THYROID EYE DISEASE

ENDOCRINE UPDATES

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PREFACE

Patients afflicted with thyroid eye disease or Graves' ophthamopathy (GO) may experience not only pain and visual loss, but also disfigurement. Full understanding of pathogenesis has been elusive, and treatment modalities are imperfect. As with other conditions, more effective intervention will follow only after a better understanding of pathogenesis is reached. The goal of this volume is to give an overview by leaders in the field of the present state of the art both in pathogenesis and clinical aspects of GO.

Much attention has been directed towards determining which cells within the orbit are targets of the autoimmune process, and how these and other cells might participate in the local inflammatory process. It is now generally agreed that orbital fibroblasts, preadipocyte fibroblasts, and adipocytes are the targeted and activated cells in GO and that full-length TSH receptor (TSHr) is expressed in these cells. Further, there is growing consensus that this receptor is up-regulated in the orbit in GO, residing primarily in newly differentiated adipocytes. However, it is also evident, given a sufficiently sensitive assay, that TSHr is detectable in fibroblasts and adipocytes from the normal orbit and other anatomic sites, as well. It will be important to determine whether the observed increase in orbital TSHr expression itself initiates the orbital autoimmune process. Also to be decided is whether orbital lymphocytes from GO patients specifically recognize this receptor, and what factor or factors unique to Graves' disease might stimulate TSHr expression in orbital cells.

Renewed interest has been focused on the concept that patients with Graves' disease may have a generalized autoimmune disease of the connective tissues, with only some patients demonstrating clinically relevant eye and pretibial skin involvement. Severe disease at these sites may reflect mechanical features, including trauma, as well as phenotypic characteristics of regional fibroblasts. It follows that patients with GO may not differ genetically from patients with Graves' hyperthyroidism not having clinically apparent eye disease. This concept highlights the importance of environmental factors in the evolution of this condition. It is likely that the development of animal models of Graves' hyperthyroidism and GO will bring insight into the role of TSHr in disease initiation and into the relative importance of environmental factors in disease expression.

Progress has also been made in diagnosis and treatment. In the past, many studies of potential treatments for GO have suffered from lack of reliable means to assess disease activity and response to treatment. Non-quantitative endpoints and activity scores that obscured, rather than highlighted, important clinical features were frequently used. Exciting new developments include the design of clinically relevant instruments to measure the quality of life in GO patients. Useful means to assess and document disease activity have been validated. In addition, emphasis has been placed on imaging, both for diagnostic precision and for quantitative assessment of therapeutic interventions. It has become apparent that there are clinical subgroups of patients with GO and that treatment must be tailored to the individual patient. Concomitantly, there has been a re-evaluation of the standard treatments for GO, including surgical approaches and orbital radiotherapy, and novel immunotherapies have been proposed.

Many challenges face scientists and clinicians interested in GO and devoted to finding ways to help patients with the condition. This volume was designed to highlight the significant progress being made by many groups of investigators worldwide. The information gained from ongoing laboratory and clinical investigations will lead to new pathophysiology-based treatments and preventive measures that may be equally applicable to other autoimmune diseases. I wish to thank all of my colleagues for their exciting contributions to this volume and for the friendships that have developed through our common interest in this disease.

Rebecca S. Bahn