thebmj

*BMJ* 2018;362:k3867 doi: 10.1136/bmj.k3867



EDITORIALS

# Dietary gluten and type 1 diabetes

## A potential association that deserves closer scrutiny

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Until recently, incidence of type 1 diabetes has been increasing in the western world, pointing towards environmental triggers in the disease process. Despite decades of intensive research, we still cannot identify the factors responsible for the increase, and therefore have no means to prevent new cases. At the moment, special interest lies in the maternal and childhood dietary factors. Large scale prospective studies with carefully collected data are needed to define and confirm associations so that effective interventions can finally be planned and implemented.

In a linked article (doi:10.1136/bmj.k3547),[1] Antvorskov and colleagues investigated the association between maternal gluten intake during pregnancy and risk of type 1 diabetes in offspring. The authors analysed data from the large Danish National Birth Cohort, covering about a third of all pregnancies in Denmark during the recruitment period of 1996-2002. More than 70 000 pregnant women reported their diet with a food frequency questionnaire during the second trimester of pregnancy, of whom 63 529 women (67 565 pregnancies) were finally included in analyses. Through registry linkage, the authors identified 247 cases of type 1 diabetes among the participants' children, and found that the child's risk of type 1 diabetes increased proportionally with the mother's gluten intake during pregnancy.

Gluten is a storage protein found in wheat, rye, and barley. In animal models of type 1 diabetes, a gluten free diet during pregnancy has been shown to markedly reduce the incidence of the disease in offspring.[2] However, previous studies in pregnant women have found no such associations.[3 4] Studies of gluten intake in children have reported inconsistent findings. These studies generally consider the timing of introduction of gluten into the diet, and do not report the amount of gluten consumed.[5-9] Physiological mechanisms that could explain an association between gluten and type 1 diabetes are unknown in humans, but studies done in animal models of the disease suggest that gluten could affect gut permeability (so-called leakiness of the gut), affect gut microbiota, and cause low grade inflammation.[10-12]

Three points are worth considering when evaluating the results of Antvorskov and colleagues' study. Firstly, is high intake of gluten associated with an unhealthy diet or other dietary characteristics that could possibly predispose individuals to type 1 diabetes? Gluten containing grains are ingested through breads, pastas, pastries, and breakfast cereals, possibly indicating the intake of refined grains and a diet of poor nutritional quality. High gluten intake might also indicate a high energy diet, although in the linked study, statistical adjustment for total energy intake made no difference to the results. Characterisation of the dietary patterns associated with a high gluten intake could provide useful information for future studies.

Secondly, gluten comes from certain grains, so could there be something else in these grains responsible for the association? For example, cereal products that are baked at high temperatures contain advanced glycation end products that have been suggested as a risk factor for type 1 diabetes.[13 14] Grains also contain several other components generally considered harmful to health but that have not yet been studied in relation to type 1 diabetes, such as mycotoxins, heavy metals, and remnants of pesticides and fertilisers.[15 16]

Thirdly, mothers with high gluten intake might provide a high gluten diet to their children, and importantly, gluten proteins (gliadin) are passed from the mother to the infant through breast milk.[17] So infants could be exposed to gluten immediately after birth through lactation. Therefore, Antvorskov and colleagues' study cannot determine whether the possible adverse effects of gluten that might eventually trigger type 1 diabetes come through prenatal exposure, childhood exposure, or both.

This is the first study to suggest a clear dose-dependent association between maternal gluten intake and risk of type 1 diabetes. If confirmed, the findings could help resolve inconsistencies in the existing literature. Nevertheless, human studies investigating the physiological effects of high gluten intake in relation to the developing immune system are needed to identify whether the proposed association really is driven by gluten, or by something else in the grains or the diet.

Given that a causal association between maternal gluten intake and type 1 diabetes in children has not yet been established, it is too early to change dietary recommendations on gluten intake in pregnancy. However, doctors, researchers, and the public should be aware of the possibility that consuming large amounts of gluten might be harmful, and that further studies are needed to confirm or rule out these findings, and to explore possible underlying mechanisms.

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Competing interests: We have read and understood the BMJ policy on declaration of interests and declare the following: none.

Provenance and peer review: Commissioned, not peer reviewed.

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