

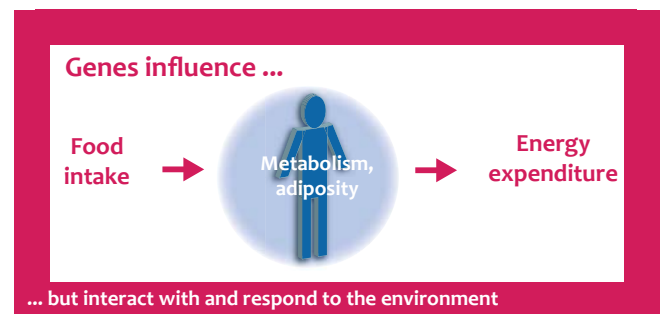
Genetics and Obesity

Patient Scenario

Jim is a 40 year old man who can't seem to control his weight. He read in a newspaper that "being fat is in your genes". Jim says that many of his family members have weight problems. Despite being told by his doctor to visit a dietitian, Jim says "what's the point in sticking to a diet if obesity is already in my genes?"

Key points for dietitians

- Obesity develops as a result of dietary and lifestyle factors, but studies also suggest a genetic influence on obesity. Many genes affect appetite, metabolism and the deposition of fat by the body.
- Some single-gene disorders and syndromes lead to severe obesity but are very rare in the population and likely to be diagnosed before referral to a dietitian. However, dietitians should be aware of their Regional Genetics Centre which can be found at www.bshg.org.uk. Referral should only be where a single-gene disorder is suspected, not for common obesity.
- Asking about family history is a routine part of dietetic assessment for conditions such as obesity and type 2 diabetes. For advice about taking a family history visit www.geneticseducation.nhs.uk.
- By discussing family history information, a patient's feelings of negativity or guilt can be acknowledged, and a dietitian can explain that diet and lifestyle can be changed to reduce obesity even if people are genetically susceptible to it.



Genetics concepts underpinning obesity

Genetics of obesity in the general population

Common obesity is caused by interaction of multiple genetic and environmental factors. Genetic differences between individuals can affect their appetite, metabolism and behaviour, putting some people at higher risk of developing obesity.

The genetic influence on Body Mass Index

A study of thousands of twins estimated that 77% of the variation in their BMI and waist circumference was due to genetic variation. The rest of the variation is attributed to environmental differences (Wardle et al., 2008).

Genetic differences affect energy intake and weight-loss

Some people may have an inborn reduction in their ability to respond to the biological signals which limit energy intake. Also, an irresistible drive to regain lost fat stores may explain why some people find it hard to sustain weight loss (Levin, 2007).

Rare single-gene disorders where severe obesity is the primary feature

There are forms of severe, young-onset obesity caused by a defect in a single gene, although these are very rare in the population as a whole. Examples are deficiencies involving the hormones melanocortin and leptin which have a key role in regulating appetite and metabolism (Farooqi and O'Rahilly, 2007).

Rare genetic syndromes where obesity is an associated feature

Some rare familial syndromes have obesity as one of many features, often associated with mental impairment, dysmorphic features and developmental abnormalities: e.g. Prader Willi syndrome, Alstrom syndrome and Fragile X syndrome (Farooqi and O'Rahilly, 2007). Although these are very rare, certain physical characteristics in children could suggest a genetic disorder, though this is most likely to be picked up by a paediatrician.

Patient Scenario

The dietitian asked Jim about his family history. His condition was not due to a single-gene disorder, but was more likely to be “common obesity” caused primarily by energy intake being higher than expenditure. Jim and his relatives could have certain variants of genes that make it harder for them to control appetite, reduce energy intake, and sustain weight loss.

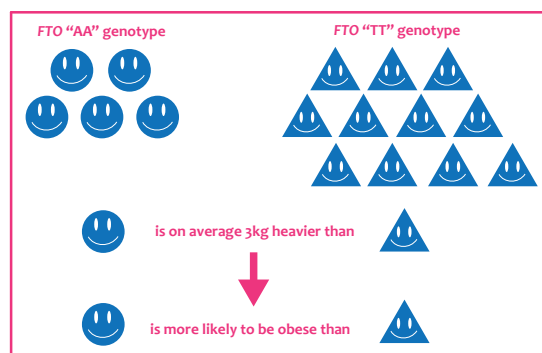
The dietitian acknowledged Jim’s feelings of negativity about obesity in his family, and explained that although he might find weight loss difficult, there are things in his lifestyle that he can change to help himself. This allowed him to think about making sustainable changes without contradicting his feelings about the role of genes. The dietitian continued the assessment and gave dietary advice, including measures to induce an energy deficit.

The search for genes involved in the development of obesity

Researchers are finding genes that are associated with susceptibility to obesity. One such gene is *FTO*, different variants (alleles) of which might partly affect how much food people eat before they are satiated. There are two versions of *FTO*: the wild-type “T” allele and a slightly different “A” allele. Everyone has two copies of the *FTO* gene, so there are three possible *FTO* genotype combinations: TT, AT, and AA. People with AT have a 30% increased risk of being obese compared to a person with TT. An AA person has a 70% increased risk of being obese compared to TT (Frayling et al., 2007).

This does not mean that AAs inevitably become obese, nor that TTs will never become obese. The *FTO* allele is just one factor that increases susceptibility to obesity. Knowledge of genotype might encourage patients to seek and comply with dietary advice. Understanding these mechanisms could lead to new obesity therapies. Even then, diet and nutrition will remain the most important part of patient care in this area.

50% of the UK population are more likely to be obese because they have a particular variant of the melanocortin receptor gene *MC4R* (Chambers et al., 2008). The variant is more common in people of Indian-Asian ancestry which may partly explain high rates of obesity in this group. These gene variants also make people more likely to develop insulin resistance and type 2 diabetes.



Connections between obesity and other conditions

Metabolic syndrome is a cluster of risk factors for cardiovascular disease including obesity, type 2 diabetes, and high blood pressure, cholesterol, and triglyceride levels. The association of these conditions may be partly explained by shared genetic risk factors that influence common pathological mechanisms.

Further information and references

Genetics resources specific to dietetic education and practice can be found at www.geneticseducation.nhs.uk

- Chambers et al. (2008) Nature Genetics. 40:716-718.
- Farooqi and O’Rahilly. (2007) Chapter 23 in Genes and Common Diseases. Cambridge University Press, UK.
- Frayling et al. (2007) Science. 316:889-894.
- Levin. (2007) Journal of Physiology. 583:425-430.
- Wardle et al. (2008) American Journal of Clinical Nutrition. 87:398-404.
- www.bda.uk.com British Dietetic Association.
- www.domuk.org Dietitians in Obesity Management UK.
- www.nationalobesityforum.org.uk National Obesity Forum.
- www.diogenes-eu.org European Diet, Obesity and Genes research collaboration.

Links to dietetic curricula and health professional competences

- This resource relates to the **BDA pre-registration curriculum framework** (page 21) “Understanding of the genetic basis of disease and its application in dietetic practice”.
- This resource relates to **UK Competences for Genetics in Clinical Practice for Non-Genetics Healthcare Staff**. 1: “Identify where genetics is relevant in your area of practice”. 9: “Communicate genetic information to individuals, families and healthcare staff”. The full Competence Framework can be downloaded from www.geneticseducation.nhs.uk
- Developed with guidance from **Dietitians in Obesity Management UK** by the National Genetics Education and Development Centre. For enquiries please contact enquiries@geneticseducation.nhs.uk