

The 'fundamental questions of obesity': Asked and answered

Scientific progress requires the ability to discover which questions are essential and which are trivial. Yet until recently, there were three fundamental questions that were ignored in nutrition & obesity research:

What is the defining characteristic of obesity?

Why would humans or non-human animals habitually consume more calories than they 'burn'?

Why would the excess calories be stored more as 'fat' than as muscle or bone?

Answer #1: The Defining Characteristic of Obesity

Animals are comprised of cells. Smaller animals have fewer cells than larger animals. So, it is not surprising that elephants have more cells than mice. This relation is also true within species. For example, *ceteris paribus*, larger humans have more cells than smaller humans. Thus, because obese individuals have more fat-cells than lean individuals, the defining characteristic of obesity is not 'diet', 'genes', 'exercise', or bodyweight and fat-mass, but a greater number of fat-cells relative to other cell types.

Answer #2: Overconsumption

There are two reasons for the chronic overconsumption of calories. First, the more fat-cells an individual has, the more calories s/he will store as fat after each meal. Yet if more calories are stored as fat, less calories are available to keep other cells alive. Therefore, excess calories must be consumed to replace the calories lost to fat storage.

The second reason is physical inactivity. As physical activity (PA) levels drop below an individual's "metabolic tipping point", appetite and fat storage increase (Fig. 1A). Thus, as fewer calories are burned, more calories are stored as fat. With extreme inactivity, you can eat very little and still gain fat.

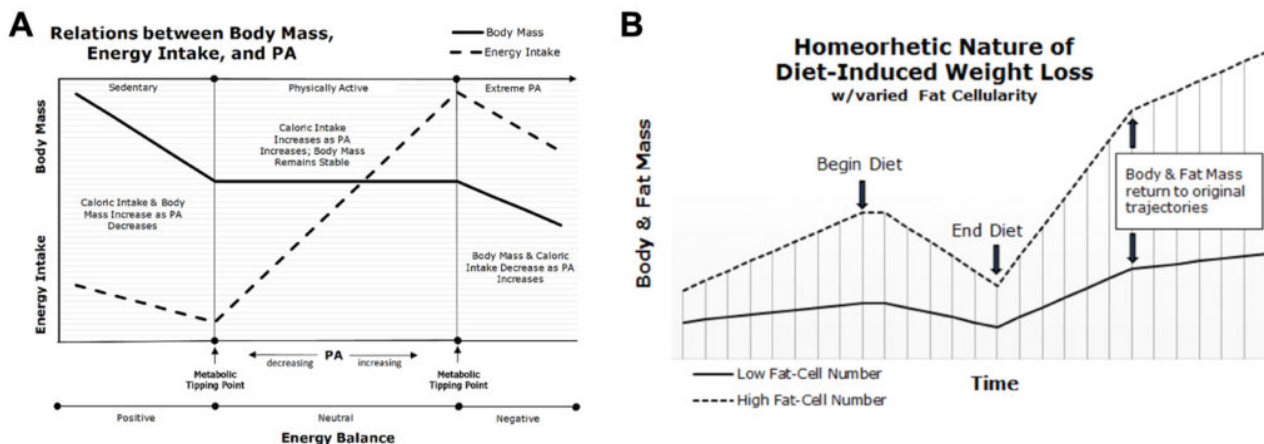


Fig. 1 A. Relations between physical activity (PA), body mass, and energy intake. As physical activity declines below the “Metabolic Tipping Point” (i.e., into the “Sedentary” range), energy intake and energy expenditure become dissociated due to insufficient metabolic-flux; as a result, body mass increases as energy balance becomes positive.

B. Body and fat mass trajectories of individuals varying in adipocyte cellularity (i.e., relative # of fat-cells). Body and fat mass trajectories return to the initial slope (i.e., rate of gain) after diet-induced weight loss. The initial slope was determined by fat-cell number.

Answer #3: Why Gain ‘Fat’ and not Muscle or Bone?

A fat-cell’s ‘job’ is not to ‘burn’ calories but to store them. Therefore, the more fat-cells a person or animal is born with, the more calories they store as fat. Conversely, a person born with more muscle-cells will ‘burn’ or store more calories in muscle-cells.

Importantly, the number of calories reaching the fetus during gestation is the major determinant of the number of muscle- and fat-cells present at birth. If too few calories reach the fetus, s/he will be born with too few muscle- and bone-cells and a stunted, unhealthy body. If too many calories reach the fetus, s/he will be born with too many fat-cells and prone to obesity and metabolic disease. Interestingly, the individual’s genes and those of his/her parents have little influence on the number of cells present at birth. In fact, a mother’s prenatal metabolism is the main determinant of obesity and health. This is known as a “*maternal effect*”.

Summary & Conclusion

The defining characteristic of obesity is not ‘genes’ nor ‘diet’, but the number of fat-cells relative to other cell-types. Obesity can be ‘inherited’ via non-genetic prenatal processes (i.e., “*maternal effects*”) or ‘acquired’ after puberty via physical inactivity and concomitant appetite dysregulation and overconsumption.

Our work suggests that ‘inherited’ obesity is irreversible because losing weight merely changes the size, but not the number of fat-cells in the body (Fig. 1B). Thus, no amount of ‘diet & exercise’ can overcome the metabolic effects of having too many fat-cells. This explains why no matter how much weight you lose, you will quickly gain it back. Conversely, ‘acquired’ obesity may be susceptible to ‘diet & exercise’, but only if no new fat cells were created.

In summary, people born with a large number of fat-cells will almost always be obese — and more importantly, their ‘diet’, ‘genes’, and physical activity levels are not the cause.

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Publication

[The Contributions of 'Diet', 'Genes', and Physical Activity to the Etiology of Obesity: Contrary Evidence and Consilience.](#)

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