Amyloidosis is a term that represents a wide spectrum of protein folding disorders. The disease may be localized or systemic. The systemic amyloidoses can be either immunoglobulin light chain derived, related to the deposition of amyloid A protein in chronic inflammatory conditions, or an inherited disorder usually related to mutant transthyretin. Normal proteins are known to misfold into amyloid, the clinically most important being native transthyretin in the form of senile systemic amyloidosis. This text attempts to comprehensively provide a framework to clinicians seeing these patients and scientists studying the disorder, with an in-depth treatment of selected world’s literature, as well as newest developments in the disorder. Because amyloidosis is so rare, many practicing clinicians are uncomfortable in the diagnosis, management, classification, prognostication, and therapy of the amyloidoses. This book calls on the clinical and scientific expertise of the world’s noted experts in the protein folding disorders.

To understand the protein folding disorders, knowledge of fibril structure and fibrillogenesis is essential. Drs. Martin, Randles, and Ramirez-Alvarado cover the essentials in the identification of amyloid fibrils, recognition of the kinetics of fibril formation, the issues associated with thermodynamic instability, and the mechanism by which the beta-pleated sheet forms. Whether it is the fully formed fibril or soluble oligomers which are responsible for the complications of the disease is also dealt with.

Drs. Palladini, Merlini, and Perlini cover what is known about the in vivo imaging of amyloid fibrils. Unlike most hematologic disorders where sensitive imaging techniques exist to stage the extent of the disease, the identification and imaging of amyloid fibrils in vivo have been a challenge for four decades. The chapter covers radionuclide imaging with SAP, ultrasound, magnetic resonance imaging, and computerized tomography and its role in identifying amyloid deposits.

Drs. Grateau and Stankovic review the diagnosis and classification of amyloidosis, reviewing correct nomenclature and clues to an appropriate clinical diagnosis. A review of available clinical techniques to establish the diagnosis, the pitfalls of histochemical staining, and the classification of the amyloidosis is dealt with.

Drs. Lavatelli, Palladini, and Merlini review the pathogenesis of systemic amyloidosis, dealing with the cellular control mechanisms that regulate misfolding and the role of the non-fibrillar components of amyloid, including serum amyloid P, glycosaminoglycans, and the impact of molecular crowding.

Drs. Lacy and Leung review supportive care for patients with amyloidosis, dealing with the role of cardiotropic agents, anti-arrhythmics, implantable defibrillators, and cardiac transplant. Renal involvement is dealt with in depth, using medical strategies
to reduce proteinuria, the role of renal transplant for amyloidosis, and the management of common complications such as pleural effusions that are recurrent.

Dr. Dispenzieri discusses response assessment and prognosis in evaluating patients with immunoglobulin light chain amyloidosis, both in terms of the hematologic response and the role of the immunoglobulin free light chain, and defining organ response. The use of a clinically relevant staging system is presented.

Since cardiac failure is the most common cause of death in systemic amyloidosis, special treatment is given to amyloid heart disease by Drs. Falk and Dubrey with specifics on the treatment of cardiac amyloidosis. Transthyretin-inherited cardiac amyloidosis and transthyretin senile systemic amyloidosis are treated independently and in depth.

Drs. Bajwa and Kelly deal with the complex issues associated with amyloid neuropathy, clinical manifestations, differential diagnosis, and the role of the sural nerve biopsy.

Dr. Gertz discusses the conventional treatment of immunoglobulin light chain amyloidosis from the first use of melphalan and prednisone through the use of the newest novel agents and their role in suppressing the light chain production by the clonal plasma cells responsible for the morbidity of the disease.

Drs. Cohen and Comenzo deal with the increasingly important role of high-dose therapy with stem cell replacement in the management of amyloidosis, including the key issues of patient selection, risk-adapted therapy, and the role of post-transplant maintenance therapy.

Dr. Zeldenrust deals with transthyretin amyloidosis, covering the diagnosis, the prognosis, and the available therapies with in-depth treatise on the use of liver transplantation to manage this devastating disorder.

Dr. Benson draws on his in-depth experience with the rarest forms of amyloid, including apolipoprotein, lysozyme, and fibrinogen amyloidosis. Without awareness of these rare forms of amyloidosis, the diagnosis is frequently overlooked and the patient is not correctly managed.

It is our hope that by comprehensively covering all forms of amyloidosis, from pathogenesis to therapy, this book can serve as a long-lasting reference volume for practicing physicians and scientists directly involved in the care of patients with amyloidosis, ultimately benefitting the patient population by shortening the diagnostic evaluation and allowing appropriate timing of necessary therapies.

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