GLOSSARY

CONGENITAL
HYPOGONADOTROPIC
HYPOGONADISM

A genetic disorder resulting from abnormalities in secretion of pituitary hormones including follicle-stimulating hormone, luteinizing hormone and gonadotropin

POLYMORPHISM

A naturally occurring, common variation in a DNA sequence that is part of normal genetic variation; most polymorphisms do not alter gene function

TRANSITION

A common DNA mutation involving the replacement of a purine base with another purine or a pyrimidine base with another pyrimidine

type of beverage consumption was not found to influence these associations.

The authors conclude that moderate alcohol consumption decreases the risk of type 2 diabetes in older, postmenopausal women, which is in line with results from previous investigations. The authors note that this might be the result of increased insulin sensitivity with a moderate intake of alcohol.

Marie Lofthouse

Original article Beulens JWJ *et al.* (2005) Alcohol consumption and risk of type 2 diabetes among older women. *Diabetes Care* 28: 2933–2938

Environmental factors can trigger development of beta-cell autoantibodies during a child's first year

The incidence of childhood-onset type 1 diabetes is increasing globally and is particularly high in Sweden. Environmental factors are known to be associated with the development of beta-cell autoantibodies, seropositivity for which precedes the onset of type 1 diabetes in genetically susceptible individuals. A new, population-based study has confirmed that these same factors can trigger beta-cell autoimmunity during the first year of life.

Seropositivity for beta-cell autoantibodies above the 99th percentile reliably distinguishes individuals at risk of type 1 diabetes from those not at risk. Wahlberg *et al.* hypothesized, therefore, that seropositivity above the 90th percentile in 1-year-old Swedish children might reveal exposure to the environmental triggers of beta-cell autoimmunity, before a fully matured destructive immune response to beta cells had developed. They found that male sex, birth in spring, low education level of the mother, gastroenteritis during the mother's pregnancy and a family history of celiac disease were associated with beta-cell autoantibody seropositivity above the 90th percentile. In addition, exposure to cow's milk by the age of 2 months, and having a relative with type 1 or 2 diabetes were associated with beta-cell autoantibody seropositivity above the 99th percentile.

Interestingly, only weak associations were seen between the development of different types of beta-cell autoantibodies in the same individual, hinting that the different types might

be triggered independently. Most children with signs of beta-cell autoimmunity do not develop type 1 diabetes, however, which suggests that the impact of these environmental triggers is strongly modified by other, protective factors.

Caroline Barranco

Original article Wahlberg J *et al.* (2005) Environmental factors related to the induction of beta-cell autoantibodies in 1-yr-old healthy children. *Pediatr Diabetes* 6: 199–205

A novel *KAL1* mutation identified in Kallmann syndrome

CONGENITAL HYPOGONADOTROPIC HYPOGONADISM comprises two disease subtypes—Kallmann syndrome (KS) and normosmic hypogonadotropic hypogonadism (nHH). Although the majority of cases are sporadic, inherited disease can occur. Candidate genes include *KAL1*, the gene for gonadotropin-releasing-hormone receptor (*GRHR*), *NELF* and *EBF2*.

Trarbach *et al.* performed a molecular analysis of these genes in a cohort of 12 men with KS and 7 with nHH. Although no mutations were detected in *GRHR*, *NELF* or *EBF2*, a novel POLYMORPHISM in *EBF2*, a TRANSITION at position 843 of exon 8 was identified in four patients with KS and three with nHH; however, this polymorphism did not change the amino acid encoded. Two previously described polymorphisms in *KAL1* were also detected.

Point mutations in *KAL1* were identified in two patients with KS. A novel single-base deletion at position 1956 of exon 12, resulting in a premature termination signal, was detected in a patient with a family history of KS. The same mutation was also identified in his brother. The second point mutation (a previously identified transition) introduced a premature termination signal at position 721 of exon 5. Both mutations were located within exons encoding the fibronectin III domain-like repeats of anosmin-1, and are speculated to result in a truncated, nonfunctional protein.

The identification of a novel *KAL1* mutation is of great interest; however, larger studies are required to determine the overall contribution to KS.

Vicky Heath

Original article Trarbach EB *et al.* (2005) Molecular analysis of *KAL-1*, *GnRH-R*, *NELF* and *EBF2* genes in a series of Kallmann syndrome and normosmic hypogonadotropic hypogonadism patients. *J Endocrinol* 187: 361–368