A.M. Joussen · T.W. Gardner · B. Kirchhof · S.J. Ryan (Eds.)
Retinal Vascular Disease

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Foreword

Angiogenesis inhibitors comprise a new class of drugs that have recently received FDA approval for use in age-related macular degeneration. They are currently in clinical trials for the treatment of diabetic retinopathy. These new drugs emerged after more than three decades of cancer research. This journey was driven by the hypothesis that tumor growth is angiogenesis dependent, and sustained by experimental demonstrations that antiangiogenic therapy could become a fourth modality to help control neoplastic disease.

At the dawning of this new field of angiogenesis research, animal models of corneal neovascularization became the test tube for discovery of angiogenesis regulatory molecules. It seems more than a coincidence that the two implantable polymers still employed by scientists today for slow release of angiogenesis regulatory molecules into the avascular cornea as a bioassay, originated from soft contact lenses or from a wearable device to treat glaucoma. In this sense, two distinct specialties of medicine, oncology and ophthalmology, are now linked. Angiogenesis has become the organizing principle.

Over the years, numerous ophthalmologists have studied in a cancer biology lab and have gone on to distinguished careers in ophthalmology. Without their contributions it is unlikely that an oncologist's armamentarium would today contain approved anti-cancer drugs that inhibit angiogenesis directly or indirectly.

It is as exciting that these new drugs have begun to increase survival for the three common cancers, colon, breast and lung, as it is that eyesight has been improved in patients with age-related macular degeneration ("A very effective treatment for neovascular macular degeneration," E.M. Stone, *N Engl J Med* 2006 355:1493).

The editors and authors of this book have brought the field of retinal vascular disease up to date, as the principles of antiangiogenic therapy are rapidly being translated to clinical practice. This book is also very valuable because it inspires the reader to think about possible future improvements in the management of retinal vascular diseases. Can biomarkers in the blood or urine be developed to detect recurrence of retinal neovascularization before symptoms or before detection by ophthalmoscopy? Can oral angiogenesis inhibitors maintain suppression of neovascular macular degeneration after sight has been improved by repeated intravitreal injections of antiangiogenic drugs? Because platelets are now known to carry high concentrations of angiogenesis regulatory molecules stored and segregated in alpha granules, will it become possible to therapeutically instruct platelets to release antiangiogenic proteins? Beyond these questions it is possible to anticipate that angiogenesis research will continue to bring new insights into the biology and molecular mechanisms of retinal vascular disease.

Judah Folkman, MD

Preface

Great progress has been made in the treatment of vascular disease in recent years, and we hope and expect this is a prelude to even greater progress in the near future. The advent of clinically applicable anti-VEGF therapies is only the "tip of the iceberg" of future additions to the clinical armamentarium. However, there is no unique formula for angiogenesis. Our understanding of complex disease specific interactions is dependent on a knowledge of the basic mechanisms involved in the vascular reactions specific to different disease entities. Despite these new treatments and the explosion of knowledge on the basic mechanisms of vascular biology, vascular disease of the retina remains to date a major cause of blindness in all age groups.

The topics covered by this book range from fundamental concepts of molecular biology to basic clinical appearance, specific pathology and treatment of retinal vascular disease.

In the first part, the current thinking in vascular biology is discussed in relation to retinal vascular disease. The emphasis is on general pathogenic concepts including ischemia, inflammation and their associated pathology. Experimental approaches are reviewed as well as animal models which might help in the investigation of the diseases.

The second part includes modern diagnostic features and general treatment strategies. Diagnostic procedures are discussed with respect to their relevance for clinical decision making. Similarly, treatment procedures are described stepwise by schematic graphics.

The third part describes each disease in a comprehensive manner including demographics, clinical course and treatment. Clinical image series including illustrated single case follow-ups are given major emphasis and provide an atlas like presentation. The book includes topics which are not currently found in other textbooks of retinal disease including case reports and clinical follow-ups. Furthermore, all the treatment procedures are explained in detail to facilitate their use by ophthalmologists in training.

More than 50 experts in the field contributed to this state of the art review of basic and clinical science, which aims to enhance our understanding of retinal vascular disease and to help the clinician in the evaluation of current and future treatment approaches. The authors are internationally recognized leaders in clinical ophthalmology, including the areas of medical retina, vitreoretinal surgery, and uveitis. In a unique way leaders and experts in their fields of molecular mechanisms and general concepts of vascular surgery have contributed to this book even though their previous major focus has not necessarily been on ophthalmic disease.

Nevertheless, the field of vascular biology and retinal vascular disease is so broad and the evolution of knowledge so rapid that the work cannot be comprehensive and the information given only resembles the current knowledge at the time of printing.

As a multiauthored text, there are many literary styles, and the editors have not sacrificed the originality and the style of the individual authors. Although

there will be some aspects that are discussed in more than one chapter, the unique interpretation by each author justifies some overlap and is an attractive feature.

The editors gratefully acknowledge the support of the contributing authors who, in addition to their large clinical load and scientific research efforts, found the time to make such a large contribution to the completion of this project. In particular, Andrew P. Schachat, MD, and his team at The Wilmer Eye Institute were of invaluable help.

At Springer, Marion Philipp and Martina Himberger helped to create this book and its unique combination of basic science and clinical application.

We hope that *Retinal Vascular Disease* will help to inspire clinicians and scientists in the future to making further efforts and advances in this field.

Düsseldorf, Hershey, Cologne, Los Angeles

August 2007

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