Introduction of Gluten to Infants

A recent research article published in JAMA Pediatrics[1] provides more information about the timing of introduction to gluten in babies first foods and the risk of developing celiac disease.

This study wanted to know if the risk of allergy to six common food allergens (peanut, sesame, egg, cow's milk, fish and wheat) could be reduced for babies by earlier introduction than the standard timing of six months of age. The study was also able to look at the number of children who developed celiac disease, depending on whether they were in the early introduction or standard introduction groups. Over 1000 babies were included and assigned by chance to the early introduction group at 4 months or to the standard group at 6 months. All the babies were breast fed for the first six months. After the study finished, it was determined that the early introduction group actually ate more gluten per week than the standard group up until 9 months of age. At 3 years of age there were no children diagnosed with celiac disease in early introduction group, while there were 7 in the standard group.

This very interesting study suggests that early introduction of gluten at 4 months of age **may** result in a decreased risk of developing celiac disease. However, this study was not perfectly designed to answer the question about risk of celiac disease because it was more interested in all six foods and allergy. It is not known if the introduction of all these foods early together influenced the findings in unexpected ways. Also, as we will discuss, there are better designed studies to address this issue for babies at a high genetic risk of celiac disease. Altogether, the number of celiac disease cases diagnosed was very low (only 7) and the follow up time was quite short, so we don't know if we followed the children for longer, whether similar numbers of celiac disease cases would be diagnosed in both groups. Also, the study does not tell us the amount of gluten babies need to be introduced to with their first foods in order to prevent an increased risk of celiac disease. This is simply not known even from other studies.

A number of other studies have attempted to address the issue of timing of introduction of first foods and risk for celiac disease. These studies all differ according to the age at which gluten was introduced, the amount of gluten given and the length of follow-up[2]. Some of the most compelling studies only included babies at genetic risk or with a family history of celiac disease[3-5] and, like the study we discussed above[1], used a group randomization approach[3,4]. Altogether, the results of these studies demonstrate that early introduction of gluten at 4-6 months **does not increase the risk of celiac disease later in life**, appears to be safe and may well actually decrease the risk of developing celiac disease.

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Study Name, Journal, yr published	Who participated in the study	What did the study do?	Study question	What did the study find?
Review, *J Pediatr* 2016[2]	Review of 15 eligible studies published up to 2014 (i.e. studies below not included)	• Review of randomized controlled trials and observational studies looking at the proper timing for gluten introduction into the infant diet, amount of gluten intake at BF weaning, effect of BF on risk of CD.	What is the evidence about the effect of time of gluten introduction and BF on the risk on developing CD?	• No evidence at the time (up to 2014) to support that early gluten introduction to the infant diet increases CD risk. • 25% increased CD risk with late (> 6 months) vs recommended (4-6 months) gluten introduction.
PreventCD, *NEJM,* 2014[3]	944 newborns at high risk of CD (ie. HLA genotype & at least 1 relative with CD)	• The infants were divided into 2 groups. • One group received a small amount of gluten (100 mg vital gluten) daily at 4-6 months, and the other did not receive early gluten. • After 6 months the gluten intake was liberalized.	How many children had CD at 3 years of age?	• 5.2% of patients developed CD by 3 years of age • No significant difference in CD between early, small amounts of gluten introduction versus placebo. • BF, exclusive or ongoing, did not influence the development of CD.
CELIPREV, *NEJM,* 2014[4]	832 newborns with a 1st degree relative with CD & HLA genotype	• The infants were randomly assigned to introduce dietary gluten at age 6 months or 12 months of age.	How many children had CD at 5 years of age?	• Delayed development of CD by 2 years of age in those introduced gluten at 12 months. • But no difference in development of CD between the 2 groups at 5 years of age.
TEDDY, *JAMA,* 2019[5]	6605 children with HLA genotypes associated with type 1 diabetes & CD	• Gluten intake was estimated from 3-day food records collected at various times until 5 years of age. • TTG measured annually from 2 years of age, followed until 5 years.	How many children had CD at 5 years of age?	• 7% of children developed CD. • Higher gluten intake in the first 5 years of life was associated with increased risk of CD when measured at 5 years of age.

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EAT, *JAMA*, 2020[1]	1004 children from the general population (ie. not only children at high risk of CD)	• Infants randomized into 2 groups: early introduction group (EIG) at 4 months or standard (SIG) at 6 months. • Infants were introduced 6 allergenic foods (cow's milk, hen's eggs, peanut, sesame, cod fish and wheat), not *only* gluten. • The amount of gluten introduced at 4 months was much higher than the PreventCD study. • TTG was measured once at 3 years of age.	How many children had CD at 3 years of age?	• 1.4% of children in the standard introduction group developed CD, while none in the EIG • Introducing high amounts of gluten (along with other allergic foods) at 4 months of age reduced celiac prevalence when measured at 3 years of age.

CD = celiac disease; BF = breast feeding

Bottom Line

It is encouraging to see another prospective study on the effect of gluten introduction on the development of celiac disease. Further studies are still needed to determine the optimal time to introduce gluten as well as the optimal amount of gluten that should be provided to minimize the risk of developing celiac disease. For now, we continue to recommend that breast feeding be encouraged, and gluten be introduced into the diet in small amounts when solids are being introduced.

References

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