

Obesity: Are genes responsible?



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The public media abound with “news” about obesity: its cost to the health and social care systems; characterisation of the parents of obese children as child abusers; exhortations to verbally abuse obese people for the public good (Liddle, 2008); and even reports of the contribution of obesity to global warming (Jackson, 2009).

Obese people are routinely blamed and stigmatised for their all too visible condition, and stereotyped as weaker-willed, lazier or less intelligent than their leaner peers. This attitude stems from lack of appreciation of the neuroregulatory systems controlling eating behaviour and their defects in obese people. Unfortunately, these views are shared by some clinical professionals (Ferrante et al, 2009), resulting in poorer medical care being extended to these people who are suffering from a chronic, progressively disfiguring and disabling condition that profoundly impacts on both quality and duration of life. First and foremost, people with obesity deserve to be treated with the same respect and care afforded to those with conditions conferring similar morbidity and mortality. They also deserve the same evidence-based approach to treatment.

The widespread assumption that people can easily modulate their weight by conscious control of food intake is at odds with the scientific evidence. Most of our nutrient choices are unconscious – a fact that the food industry and supermarkets exploit to promote the purchase and consumption of unhealthy, but profitable food (Cohen, 2008). Furthermore, BMI, waist circumference and adiposity are all highly heritable traits, mediated primarily through genes expressed in the hypothalamus, and regulating feeding and satiety (Walley et al, 2009). This is not to discount the influence of the obesogenic “Westernised” environment, but to recognise that there are certain individuals in the population who are genetically more sensitive to our current superabundance of calorie-dense food and stressful, sedentary lifestyles. These people become obese.

While it is obvious that diet and exercise programmes produce short-term gains in terms of weight loss and improved general health, the evidence is overwhelming that these measures are ineffective in the long-term management of pre-existing severe and morbid obesity (Mann et al, 2007; Sjöström, 2008).

The more severe the obesity and the earlier its onset, the more intractable it is. This is because morbidly obese children are more likely to be exhibiting the effects of a single-gene disorder, resulting from mutations in key genes in the leptin-melanocortin or related pathways. At least one in twenty severely obese children have a primary appetite dysregulation resulting from a deleterious mutation in one of these genes (Lubrano-Berthelie et al, 2003). This is likely to represent the tip of the genetic obesity iceberg: many more such genes may be revealed by next generation DNA sequencing. There is currently no way for these children to avoid obesity, yet they suffer the dual disadvantages of poor health and societal disapproval and are even sometimes removed from their family amid allegations of parental abuse.

It is also becoming clear that more subtle genetic variants play a role in less severe forms of obesity. At least 30 genes modestly and additively increase the risk for severe obesity. Importantly, there is emerging evidence that physical activity is able to diminish the effects of some gene variants responsible for predisposition to obesity (Cauchi et al, 2009) and, thus, exercise may be useful as a preventative strategy.

It remains unclear, however, how individuals who are already severely obese should be managed. Existing drug therapies have limited efficacy and the only effective approach to severe and morbid obesity is bariatric surgery (Sjöström, 2008). Persistence of essential appetite dysregulation, however, means that many surgically treated people are at risk of regaining weight. People experiencing such weight regain may avoid care providers because of feelings of shame and embarrassment, but this can be minimised by respectful and sensitively-delivered long-term aftercare by an experienced multidisciplinary core team.

The attitude of healthcare professionals is critical for the implementation of strategies to prevent progression of overweight to frank obesity, for the management of severe obesity and for prevention of weight regain. A sea change is urgently needed in the way that severe obesity is viewed to avoid unhelpful and simplistic attitudes that exacerbate suffering and obstruct successful treatment of people with obesity. ■