Amyloid and Related Disorders

Surgical Pathology and Clinical Correlations
This book is dedicated to our patients, past and present, with the hope that it will make a difference in the lives of future amyloidosis patients.
Preface

Amyloidosis, although known since the nineteenth century, retained for a long time the aura of a rare and obscure disease that was mainly of purely academic interest. This perception was augmented by the fact that the disease was only ever diagnosed once it had progressed to an advanced stage and because no effective therapies were available for its treatment.

This state of affairs has, however, changed dramatically during the last decade or so. With the new therapies that are now available for systemic amyloidoses, patients who are diagnosed with light chain amyloidosis (AL) may achieve a durable response and live for more than a decade from the time of their initial diagnosis. Treatments for other types of systemic amyloidosis are also improving. Thus, since the 1990s, solid organ transplantation has been introduced for the management of patients diagnosed with hereditary amyloidoses. Newer pharmacologic therapies are in clinical trials. However, treatment outcomes are clearly optimal when they are applied early in the disease process. Thus, now more than ever, early diagnosis is imperative. Although there are a number of excellent amyloidosis treatment centers worldwide, early diagnosis of affected patients is reliant upon widespread and effective screening and, despite advances in laboratory medicine, this still depends upon the detection of deposits in tissues. Thus, the role of the pathologist in this process is critical for successful completion of this first crucial step, which is then instrumental in directing the patient toward further workup conducted by specialized centers.

This whole process is dependent upon an adequate state of awareness of the disease among general surgical pathologists at large and their close collaboration with clinicians. This book therefore has, as its primary focus, the diagnosis of amyloidosis in surgical pathology. Although written primarily for pathologists, it is hoped that this book is also helpful to those who would wish to gain insight into recent diagnostic and treatment options. It brings together, for the first time, a collection of articles by both pathologists and clinicians, with a focus on practical issues, in the hope that this information will serve as a guide for practitioners in both fields who are concerned with the early diagnosis of the amyloidoses.

This book begins with general information on the amyloidoses: the history of amyloid investigations, the modern nomenclature, the mechanism of amyloidogenesis and an overview of AL, hereditary, AA, dialysis, and localized amyloid. Newly emerging conditions associated with amyloidosis (such as
periodic fevers) and newly recognized amyloid types are also included. Since cerebral amyloidoses are usually dealt with by neuropathologists, in this book, we provide only a brief overview and to the extent that the issues involved are of interest to general surgical pathologists. In Part II, diseases that mimic amyloid and related disorders are discussed. Part III is entirely devoted to pathologic diagnosis and discusses in detail issues pertaining to the generic diagnosis of amyloid, Congo red stains and its more sensitive alternatives useful for screening purposes, as well as issues pertaining to amyloid typing that involve both antibody-based and proteomic methods. This part also contains extensive discussion of pitfalls encountered in the diagnosis of amyloidosis, and provides guidance on how to avoid them. Part IV provides an overview of laboratory support for the diagnosis of amyloidosis, including serum and urine studies (including the free light chain assay), bone marrow examination, and genetic studies. Part V provides an overview of the organ-specific pathologies that are encountered in the examination of tissues from the genitourinary tract, cardiac, gastrointestinal, liver, and peripheral nerve specimens. Part VI discusses clinicopathologic interactions, the role of solid organ transplantation, emerging therapies for amyloidoses in general, and modern therapies for AA amyloidosis. This part also emphasizes the importance of accurate diagnosis of amyloidosis in view of the serious consequences that may follow from misdiagnosis of the disease entity or, more specifically, the amyloid type. Brief chapters on relevant legal issues and the patient’s perspective conclude Part VI.

It behooves us to acknowledge that abnormal protein folding, the very essence of amyloid fibril formation, affects many more aspects of our lives than those covered by the chapters in this book. Protein misfolding may represent a fundamental biochemical process that is also operational in the course of neurodegenerative diseases and human aging. Thus, understanding the amyloidoses may help us to understand the aging process in general and, perhaps, even aid in devising antiaging strategies. Those who are interested in the amyloidoses are encouraged to review the International Society of Amyloidosis Web site (www.amyloidosis.nl) and the past and future contents of the journal “Amyloid.”

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Maria Mrozowicz Picken MD, PhD, Chicago, October 2011
## Contents

### Part I Introduction/General

1. **Aspects of the History and Nomenclature of Amyloid and Amyloidosis** ................................................................. 3  
   Per Westermark

2. **Amyloid Diseases at the Molecular Level: General Overview and Focus on AL Amyloidosis** ................................. 9  
   Mario Nuvolone, Giovanni Palladini, and Giampaolo Merlini

3. **AA Amyloidosis** ............................................................................ 31  
   Amanda K. Ombrello and Ivona Aksentijevich

4. **The Hereditary Amyloidoses** ....................................................... 53  
   Merrill D. Benson

5. **Dialysis-Associated Amyloidosis** ................................................. 69  
   Paweeana Susantitaphong, Laura M. Dember, and Bertrand L. Jaber

6. **Localized Amyloidoses and Amyloidoses Associated with Aging Outside the Central Nervous System** ............. 81  
   Per Westermark

7. **Cerebrovascular Amyloidoses** ..................................................... 105  
   John M. Lee and María M. Picken

### Part II Non-Amyloid Protein Deposits

8. **Differential Diagnosis of Amyloid in Surgical Pathology: Organized Deposits and Other Materials in the Differential Diagnosis of Amyloidosis** ................................................................. 113  
   Guillermo A. Herrera and Elba A. Turbat-Herrera

9. **Light/Heavy Chain Deposition Disease as a Systemic Disorder** .............................................................................. 129  
   Guillermo A. Herrera and Elba A. Turbat-Herrera
Contents

10 Non-Randall Glomerulonephritis with Non-organized Monoclonal Ig Deposits ............................................................... 143
Pierre Ronco, Alexandre Karras, and Emmanuelle Plaisier

11 Pathologies of Renal and Systemic Intracellular Paraprotein Storage: Crystalopathies and Beyond .................. 155
Maria M. Picken

Part III Diagnosis

12 Diagnosis of Amyloid Using Congo Red .................................... 167
Alexander J. Howie

13 Diagnosis of Minimal Amyloid Deposits Using the Congo Red Fluorescence Method: A Review ......................... 175
Reinhold P. Linke

14 Thioflavin T Stain: An Easier and More Sensitive Method for Amyloid Detection ................................................... 187
Maria M. Picken and Guillermo A. Herrera

15 Fat Tissue Analysis in the Management of Patients with Systemic Amyloidosis .......................................................... 191
Johan Bijzet, Ingrid I. van Gameren, and Bouke P.C. Hazenberg

16 Generic Diagnosis of Amyloid: A Summary of Current Recommendations and the Editorial Comments on Chaps. 12–15 ........................................................................... 209
Maria M. Picken

17 Routine Use of Amyloid Typing on Formalin-Fixed Paraffin Sections from 626 Patients by Immunohistochemistry ........................................................... 219
Reinhold P. Linke

18 Amyloid Typing: Experience from a Large Referral Centre ................................................................................... 231
Janet A. Gilbertson, Toby Hunt, and Philip N. Hawkins

19 Options for Amyloid Typing in Renal Pathology: The Advantages of Frozen Section Immunofluorescence and a Summary of General Recommendations for Immunohistochemistry (Chaps. 17–19) ................................................... 239
Maria M. Picken

20 Amyloid Typing: Immunoelectron Microscopy ......................... 249
Laura Verga, Patrizia Morbini, Giovanni Palladini, Laura Obici, Vittorio Necchi, Marco Paulli, and Giampaolo Merlini

21 Classification of Amyloidosis by Mass Spectrometry-Based Proteomics ........................................................................ 261
Ahmet Dogan

Classifcation of Amyloidosis by Mass Spectrometry-Based Proteomics

Ahmet Dogan
Part IV Ancillary Studies of Amyloidosis

22 Laboratory Support for Diagnosis of Amyloidosis .......... 275
   David L. Murray and Jerry A. Katzmann

23 Bone Marrow Biopsy and Its Utility in the Diagnosis of AL Amyloidosis and Other Plasma Cell Dyscrasias .......... 283
   Sujata Ramamurthy, Lawreen H. Connors, and Carl J. O’Hara

24 Laboratory Methods for the Diagnosis of Hereditary Amyloidoses ................................................................. 291

Part V Organ Involvement in Amyloidoses

25 Amyloidoses of the Kidney and Genitourinary Tract .......... 305
   Maria M. Picken

26 Cardiac Amyloidosis .......................................................... 319
   Carmela D. Tan and E Rene Rodriguez

27 Amyloidosis of the Gastrointestinal Tract and Liver .......... 339
   Oscar W. Cummings and Merrill D. Benson

28 Peripheral Nerve Amyloidosis ........................................... 361
   Adam J. Loavenbruck, Janean K. Engelstad, and Christopher J. Klein

Part VI Clinical Issues and Therapy

29 Clinical and Pathologic Issues in Patients with Amyloidosis: Practical Comments Regarding Diagnosis, Therapy, and Solid Organ Transplantation ................................................................. 377
   Jay S. Dalal, Kevin Barton, and Maria M. Picken

30 Emerging Therapies for Amyloidosis ............................... 393
   Merrill D. Benson

31 Modern Therapies in AA Amyloidosis ................................ 399
   Amanda K. Ombrello

32 Medicolegal Issues of Amyloidosis ................................. 405
   Timothy Craig Allen

33 Amyloidosis from the Patient’s Perspective ...................... 413
   Muriel Finkel

Index .......................................................................................... 419
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