RENAL DISEASE

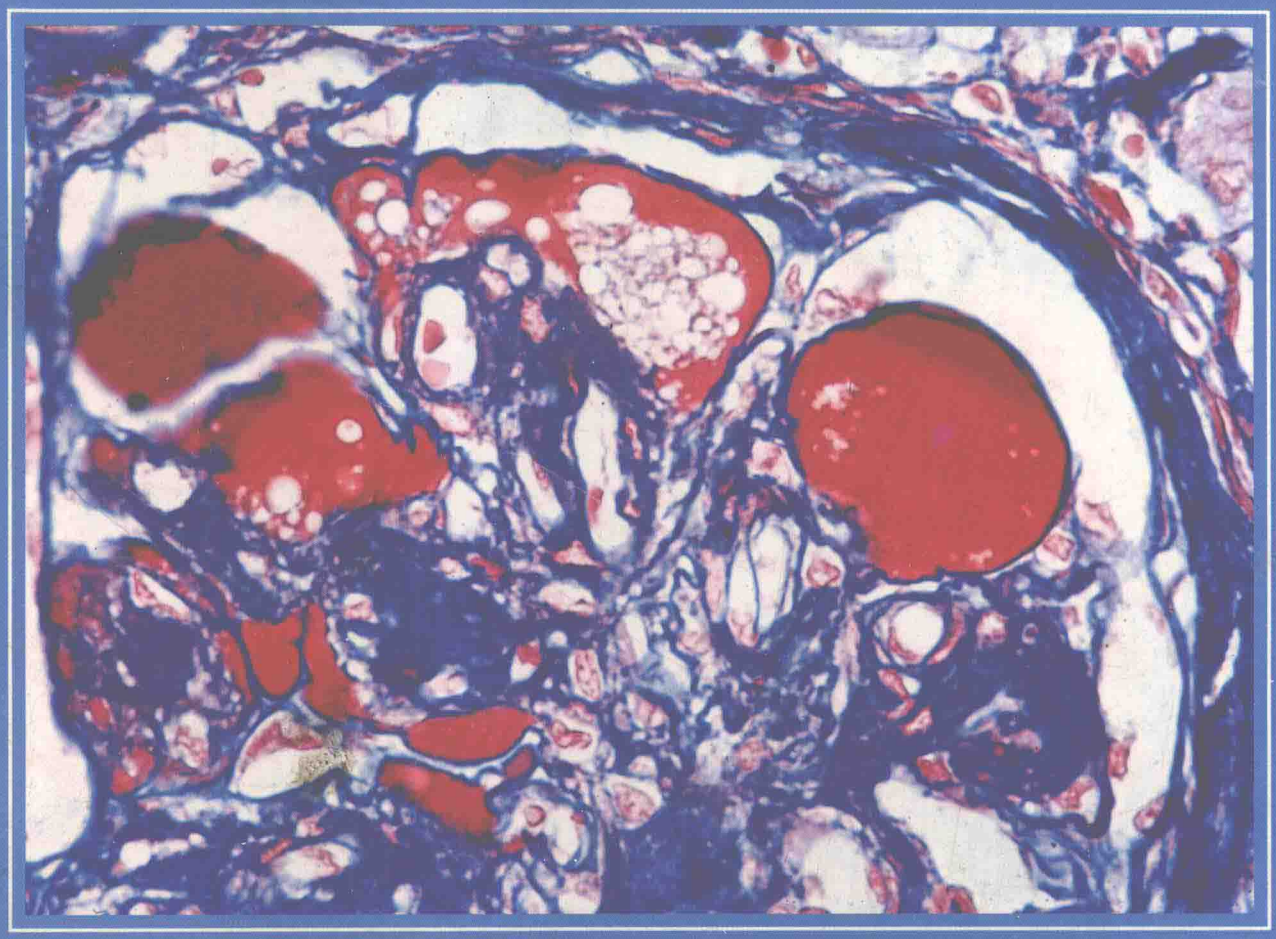
Classification and Atlas of Glomerular Diseases

JACOB CHURG

in collaboration with

L.H. SOBIN

and pathologists and nephrologists
in 14 countries



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Classification and Atlas of Glomerular Diseases

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Preface

Among the prerequisites for comparative studies on renal diseases are international agreement on criteria for diagnosis, a standardized nomenclature and a uniform system for classification. Without these ingredients, nephrologists, pathologists and epidemiologists, among others, would be uncertain whether studies carried out in one country were comparable to those from another.

Two notable recent efforts were made by international groups to bring order into this field.

The International Committee for Nomenclature and Nosology of Renal Disease working through subcommittees on anatomy, immunology, pathology, physiology, radiology and clinical medicine published "A Handbook of Kidney Nomenclature and Nosology" in 1975.

The International Collaborative Study of Kidney Disease in Children recognized the need to establish uniform criteria in this field owing to the special task they were undertaking. Their use of a panel of pathologists to review the material in the study helped pave the way towards developing acceptable terms and criteria for diagnosis.

Building on the experience of these groups, the World Health Organization in 1974 established a Collaborating Centre for the Histological Classification of Renal Diseases at the Department of Pathology, Mount Sinai School of Medicine, The City University of New York, in New York City, under the direction of Dr. J. Churg. The Centre worked with pathologists and nephrologists from fourteen countries to elaborate the material in this volume.

It is recognized that the classification reflects the present state of knowledge and modifications are almost certain to be needed as experience accumulates. Although some may wish to dissent from the views expressed, it is hoped that, in the interests of international cooperation, all will try to use the classification as put forward, particularly when international communication is intended.

Introduction

This monograph consists of two sections. The first provides a listing of glomerular lesions (Tables I and II) and gives their definitions. It also presents the main clinical and morphological features of glomerular processes in a tabular form (Tables III, IV and V). The second section describes in detail and illustrates the various glomerular processes. An Appendix contains information about some of the more useful histologic techniques and about examination of renal specimens.

Ideally, a classification of diseases should be based on etiology. However the current knowledge of etiology or even of pathogenesis of glomerular diseases is too limited to be of much value. As is well known, clinical classifications have proven unreliable because of considerable overlap in symptomatology. At the present time the most consistent classification is that based on morphology. This too has its limitations, because the pattern of glomerular change often lacks clinical specificity. It is to be understood that what is being classified here are histological patterns rather than diseases. Sometimes a pattern is sufficient to establish a specific diagnosis but in many cases it is necessary for that purpose to combine the morphological with the clinical data.

For some purposes the histological material has a further advantage over the clinical data: slides and photographs can be stored for a long period of time and retrieved for review whenever new clinical information in the individual cases, or a new way of classification becomes available. If need be, they can also be sent out for consultation over long distances.

The classification here presented harks back to Volhard and Fahr, but wears a modern dress. It is based primarily on light microscopy but also provides information about electron microscopic and immunofluorescent features. To avoid the increasing complexity of some of the current classifications, the glomerular lesions are divided into two categories: those representing the Basic Glomerular Patterns (Table I) and those considered to be the Qualifying Features (Table II). The lesions included in Table I are the constant changes, while those in Table II modify the appearance and sometimes even the evolution of the Basic lesion but do so inconstantly and only in some cases. For a complete definition of the histologic pattern in each individual case, the appropriate category from Table I should be supplemented by additional feature or features from Table II.

Perusing the Tables I and II makes it obvious that selection of the Basic Patterns is to a certain degree arbitrary. By combining sufficient number of Qualifying Features, it is feasible to define almost any entity in Table I, and if one so wishes, remove it from that Table. By this process one can reduce the number of Basic Patterns to very few, perhaps only two, in a manner reminiscent of Ellis' division of glomerulonephritis into Type 1 and

Type 2. For example, Table I could contain only Minor Changes and Mesangial Glomerulonephritis and all other entities would be defined by attaching appropriate qualifiers from Table II. However such classification would place under one heading entities with entirely different clinical behavior and would aggravate the problem of relating the clinical to the morphologic manifestations. The committee felt that the classification used in this monograph provides a reasonable compromise, which does not deviate too far from the current terminology and which offers a fairly consistent basis for clinicopathological correlation.

This monograph is meant not only for the specialist in renal diseases, but also for the general pathologist faced with examination of a renal biopsy or autopsy specimen. The first and most essential step of such examination is a careful study by light microscopy. This requires good tissue sections and proper stains (see Appendix). Information derived from such study, combined with the clinical and laboratory data and sometimes also with response to treatment, will be sufficient for diagnostic and prognostic purposes in a large majority of patients. In some cases the diagnosis should be considered provisional until it is further refined by electron microscopy and/or immunofluorescence microscopy, particularly in cases showing only minor changes by light microscopy, since clinically significant disease may occur with only slight glomerular changes. If only limited facilities are available, it is advisable to process and embed some of the renal biopsy tissue for electron microscopy (see Appendix for procedure). Such tissue can be examined at some future date, or be sent to an electron microscopy laboratory. A similar approach can be taken to immunofluorescence microscopy, though this may be somewhat more difficult to put into practice.

It is our sincere hope that pathologists and nephrologists will find this monograph useful as a basis for communication with their fellow workers throughout the world.

Key to Abbreviations

Am = amyloid
B = cytoplasmic bleb
BC = Bowman's capsule
BM, bm = basement membrane
BMM = basement membrane material
Br = break or defect of basement membrane
Cap = capillary
Col = collagen
Cr = crescent
Cr cell = cell of crescent
D = deposit
En = endothelial cell
Ep = epithelial cell
F = fibrin
FC = foam cell
FP = foot process or processes
Gr = granular material or granules
H = hyalin
I = interstitial tissue
JGC = juxtaglomerular cell
L = capillary lumen
l = lacuna or lucent area
LD = lamina densa
LRE = lamina rara externa
LRI = lamina rara interna
M = mesangium
MC = mesangial cell
MI = mesangial interposition in the capillary wall
MM = mesangial matrix
MN = mesangial nodule
Mon = mononuclear cell or monocyte
MV = microvillus or microvilli
P = podocyte
PAS = periodic acid-Schiff's reagent
PASM = periodic acid-silver methenamine
Pmn = polymorphonuclear leukocyte
PTA = phosphotungstic acid
PTAH = phosphotungstic acid-hematoxylin
RBC = red blood cell
S = spike or spikes
SM = smooth muscle
TBM = tubular basement membrane
TC = tubular cell
U = urinary space

Contents

Section I

Classification of Glomerular Diseases

GLOSSARY OF TERMS

Diffuse: A lesion involving all or nearly all glomeruli (i.e. $> 80\%$).

Focal: A lesion involving some but not all glomeruli ($< 80\%$).

Global: A lesion involving the whole glomerulus.

Segmental: A lesion involving a portion of the glomerulus (i.e. some capillary lumina remain uninvolved).

Hyalinosis: A lesion containing an acellular, structureless material (by light microscopy) consisting of glyco-proteins and sometimes incorporating lipids. The hyaline material stains intensely with eosin and PAS, red with Trichrome, and does not stain with periodic acid-silver methenamine (PASM).

Sclerosis: A lesion consisting of fibrillar material resulting from an increase in mesangial matrix and/or collapse and condensation of the basement membrane. The sclerotic material stains with eosin and PAS regent, blue/green with Trichrome stains and stains positively with PASM.

Fibrosis: A lesion consisting of collagen fibers which may be differentiated from sclerosis by *not* staining with PAS regent or PASM.

Necrosis (Glomerular): A lesion characterized by fragmentation of nuclei and/or disruption of the basement membrane, often associated with fibrin rich material.

Cellular Crescent: A lesion consisting of cellular proliferation (probably epithelial) which fills part or all of Bowman's space. Minimum requirement for this definition is the presence of at least two layers of cellular proliferation. Fibrin may often be associated with such lesions.

Fibro-cellular Crescent: A lesion which is similar to a cellular crescent but with the addition of a variable amount of fibrillar material. This fibrillar material may be either basement membrane-like material or collagen.

N.B. This category includes those crescents with *almost* complete fibrous replacement.

Fibrous Crescent: A lesion within Bowman's space which is predominantly composed of fibrous tissue. This lesion may be the scarred remains of cellular and fibro-cellular crescents. However, it is important to note that identical lesions also occur in ischemic glomeruli where no evidence of glomerulonephritis can be obtained.

Note: Other terms in this monograph are used in a generally accepted sense as in standard textbooks of pathology and nephrology. A complete Glossary of terms can be found in a Handbook of Kidney Nomenclature and Nosology (see references). Histologic and clinical definitions follow Tables I, II and V in this monograph.

Table I BASIC GLOMERULAR ALTERATIONS.

1. Primary Glomerular Diseases (Glomerulonephritis and Related Conditions)
- A. Minor Glomerular Abnormalities
- B. Focal/Segmental Lesions (with only minor abnormalities in other glomeruli)
- C. Diffuse Glomerulonephritis
  - a. Membranous Glomerulonephritis (Membranous Nephropathy)
  - b. Proliferative Glomerulonephritis
    - Mesangial Proliferative Glomerulonephritis
    - Endocapillary Proliferative Glomerulonephritis
    - Mesangiocapillary Glomerulonephritis (Membranoproliferative Glomerulonephritis Types 1 and 3)
    - * Dense Deposit Glomerulonephritis (Dense Deposit Disease) (Membranoproliferative Glomerulonephritis Type 2)
    - Crescentic (Extracapillary) Glomerulonephritis
  - c. Sclerosing Glomerulonephritis
- D. Unclassified Glomerulonephritis

2. Glomerulonephritis of Systemic Diseases
- Lupus Nephritis
- Nephritis of Henoch-Schönlein Purpura (Anaphylactoid Purpura)
- Berger's Disease (IgA nephropathy)
- Goodpasture's Syndrome
- Glomerular Lesions in Systemic Infections
  - Septicemia
  - Infective Endocarditis
  - Shunt Nephritis
  - Syphilis
- Parasitic Nephropathies
  - Malarial Nephropathy
  - Schistosomal Nephropathy
  - Strongyloides Nephropathy

3. Glomerular lesions in Vascular Diseases
- Periarteritis Nodosa
- Wegener's Granulomatosis
- Thrombotic Microangiopathy (Hemolytic-Uremic Syndrome and Thrombotic Thrombocytopenic Purpura)
- Glomerular Thrombosis (Intravascular Coagulation)
- Benign Nephrosclerosis
- Malignant Nephrosclerosis
- Scleroderma (Systemic Sclerosis)

4. Glomerular Lesions in Metabolic Diseases
- Diabetic Glomerulosclerosis
- Amyloidosis
- Nephropathy in Dysproteinemias
  - Multiple Myeloma
  - Waldenstrom's Macroglobulinemia
  - Cryoglobulinemia

* May belong in a different category — Metabolic Disease?

Nephropathy of Liver Disease
Nephropathy of Sickle Cell Disease
Nephropathy of Cyanotic Congenital Heart Disease and in Pulmonary Hypertension

5. Hereditary Nephropathies

Alport's Syndrome
Benign Recurrent Hematuria
Thin Basement Membrane Syndrome
Nail-Patella Syndrome (Osteo-onychodysplasia)
Congenital Nephrotic Syndrome (Finnish Type)
Infantile Nephrotic Syndrome (French Type) (Diffuse Mesangial Sclerosis)
Fabry's Disease and Other Lipidoses

6. Miscellaneous Glomerular Diseases

Nephropathy of Toxemia of Pregnancy (Pre-eclamptic Nephropathy)
Radiation Nephritis

7. End Stage Kidney

8. Glomerular Lesions Following Transplantation

Definitions to Table I will be found in Section II of this monograph together with clinical and morphological descriptions and illustrations of each entity.

Table II SIGNIFICANT QUALIFYING GLOMERULAR CHANGES.

The lesions may be diffuse or focal. If focal, then give percentage of glomeruli affected.

(a) Segmental Mesangial/Endocapillary Proliferation
(b) Segmental Hyalinosis
(c) Segmental Sclerosis
(d) Segmental Necrosis
(e) Segmental Capillary Wall Abnormality
(f) Capillary Thrombosis
(g) Adhesions
(h) Cellular and/or Fibrocellular Crescents
(j) Global Sclerosis
(k) Leukocytic Infiltration
(l) Subepithelial Deposits
(m) Transmembranous and Intramembranous Deposits
(n) Subendothelial Deposits
(p) Mesangial Deposits

Additional Non-Glomerular Lesions: Specify Type and Extent.

Vacular
Tubular
Interstitial
