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The prevention of coeliac disease



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A B S T R A C T

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Primary prevention of coeliac disease is currently not possible. Previously, a 'window of opportunity' was suggested for primary prevention, by introducing gluten between four and six months of age. However, results from recent prospective studies establish that the timing of gluten introduction and the duration or maintenance of breastfeeding do not influence the development of the disease. Secondary prevention is possible through early diagnosis and treatment. Since coeliac disease is severely underdiagnosed, the only way to achieve large-scale secondary prevention is by mass screening. Prospective studies indicate that important health problems, such as reduced foetal growth and birth weight, delayed growth in height and weight in children, and reduced bone mineral density in both children and adults can be prevented by mass screening. Adherence to a strict gluten-free diet may be considered as tertiary prevention.

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Coeliac disease (CD) is a common but frequently unrecognized disease, partially because of its variable clinical presentation and symptoms that range from malabsorption with chronic diarrhoea, poor growth in children, abdominal distension and weight loss, to nonspecific signs and symptoms like fatigue, osteoporosis or iron deficiency anaemia [1]. Extra-intestinal symptoms such as arthritis or neurologic manifestations are also frequent [2,3]. In addition, CD may be asymptomatic as in the case of 43% of the children identified by family screening [4]. For every child diagnosed with CD there are

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seven who have unrecognised, and therefore, untreated disease [5–7]. Screening studies have shown that CD has a frequency of 1%–3% among Europeans, corresponding to about five million people in the European Community. These studies further suggest that CD is the most common food intolerance in Europe and the USA [3,5,6,8,9]. CD increases the overall mortality risk [10], reduces the quality of life [11] and yields extensive negative economic consequences [12]. According to an estimate by the Dutch Celiac Disease Society (www.glutenvrij.nl) the necessary gluten-free diet results in an added cost of €1200–1300 per patient a year, corresponding to €6.0–6.6 billion in financial burden to Europe if all five million cases of CD were considered (www.CDEUSA.com). The patient's health status improves with a gluten-free diet, but primary prevention would even be more beneficial [13]. For these reasons, CD may be considered a public health problem [3,14]. Prevention is defined as any activity that reduces the burden of mortality or morbidity from disease, taking place at the primary, secondary or tertiary level [15]. Primary prevention avoids the development of a disease. Secondary prevention is aimed at early disease detection, thereby increasing opportunities for interventions to halt disease progression and the emergence of symptoms. Tertiary prevention focuses on reducing the negative impact of an already existing disease by restoring function and reducing disease-related complications.

Primary prevention

Primary prevention in CD implies that gluten tolerance is acquired, since CD patients do not develop it or lose it later on in life [16]. This hypo-responsiveness to dietary protein antigens in the intestine is a phenomenon termed 'oral tolerance' [17]. Animal experimental models have suggested possibilities for induction of gluten tolerance: intravenous or intranasal administration of multiple doses of gliadin to mice allowed down-regulation of the specific immune response [18]. Breastfeeding protected young inbred AVN strain rats from CD-like lesions [19]. Currently, however, primary prevention of CD is not possible. Previous retrospective studies suggested a 'window of opportunity' for primary prevention by introducing gluten between four and six months of age [20,21] during which breast feeding provided a protective effect [22]. Based on these results, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommends that gluten should not be introduced before 17 weeks of age and not later than at 26 weeks, preferably concurrent with the period of breastfeeding [23].

Breastfeeding is an environmental factor that has been associated with the induction of oral tolerance [24]. Many studies have evaluated the role of breastfeeding and the risk of developing CD. A systemic review and meta-analysis which included all the studies published on this topic between 1966 and 2004 found that breast fed children had a 52% risk reduction of being affected by CD compared to those who were not breast fed during the time of gluten introduction [pooled OR 0.48; 95% CI: 0.40–0.59] [22]. Some studies on this topic reported CD prevention [22,25–27] while others did not [28,29]. A systematic review published by the PreventCD group (www.preventcd.com) showed that the principal difficulties in interpreting and comparing studies investigating the effect of early nutrition in the development of CD arise from the inability to randomise and blind such studies, their retrospective nature and its associated parental recall bias [30]. The best method to investigate the effect of environmental factors in the development of CD, nutritional or otherwise, is to perform prospective, randomised, placebo-controlled interventions among young children with long-term follow up. However, results from the recent prospective studies PreventCD, CELIPREV, MoBa, Generation R and TEDDY, establish that the timing of gluten introduction and the duration or maintenance of breast-feeding do not influence the development of CD [4,29,31–33].

PreventCD (Prevent Coeliac Disease) is an international, prospective, randomised, placebo-controlled interventions study among 994 infants with the HLA-DQ2 and/or -DQ8 alleles and a first degree family member with CD [4]. From 2007 to 2010, infants were randomised to a double-blind dietary intervention with either 100 mg of gluten daily or a placebo. The intervention took place when the children were between four and six months of age. The children were screened regularly for CD. Breastfeeding for at least six months was encouraged. Gluten intake was quantified and the breast feeding analysed. The results showed that the development of childhood CD is not

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