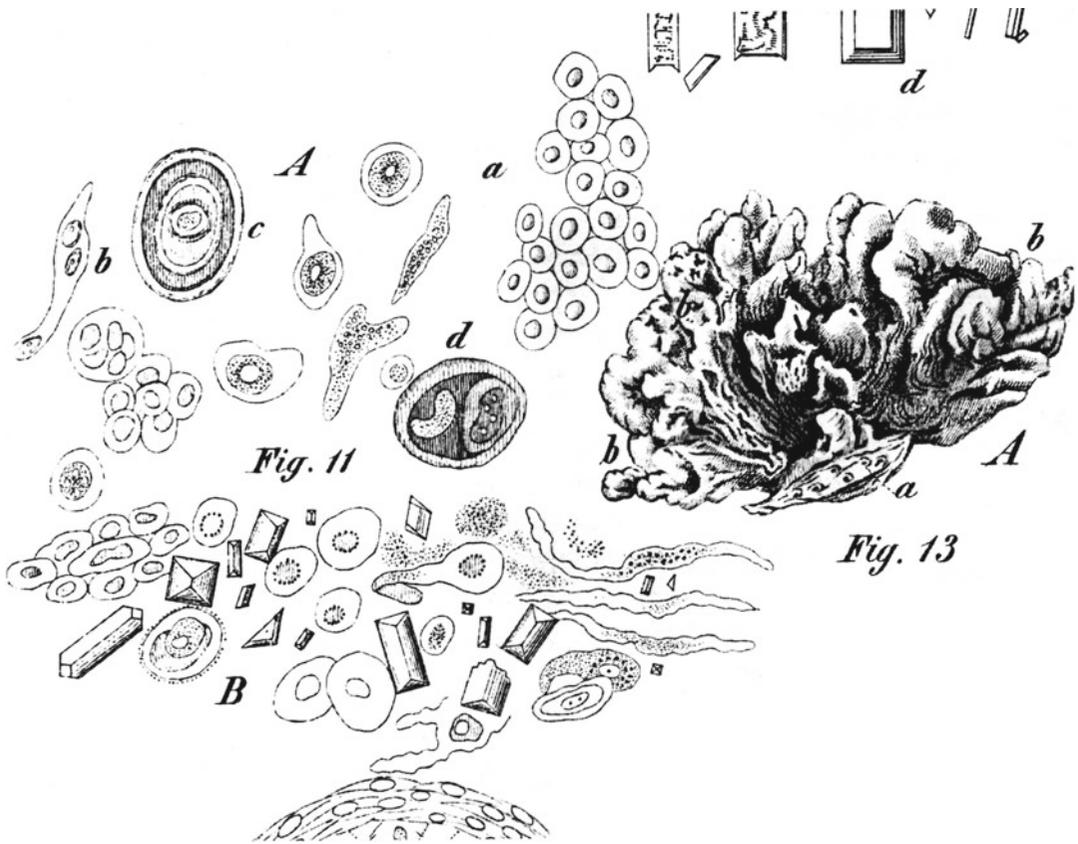


Fig. 1.3 Figure 11 (left) from Lambi's 1856 paper, illustrating various cells and crystals observed in the urinary sediment. Figure 13 (right) shows "papillary pseudoplasma from the urethra of a girl"—undoubtedly a condyloma acuminatum

Careful microscopic analysis of cells in the urinary sediment began in the middle of the nineteenth century. In 1856 Wilhelm Duschlan Lambi (also known as Vilem Dusan Lambi), a Czech physician from Prague, wrote in German a beautifully illustrated article entitled "Ueber Blasenkrebs. Ein Beitrag zur mikroskopischen Diagnostik am Krakenbette" [On cancer of the bladder. A contribution to microscopic diagnosis at bedside], in which he said the following: "The diagnosis of cancer of the bladder by microscopy of the urinary sediment has received no thorough treatment in the available literature—or rather has not been mentioned at all." He then proceeded to describe in considerable detail the cytologic findings in six tumors of the bladder, one uterine carcinoma involving the bladder, one "benign papilloma" of the urethra observed in a girl (presumably a condyloma acuminatum), and two inflammatory conditions serving as controls (Fig. 1.3). Lambi's life story and contributions were described in some detail by two meritorious historians of human cytology, Heinz Grunze and Arthur Spriggs (1986). It is of incidental interest that Lambi's contributions were not limited to bladder cancer. He was immortalized in the name of the parasite *Giardia lamblia*.

Other nineteenth-century observers reported on the diagnostic value of cytology in tumors of the urinary tract. The great British microscopist Beale, who in 1854 published one of the most comprehensive and astute books on the subject of clinical microscopy, subsequently wrote extensively on urinary cytology and in 1864 described cancer cells in the urine. In the same year, a Scottish physician, Sanders, described in *Edinburgh Medical Journal* a patient in whose urinary sediment fragments of cancerous tissue were observed. Shortly thereafter, in 1869, a British physician, Dickinson, reported

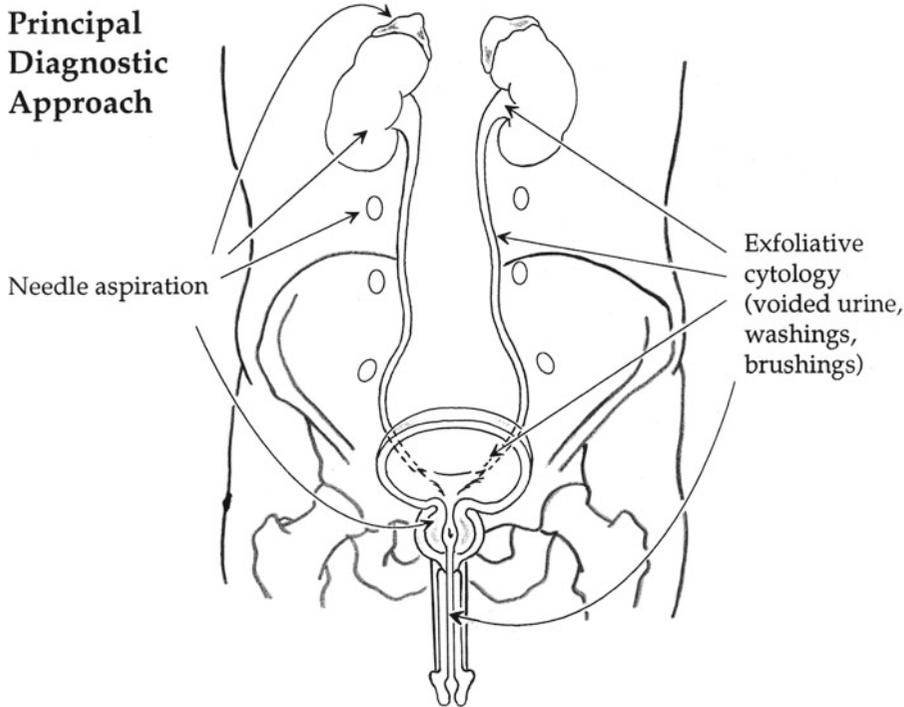


Fig. 1.4 A diagram of the principal organs of the urinary tract and the methods of investigation by either exfoliative or aspiration cytology. (Diagram by Dr. Diane Hamele-Bena, Columbia Presbyterian Hospital, New York, NY). In this book, fine needle aspiration of the kidney is not described (see Koss LG, Melamed MR. Koss's Diagnostic cytology and its histopathologic bases. 5th ed. Philadelphia, PA: Lippincott; 2006. p. 1457–1482)

a similar observation. While there may have been other sporadic reports on this subject that are not known to us, it is noteworthy that in 1892, a New York pathologist, Frank Ferguson, stated at a meeting of the New York Pathological Society that the microscopic examination of histologic sections of paraffin-embedded urinary sediment is one of the most important diagnostic procedures in bladder cancer.

There is no evidence that Ferguson's observations were noted by the medical community: there are no records of cytologic diagnosis of cancer of the lower urinary tract before 1945. In that year Papanicolaou and the urologist, Marshall, reported on the cytologic examination of the urinary sediment in 83 patients. The diagnostic results were reported as 88.8% correct "positive" and 60% correct "negative," thus hardly worthy of note, were it not for the illustrious authors and the fact that the article appeared in the exclusive scientific journal *Science*. In the 1950s, Geoffrey Crabbe, a British cytopathologist, published several papers on the application of voided urine cytology to the surveillance of workers at high risk for bladder cancer who were employed in the dyestuff industries in England, where carcinogenic aromatic amines were produced in open systems. Crabbe's contributions proved to be of seminal value, as they led to a series of observations of workers exposed to a potent bladder carcinogen, paraaminodiphenyl, in the United States. A series of publications by Koss et al. in 1960, 1965 and 1969 defined the diagnostic limits and achievements of cytology of voided urine and introduced the concept of *nonpapillary carcinoma in situ* as the principal precursor lesion of invasive cancer of the urinary bladder. These observations have completely modified the approach to the diagnosis and treatment of tumors of the bladder (for further comments see Chap. 5).

The examination of voided urine is an efficient method of diagnosis of some diseases of the lower urinary tract, i.e., bladder, urethra, ureters, and renal pelvis. With the passage of time, examination of