New Treatments in Noninfectious Uveitis
Contents

VI  List of Contributors
IX  Preface
    Miserocchi, E.; Modorati, G. (Milan); Foster, C.S. (Cambridge, Mass.)

1  The Philosophy of Treatment of Uveitis: Past, Present and Future
    Kruh, J.; Foster, C.S. (Cambridge, Mass.)

7  The Gold Standard of Noninfectious Uveitis: Corticosteroids
    LeHoang, P. (Paris)

29  Corticosteroid-Sparing Agents: Conventional Systemic Immunosuppressants
    Kruh, J.; Foster, C.S. (Cambridge, Mass.)

47  Corticosteroid-Sparing Agents: New Treatment Options
    Tomkins-Netzer, O.; Taylor, S.R.J.; Lightman, S. (Guildford/London)

57  Mycophenolate Mofetil Use in the Treatment of Noninfectious Uveitis
    Klisovic, D.D. (Dublin, Ohio)

63  Anti-Tumor Necrosis Factor-α Agents in Noninfectious Uveitis
    Gueudry, J. (Rouen); LeHoang, P.; Bodaghi, B. (Paris)

79  New Biologic Drugs: Anti-Interleukin Therapy
    Tappeiner, C.; Möller, B. (Bern); Hennig, M.; Heiligenhaus, A. (Münster/Essen)

90  Interferon-α Therapy in Noninfectious Uveitis
    Deuter, C. (Tübingen); Stübiger, N. (Berlin); Zierhut, M. (Tübingen)

98  Rituximab for Noninfectious Uveitis
    Miserocchi, E.; Modorati, G. (Milan)

110 Intravitreal Injection Therapy in the Treatment of Noninfectious Uveitis
    Modorati, G.; Miserocchi, E. (Milan)

122 Corticosteroid Intravitreal Implants
    de Smet, M.D. (Lausanne/Amsterdam)

134 New Treatment Options for Noninfectious Uveitis
    Gomes Bittencourt, M.; Sepah, Y.J.; Do, D.V.; Agbedia, O.; Akhtar, A.; Liu, H.; Akhlaq, A.;
    Annam, R.; Ibrahim, M.; Nguyen, Q.D. (Baltimore, Md.)

162 Subject Index
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Preface

Uveitis is a potentially blinding inflammatory disease that presents a therapeutic challenge for the general ophthalmologist and even for the uveitis specialist. The importance of this sight-threatening disease is translated into numbers, with important studies demonstrating that uveitis is the cause of 2.8–10% of all cases of blindness.

The primary goal of therapy in patients with uveitis should be controlling intraocular inflammation, reducing the risk of ocular complications and secondary visual loss. However, when we are faced with severe inflammatory ocular disease, we always have to balance the risk and benefit of preserving vision versus the occurrence of potentially severe treatment-related adverse events.

The dawn of the modern age for the treatment of uveitis came in 1950, with the employment of corticosteroids that have completely revolutionized the treatment of ocular inflammatory disease. But, with the increasing use of corticosteroids over time and the discovery of exciting results both for patients and physicians in treating uveitis, the long-term adverse events of corticosteroids become rapidly evident. It became clear that corticosteroids were potent and excellent drugs to control autoimmune uveitis, leading to rapid resolution of intraocular inflammation, but their safety profile and the secondary occurrence of systemic side effects render their use a double-edged sword.

Due to the high morbidity related to long-term treatment with corticosteroids, physicians were stimulated to find corticosteroid-sparing therapeutic agents, such as the chemotherapeutic agents.

Most of the systemic immunomodulatory drugs employed in ophthalmology have been adopted from other specialties, such as rheumatology and dermatology.

The new era of corticosteroid-sparing drugs created a ‘new therapeutic philosophy’ in the management of intraocular inflammation among uveitis specialists around the world. The first generation of immunosuppressive agents employed in uveitis were the alkylating agents in the early 1950s, followed by the antimetabolites methotrexate and azathioprine in the 1960s and cyclosporin A in the 1970s. Cyclosporin A has remained one of the only immunosuppressants prescribed on-label for ocular immune-mediated disorders.
Better understanding of the immune system and inflammatory pathways were further discovered between the 1980s and the 1990s. During this period, the interactions between specific cytokines and cell surface receptors led to the development of novel therapeutic approaches.

The great revolution in the treatment of uveitis came in the 1990s with the introduction of the so-called ‘new therapeutic agents’, known as a biologic response modifiers. These agents, created through modern bioengineering techniques, were designed to act as cell-specific immunosuppressants by the direct inhibition of cytokines or cell surface molecules. This would allow for more precise modulation of the immune system without having the effects of a systemic and global immune suppression.

During the last decade, an increasing number of new drugs have been introduced in the field of rheumatology for the treatment of autoimmune diseases, such as rheumatoid arthritis, and have been subsequently explored in the treatment of uveitis patients with exciting results.

The therapeutic armamentarium of the uveitis specialist has expanded enormously compared to previous generations. New randomized clinical trials are investigating the use of new treatment options for ocular inflammatory diseases.

The desire to avoid systemic side effects from corticosteroids and immunosuppressants has driven the continuing search for effective agents with an improved safety profile, but also the increasing use of local drug administration, which can avoid systemic side effects.

For this reason, the development of intraocular therapy has generated an increasing interest in the last decade as an alternative treatment to control ocular inflammatory diseases and inflammatory macular edema, which is the most important cause of visual loss in patients with uveitis.

Intraocular implants which release corticosteroids for a prolonged period within the vitreous cavity have been recently developed for treating ocular inflammation. The first implant designed was a nonerodible implant device that released fluocinolone acetonide, while the one most recently introduced on the market is the bioerodible polymer that releases dexamethasone. In clinical trials, both implants have been shown to be effective in reducing intraocular inflammation in patients with intermediate or posterior uveitis. Certain clinical situations, particularly with asymmetric uveitis or severe inflammatory macular edema, may in fact favor intravitreal treatment over systemic treatment. Short-term intravitreal therapy can be employed as well, with intravitreal corticosteroid or methotrexate injections.

Patients with uveitis and ocular inflammatory diseases are in desperate need of effective therapeutic agents which cannot only eliminate inflammation and prevent recurrences but also protect the patients from potential side effects. In addition, we believe that all currently available drugs should be approved by the regulatory bodies as soon as possible so that they can be of benefit to all patients.

Today, the horizon of uveitis treatment appears very bright compared to a decade ago given the many therapeutic agents and approaches for uveitis and ocular
inflammatory diseases. Different classes of new agents, delivery systems and novel methods of safe and effective administration of pharmacologic agents are under investigation. Hopefully, in the near future such efforts will lead to an increasing number of therapeutic options for our patients that will improve not only the vision but also the quality of life of these patients.

This book was designed to bring together the principles of therapy of patients with noninfectious uveitis and the most recent therapeutic options that can be offered to the patient. Its aim is to help educate residents, update general ophthalmologists and uveitis specialists on the latest innovative treatment options for patients who have noninfectious uveitis. After an outline of the treatment principles and the most conventional treatment options, the book covers a large number of topics on the newer available agents for intraocular inflammation.

The authors bring together their personal experience and full teaching acumen to each chapter, culminating in a single book that brings to the forefront the importance of the challenge in the treatment of uveitis. We hope that each chapter will stimulate the interest of readers working in this particular field of uveitis.

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