Early Feeding Practices and Their Impact on Development of Celiac Disease

Alessio Fasano and Carlo Catassi

Celiac disease (CD) is an immune-mediated enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. Gluten is a protein component in wheat and other cereals like rye and barley that are generally introduced in the infant’s diet at weaning [1]. At present, there is an active and far from being settled debate on early feeding practices and their impact on the onset of CD. While epidemiological studies strongly support the notion that early exposure (before 4 months of life) to gluten increases the risk of CD development [2], no conclusive data are available on the impact of delaying gluten introduction on the onset of CD. The two main schools of thought on this topic claim that delaying gluten introduction in at-risk infants can either prevent the onset of the disease or merely delay its onset. The uncertainty on which of the two theories is correct is based on the fact that no prospective, well-designed studies to address this issue have been performed so far. However, recent advances have increased our understanding of the molecular basis of this disorder and provide the rationale to perform prospective studies to establish the proper timing of gluten exposure to minimize the risk of developing CD.

In a prospective, observational study conducted in Denver, Colo., USA, on 1,560 children at increased risk for CD, it was determined that children exposed to gluten-containing cereals in the first 3 months of life had a 5-fold increased risk of celiac serum autoimmunity compared with children exposed to gluten-containing foods at 4–6 months [2]. Interestingly, the investigators reported a marginally increased risk of celiac serum autoimmunity in infants in whom gluten was introduced after 7 months of age compared with those exposed at 4–6 months. Based on these results, authors suggested that a favorable ‘window of exposure’ to gluten exists between 4 and 6 months [3]. This ‘tolerance window’ hypothesis has not found confirmation
in a similar prospective study performed on 1,511 genetically at-risk German infants [4]. To attempt clarifying these discrepancies, at least two prospective, nutrition intervention studies have been recently initiated. The family study of PREVENTCD is currently performed in 10 European countries and a total of 1,000 children will be involved. The project will study the influence of the dietary history in the prevention of CD. The general concept is that small amounts of food substances are administered gradually to ‘teach’ the immune system not to respond to this foodstuff (oral tolerance). The Italian baby study is another initiative aimed at evaluating the role of age at gluten introduction on CD-related autoimmune serological changes in a large cohort of at-risk infants. Since October 2004, 722 infants at increased risk for CD have been enrolled in this prospective, multicenter intervention study. At weaning, infants were blindly assigned to a diet in which gluten was introduced either between the 4th and 6th month or after the 12th month, then entered a follow-up period of 5 years (fig. 1). At the 3-year follow-up, the proportion of infants developing biopsy-proven CD was 4-fold higher among those weaned with gluten at 6 (8%) than at 12 months of age (2%). Despite these promising results, long follow-ups are necessary to clarify whether the delayed gluten introduction

**Fig. 1.** Study design of the Italian baby study. GFD = Gluten-free diet; TTG = IgA anti-transglutaminase antibody; AGA = IgG antigliadin antibodies.
effectively protects from CD development or merely delays the onset of the disease and to establish the role of other environmental factors, including the gut microbiota, in triggering loss of tolerance to gluten in genetically predisposed infants.

References