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Coeliac disease: changing views

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A continuing flow of new scientific developments concerning coeliac disease in the last decade asks for the formulation of new concepts of pathophysiology and clinical considerations. Immunogenetic studies have shown a correlation of the disease to the HLA region on the short arm of chromosome 6, immunological research has led to the concept of a T-cell driven immunologic response of the small intestine, with the identification of highly sensitive and specific antibodies. The understanding of the histopathology of coeliac disease has changed dramatically, initiated by the proposition of a spectrum of gluten sensitive enteropathy by Marsh in 1992. Clinical studies report a significant change in patient characteristics and epidemiology. The incidence of the disease has shifted to a majority of adult coeliacs, the disease may present with less severe symptoms of malabsorption and the screening studies suggest an overall prevalence of up to 1 in 200–300.

Histopathology has been standardized; lymphocytic enteritis (Marsh I), lymphocytic enteritis with crypthyperplasia (Marsh II), and villous atrophy, subdivided in partial, subtotal and total (Marsh IIIABC). Special attention is given to a subgroup of 'refractory coeliacs', including the identification of pre-malignant T-cells in the intestinal mucosa. The management of coeliacs primarely consists of monitoring for compliance and complications. Dietetic and medical associations need to establish protocols and offer additional training to undergraduetes, internships, general practitioners and other allied health professionals.

It might be relevant to have a low threshold for intestinal biopsies. However, screening asymptomatics may be harmful for individuals. Research is needed to assess the benefits of mass-screening in the future. HLA analysis can contribute towards recognising populations at increased risk.

Keywords: coeliac disease; serology; marsh-classification; screening; refractory coeliac disease; HLA-typing; pathology; quality of life; gluten-free products.

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DIAGNOSTIC CRITERIA (1969–2001)

Until the 1950s, the diagnosis of coeliac was made when a child or adult had malabsorption in the absence of infection. When techniques for peroral small bowel biopsy were introduced during the 1960s, patients with malabsorption were found to have either a normal or a grossly abnormal jejunal biopsy. It is now more than 35 years since the diagnostic criteria for coeliac disease (CD) were proposed at the Interlaken Meeting of the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) in 1969.[1]

These criteria were further enunciated at the Second International Symposium of Coeliac Disease in 1974, and are as follows (A) structurally abnormal jejunal mucosa when taking a diet containing gluten; (B) clear improvement of villous structure when taking a gluten-free diet (GFD); (C) deterioration of the mucosa during gluten challenge.[2]

The 'Interlaken criteria' were reviewed by ESPGAN in 1990.[3] Challenge was no longer required except for children under 2 years of age, where it still is. Criteria for the diagnosis of CD in adults have been defined in anticipation of the 2001 United European Gastroenterology Week (UEGW) in Amsterdam.[4] It was concluded that CD does not require further confirmation if is based on duodenal histology showing villous atrophy (VA), crypt hyperplasia and intraepithelial lymphocytosis while using a gluten-containing diet, which normalizes on a GFD. It was stated that pathologists and clinicians become familiar with the pitfalls in diagnosis. Findings of circulating antibodies such as against endomysium and/or tTG before a GFD support the diagnosis, but are not essential. HLA-DQ_2 or HLA-DQ_8 are still considered circumstantial evidence. Gluten challenge might be useful for minor histological abnormalities, such as intraepithelial lymphyocytosis.[5,6]

Traditionally, the coeliac condition was known as a disease of childhood, managed by paediatricians and characterised by severe malabsorption due to VA, with a clear response to GFD. In the 1990s intensified scientific interest led to impressive steps forward in the understanding of the disease. Through in vitro studies, Marsh demonstrated a spectrum of consecutive stages of mucosal abnormalities that can be seen in gluten sensitivity, which was in contrast to the on/off phenomenon of total VA that was previously believed to be present in the 'allergic' reaction of the intestinal mucosa to gluten.[7] Immunological studies demonstrated that in active coeliac disease antibodies to endomysium and tissue transglutaminase can be detected, which opened the way for new diagnostic strategies and population screening.[8] Immunogenetic research located coeliac related patterns on the immunology-related HLA region on the short arm of chromosome 6, giving way to the formation of new concepts of the etiology of the inflammatory response that is seen in coeliac disease.[9] Clinical studies, including population screening with antibodies, suggested that CD can present with milder symptoms than severe malabsorption, and that case-finding was disappointing in medical practice. Catassi even proposed the analogy of 'a coeliac iceberg', when in screening studies in a population of Italian school children he found an incidence of coeliac disease of up to 1 in 200, implicating a prevalence more than 10-fold higher than previously found.[10] This 'iceberg' of coeliac disease has been confirmed by many studies.

THE COELIAC SPECTRUM ACCORDING TO MARSH

The spectrum of gluten sensitive enteropathy as Marsh described, consists of consecutive stages of progressive abnormalities of the small intestinal mucosa,