

Preface

Celiac disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten-containing grains (including wheat, rye and barley) in genetically susceptible individuals. Epidemiological studies conducted during the past decade revealed that CD is one of the most common lifelong disorders worldwide. CD can manifest itself with a previously unappreciated range of clinical presentations, including the typical malabsorption syndrome and a spectrum of symptoms potentially affecting any organ system. Since CD often presents in an atypical or even silent manner, many cases remain undiagnosed and carry the risk of long-term complications, including anemia, osteoporosis, infertility or cancer. The high prevalence of the disease and its variety of clinical outcomes raise several interesting questions. Why is a disease that, if not treated, is associated with a high rate of morbidity and increased mortality yet not segregated by genetic evolution, and why does it remain one of the most frequent genetically based disorders of humankind? One possible explanation is that gluten, a protein introduced in large quantities in the human diet only after the advent of agriculture, activates 'by mistake of evolution' mechanisms of innate and adaptive immunity that are too important for human survival to be eliminated.

Another unresolved issue concerns the variable(s) that dictates the length of clinical latency and the type of symptoms experienced by CD patients when the disease becomes clinically apparent. In recent years, there have been noticeable shifts in the age of onset of symptoms and in the clinical presentation of CD, changes that seem to be associated with a delayed introduction of gluten coupled with its reduced amount in the diet. Another controversial topic concerns the complications of untreated CD. Multiple studies that have focused on the biochemistry and toxicity of gluten-containing grains and the immune response to these grains suggest that individuals affected by CD should be treated, irrespective of the presence or absence of symptoms and/or associated conditions. However, well-designed prospective clinical studies to address this point have not been performed, nor can they be conceived, given the ethical implications of such studies. Nevertheless, there is general agreement that the persistence of mucosal injury, with or without typical symptoms, can lead to severe complications in CD patients who do not strictly comply with a gluten-free diet. Another controversial issue is related to screening policies in terms of who should be screened for CD. The prevalence of the disease and the burden of

illness related to this condition, particularly if not treated, are so high as to possibly support a policy of general population screening. However, cost-effective analyses and 'return on investment' for patients, healthcare providers and policy makers keep the debate open.

This book covers most of the aforementioned controversial and yet unresolved topics by capitalizing on the contribution of opinion leaders expert in CD and of its multidisciplinary ramifications. What the reader will surely find stimulating about this book is not only its exhaustive coverage of our current knowledge of CD, but also of provocative new concepts in disease pathogenesis, treatment and prevention that can be extrapolated to other immune-mediated pathologies. Indeed, given the undisputable role of gluten in causing inflammation and immune-mediated tissue damage, CD represents a unique model of autoimmunity in which, in contrast to most other autoimmune diseases, a close genetic association with HLA genes (DQ2 and/or DQ8), a highly specific humoral autoimmune response (autoantibodies to tissue transglutaminase) and,

most importantly, the triggering environmental factor (gluten) are known. This information provides the rationale for the treatment of the disease based on complete avoidance of gluten-containing grains from the patients' diet. Therefore, CD represents the only autoimmune disorder for which a treatment is available, since the trigger(s) involved in the pathogenesis of other autoimmune diseases remain elusive at best. This also implies that CD could represent the best model to study autoimmune pathogenesis and, eventually, to develop novel therapeutic strategies for the treatment of conditions still orphan of any possible solution.

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