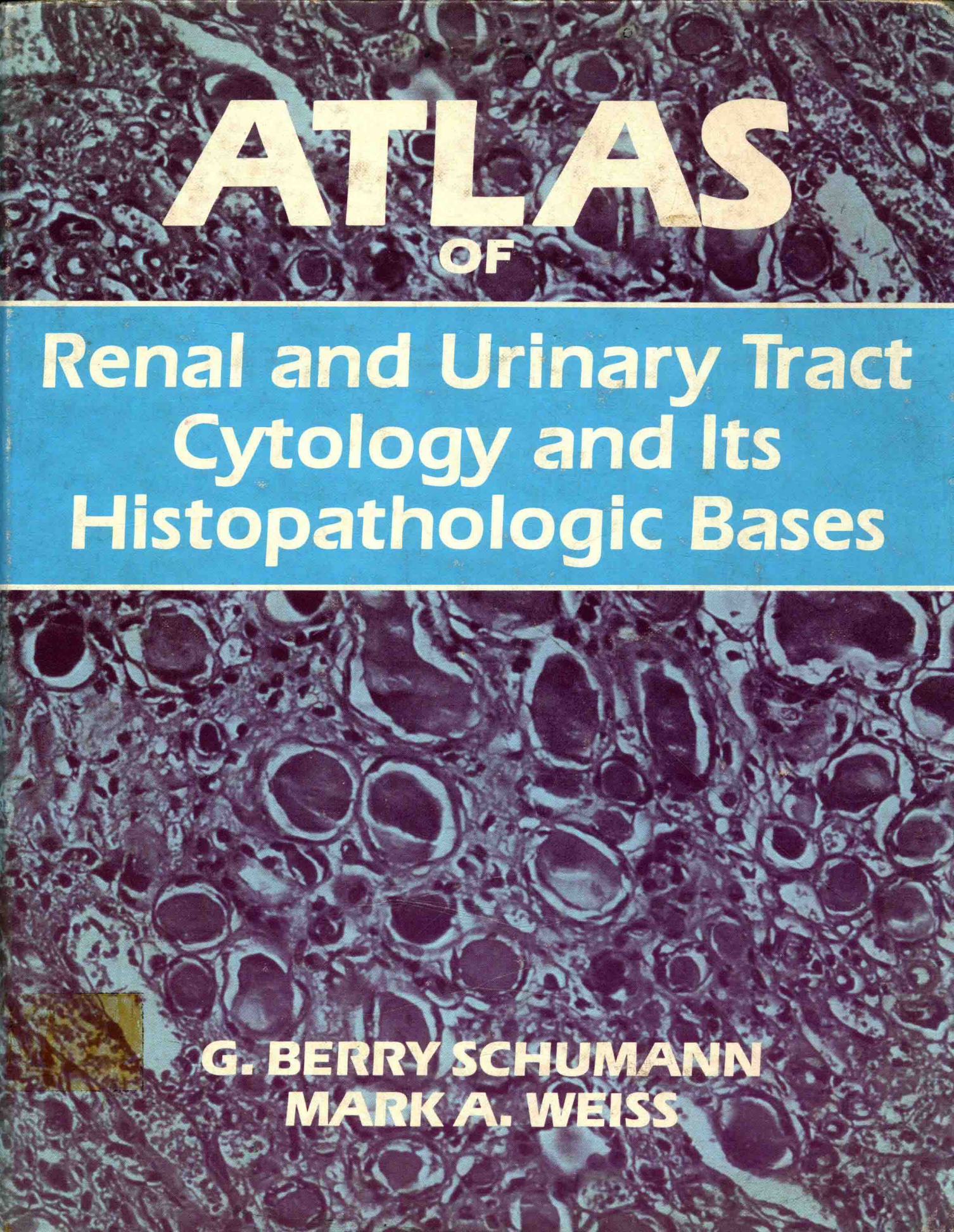
ATLAS OF

Renal and Urinary Tract Cytology and Its Histopathologic Bases



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To our mentors, parents and family

INTRODUCTION

The examination of urine (urinalysis) represents one of the oldest medical laboratory procedures for the evaluation of renal parenchymal and urinary tract disorders. Early popularity was based upon the ease of specimen collection. Although crude procedures, such as smelling, tasting, boiling and adding reagents (acids) were initially described in medical textbooks, it was not until the microscope became available that urinalysis became a valuable method of clinical diagnosis. Fascination with the capabilities of this simple technique frequently led physicians into the habit of examining the urine before the patient.

Historically, the laboratory urinalysis procedure has been divided into *macroscopic* and *microscopic* components. The *macroscopic* urinalysis, as a measure of functional change, involved physicochemical testing for the assessment of color, appearance (turbidity), specific gravity, pH and chemical constituents (glucose, protein, ketones, etc.). The *microscopic* urinalysis involved an interpretation of urine sediment to provide structural (morphologic) evidence of infections, hematuria and inflammation.

In the mid 1960's, the development of reagent-strip physicochemical testing led to a major modernization of the urinalysis laboratory. When properly performed, this provided a cost effective semi-quantitative method for screening and functional monitoring of patients with renal disease. Interest in the microscopic urinalysis declined, because of crude microscopic methods, poor clinico-pathologic correlations and the inability to adapt to mass screening. Requirements for quality control and continuing education widened the gap between the microscopic and macroscopic urinalysis and resulted in routine urinalyses being performed in the clinical chemistry laboratory.

Attempts to improve the urine sediment examination, especially for renal disease, primarily occurred in microscope modifications, urine staining and counting chamber methods. The wet mount (unstained brightfield microscopy) was criticized, and phase-contrast and interference-contrast microscopy were suggested. Supra-vital staining techniques, such as the Sternheimer-Malbin, never gained popularity.

Poor visualization, standardization and quality control continued to be major deficiencies.

While interest in utilizing sediment examinations for renal disease declined, the detection of cancer cells in the sediment using cytologic techniques was rapidly developing. In the early 1950's, the field of diagnostic cytology was detecting and modifying the clinical course of cervical cancer. By using the Papanicolaou staining method, impressive cellular detail could be achieved that correlated with histologic material. Other microscopists, especially in Europe, found the permanent Wright-Giemsa staining method valuable. Unfortunately, cytologists concentrated primarily on neoplastic disease of the lower urinary tract.

With the advent of renal transplantation, the common use of immunosuppressive and chemotherapeutic agents and industrial exposure to nephrotoxic agents and carcinogens, a new approach to the sediment examination was required. Semi-quantitative methods were needed to document chronologic sediment changes.

This atlas on renal and urinary tract cytology provides the histologic bases for urine sediment findings. In addition, it provides a practical diagnostic approach, termed *cytodiagnostic urinalysis*, for the evaluation of urine sediment. *Atlas of Renal and Urinary Tract Cytology and Its Histopathologic Bases* is divided into four parts. Part I briefly discusses the cytologic and histologic techniques used. Part II defines common morphologic entities and criteria for accurate identification. Parts III and IV utilize case material for the demonstration of various types of urine sediment patterns and their differential diagnoses.

Data derived from an accurate urine sediment examination will provide important information for the diagnosis and management of patients with urinary system disease. In the future, with incorporation into the cytodiagnostic urinalysis of more sophisticated techniques, such as transmission and scanning electron microscopy, immunofluorescence, cytochemistry, and chemical analyses of heavy metals, the urine sediment evaluation is sure to regain medical popularity.

PREFACE

Accurate interpretation of morphologic urinary sediment findings is essential for defining and documenting the dynamic changes involving the urinary system during disease. In the past, little information was derived from the urine sediment examination because imprecise techniques were utilized. The authors have evaluated several thousand urine sediments using the Papanicolaou staining technique and found this method far superior in demonstrating the cellular detail required for accurate interpretation and precise diagnosis.

Over the last two years, numerous urine sediments have been examined by a cytologist and nephropathologist to establish a histologic basis. Unlike most traditional textbooks on microscopic urinalysis or urine cytology, this atlas provides correlates of renal parenchymal and lower urinary tract conditions. Numerous photographs demonstrate the remarkable morphologic similarity between exfoliated cells or structures and their appearance in histologic material. While examples of traditional findings of infectious (bacterial, fungal, viral), inflammatory, and neoplastic disease involving the lower urinary tract are presented, special emphasis has been given to the criterion for recognition of entities associated with renal parenchymal disease. Much of the correlation has been achieved through evaluation of renal transplant biopsies and corresponding serial urine sediment examinations. Hopefully this atlas will provide a diagnostic approach for systematic evaluation of the urine sediment and its histologic bases.

G. Berry Schumann, M.D. and Mark A. Weiss, M.D.

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CONTENTS

PART I

MATERIALS AND METHODS

1

CYTOLOGIC PROCEDURES AND TECHNIQUES

SPECIMEN COLLECTION

Urine sediment examinations are usually of spontaneously voided clean-catch urine or following instrumentation (catheterization). If catheterized urine is being submitted, it should be noted on a requisition form. Because excoriation of epithelial surfaces may occur during instrumentation, this notation is imperative. Detailed information regarding specimen collection is given in standard textbooks.

CELLULAR PRESERVATION

Morphological detail of cellular elements will be preserved if the specimen is submitted to the laboratory within a 2-hr period. Refrigeration (2–8°C) will minimize cellular degeneration up to 48-hr period. It should be noted that hyaline and granular casts will dissolve with prolonged unfixed storage. When it is anticipated that a period of longer than 48-hr will occur before the urine specimen is submitted to the laboratory, an appropriate fixative should be used. The use of equal volumes of urine and 50% alcohol, Saccomanno's or Mucolexx fixative is recommended. Alcohol-fixed urine sediments should be stored in the refrigerator until time for preparation. A major advantage of the Saccomanno and Mucolexx fixatives is that the specimen can be stored at room temperature.

PREPARATORY METHODS

The material and methods used for preparation of urine sediment are given in standard textbooks. Methods of cell recovery vary to improve cellular yield. The two techniques that have proved of most value are the cytocentrifugation and membrane filter techniques. Following notations of volume, color, appearance (turbidity or cloudiness), specific gravity, and reagent-strip testing, the urine is initially centrifuged 10 min at 1200 rpm. The visual examination of the urine specimen is useful in determining which technique should be utilized. If *no* sediment button is visible following centrifugation, the membrane filter technique is employed (Fig. 1-1). If a sediment button *is* observed, the supernatant should be carefully removed leaving a 1- to 3-ml total volume of supernatant and sediment. Cytocentrifugation is then performed (Fig. 1-2). Following