

BBS-D-16-00532_ Nettle_ Wells**<CT>Obesity is not just elevated adiposity, it is also a state of metabolic perturbation**

<CA>Jonathan CK Wells

<CAA>*Childhood Nutrition Research Centre, UCL Great Ormond Street Institute of Child Health, London WC1N 1EH, United Kingdom.*

<C-AB>**Abstract:** Nettle et al. miss the crucial difference between adaptive models of storing energy and explanations for the pathological metabolic state of obesity. I suggest that the association of food insecurity with obesity in women from industrialized settings is most likely due to reverse causation: Poverty reduces agency to resist obesogenic foods, and this scenario is compounded by perturbations of insulin metabolism stemming from high adiposity and lipogenic diets.

<C-Text begins>

Undoubtedly, multidisciplinary approaches are required to explain differential susceptibility to obesity, but this article suffers from lack of reference to several key literatures, and I find the conclusions seriously flawed. In my own work, I have proposed and tested several adaptive hypotheses relating to adiposity (Wells 2006; 2009; 2010a;

2011a; 2012a; 2012d; 2012e; 2012f). Paleo-climate data indicate that hominins were exposed to growing ecological stochasticity in comparison with non-human apes and evolved many components of physiological flexibility in response (Wells 2012d), of which adipose tissue was particularly important. There is little evidence that starvation was the primary selective pressure; rather there are several “fitness functions” of adipose tissue (Wells 2010a) broadly connected to tolerating short-term or seasonal changes in energy balance. I have provided empirical support for body composition variability enabling adaptation to diverse stresses including climate, pathogen burden, and seasonality, while buffering health, growth, and reproduction (e.g., Wells 2012c; 2012g; Wells & Cortina-Borja 2013; Wells et al. 2010). Crucially, I restricted these analyses to populations in non-Western settings, and I have repeatedly emphasized that the adaptive biology of adipose tissue must be clearly differentiated from the pathological scenario of obesity and the impact of obesogenic environments (Wells 2010a; 2012e; 2012f). Nettle et al. are aware of this literature, having cited it elsewhere (Nettle et al. 2013), but have adopted the opposite approach: proposing that adaptive models explain obesity itself.

Nettle et al.’s approach posits that psychological mechanisms underlie “decisions” about “how much to eat,” though they do not specify whether this involves conscious deliberation or not. They then argue that it is adaptive to assess food security (again, without specifying how) and select an appropriate level of fat-insurance to acquire. Regardless of how these cost-benefit decisions are made, their “appropriate level” model explicitly assumes that individuals must decide both *when to acquire fat* and *when to stop acquiring it*, as their model proposes rising fitness costs. But the fundamental problem of

obesity, well known to all in the field, is that *fat individuals become even fatter*, and far from supporting their adaptive arguments, their meta-analysis directly contradicts them.

According to adaptive principles, food insecurity should predict the greatest weight gain in thin individuals. This is very evident in the bird literature they reviewed – for example, the experimental study of greenfinches where food insecurity promoted weight gain inversely in association with baseline weight (Ekman & Hake 1990). Paradoxically, however, food insecurity showed significantly stronger associations with excess weight in the meta-analysis for obesity than for overweight. From an allometric perspective, birds have adequate fat stores to buffer only short periods of starvation, whereas men and women of average U.K. height with a body mass index (BMI) of 30 kg/m² have sufficient energy reserves to endure total starvation for ~75 and ~88 days and to endure half-rations for 150 and 175 days, respectively. Larger individuals with BMI of 40 kg/m² could tolerate half-rations for over nine months simply by oxidizing fat reserves (though in practice for even longer, as lean mass also declines during extended weight loss). That food insecurity should predict excess weight more strongly *among those already with substantial energy stores* than among those with lower reserves contradicts their adaptive model. Their “positive” findings thus derive from high-income populations analogous to “fat greenfinches,” whereas what we really need to know is whether food insecurity promotes weight gain in thin humans.

If their findings fit poorly with their energy insurance hypothesis for obesity, what other explanations are more likely? It is baffling that they make no reference to the

neurobiology of appetite regulation; the role of key hormones such as insulin, leptin, and ghrelin; or the role of insulin resistance in driving hyperphagia among those obese. High circulating insulin levels in obese individuals make them highly susceptible to energy-dense diets, particularly those high in sucrose (Lustig 2006; 2008; Wells & Siervo 2011). This means that certain foods can themselves drive hunger and lethargy, helping explain why those who are already fat keep getting fatter (Lustig 2006; 2008; Wells & Siervo 2011).

A much simpler explanation for Nettle et al.'s finding, therefore, is reverse causation. Food-insecure individuals are also poorer, which shapes their dietary choices, and poorer groups are well established to have greater geographical exposure to junk food and other obesogenic factors (Block et al. 2004; Drewnowski & Specter 2004; Larson et al. 2009). Indeed, I have argued that poor and food-insecure groups have the least agency to resist commercial interests, and that this lack of agency is itself promoted by corporate manipulation of dietary quality and food availability (Wells 2016). This looks less like adaptive energy insurance acquisition and more like the interaction of perturbed metabolism with material deprivation and disempowerment – thus, from obesity to morbid obesity.

I have similar concerns over Nettle et al.'s perspective on the developmental origins of obesity. Their proposal that offspring acquire energy reserves in anticipation of future food insecurity reiterates the predictive adaptive response hypothesis (Gluckman & Hanson 2004), yet this has been extensively criticized specifically in relation to growth

and metabolism (Wells 2010b; 2012b). Early growth patterns primarily predict later size and lean mass (Wells 2011a; 2011b) rather than adiposity, and associations of birth weight or infant weight gain with later obesity appear restricted to obesogenic settings (Wells et al. 2007). In Peru, early-life exposure to food insecurity following the 1998 El Nino event reduced childhood height and lean mass but had no effect on fat mass (Danysh et al. 2014).

Obesity is a serious public health issue because even when people strongly desire to lose weight, their metabolism overrides their intentions. This is most powerfully demonstrated by the effects of bariatric surgery: Long before any change has occurred in energy stores, profound alterations in hormone levels lead to reduced appetite and improved metabolic health (Rubino et al. 2004).

It would be interesting to test the food insecurity–energy insurance hypothesis in those of poorer nutritional status, but the authors have failed to provide evidence that it drives human obesity.

Block, J. P., Scribner, R. A. & DeSalvo, K. B. (2004) Fast food, race/ethnicity, and income: A geographic analysis. *American Journal of Preventive Medicine* 27(3):211–17. [JCKW]

Danysh, H. E., Gilman, R. H., Wells, J. C., Pan, W., Zaitchik, B., Gonzalez, G., Alvarez, M. & Checkley, W. (2014) El Nino adversely affected childhood stature and lean mass in northern Peru. *Climate Change Responses* 1:7. [JCKW]

- Drewnowski, A. & Specter, S.E. (2004) Poverty and obesity: The role of energy density and energy costs. *American Journal of Clinical Nutrition* 79(1):6–16. [JCKW]
- Ekman, J. B. & Hake, M. K. (1990) Monitoring starvation risk: Adjustments of body reserves in greenfinches (*Carduelis chloris L.*) during periods of unpredictable foraging success. *Behavioral Ecology* 1(1):62–67. [JCKW]
- Gluckman, P.D. & Hanson, M.A. (2004) The developmental origins of the metabolic syndrome. *Trends in Endocrinology and Metabolism* 15(4):183-7.
- Larson, N. I., Story, M. T. & Nelson, M.C. (2009) Neighborhood environments: Disparities in access to healthy foods in the U.S. *American Journal of Preventive Medicine* 36(1):74–81. [JCKW]
- Lustig, R. H. (2006) Childhood obesity: Behavioral aberration or biochemical drive? Reinterpreting the first law of thermodynamics. *Nature Clinical Practice Endocrinology and Metabolism* 2(8):447–58. [JCKW]
- Lustig, R. H. (2008) Which comes first? The obesity or the insulin? The behavior or the biochemistry? *Journal of Pediatrics* 152:601–02. [JCKW]
- Nettle, D., Frankenhuys, W. E. & Rickard, I. J. (2013) The evolution of predictive adaptive responses in human life history. *Proceedings of the Royal Society B: Biological Sciences* 280: 20131343. [JCKW]
- Rubino, F., Gagner, M., Gentileschi, P., Kini, S., Fukuyama, S., Feng, J. & Diamond, E. (2004) The early effect of the Roux-en-Y gastric bypass on hormones involved in body weight regulation and glucose metabolism. *Annals of Surgery* 240(2):236–42. [JCKW]

- Wells, J. C. (2006) The evolution of human fatness and susceptibility to obesity: An ethological approach. *Biological Reviews of the Cambridge Philosophical Society* 81(2):183–205. [JCKW]
- Wells, J. C. (2009) Ethnic variability in adiposity and cardiovascular risk: The variable disease selection hypothesis. *International Journal of Epidemiology* 38(1):63–71. [JCKW]
- Wells, J. C. (2010a) *The evolutionary biology of human body fatness: Thrift and control*. Cambridge University Press. [JCKW]
- Wells, J. C. (2010b) Maternal capital and the metabolic ghetto: An evolutionary perspective on the trans-generational basis of health inequalities. *American Journal of Human Biology* 22:1–17. [JCKW]
- Wells, J. C. (2011a) An evolutionary perspective on the trans-generational basis of obesity. *Annals of Human Biology* 38:400–409. [JCKW]
- Wells, J. C. (2011b) The thrifty phenotype: An adaptation in growth or metabolism? *American Journal of Human Biology* 23:65–75. [JCKW]
- Wells, J. C. (2012a) The capital economy in hominin evolution: How adipose tissue and social relationships confer phenotypic flexibility and resilience in stochastic environments. *Current Anthropology* 53(S6): S466–S478. [JCKW]
- Wells, J. C. (2012b) A critical appraisal of the predictive adaptive response hypothesis. *International Journal of Epidemiology* 41(1):229–35. [JCKW]
- Wells, J. C. (2012c) Ecogeographical associations between climate and human body composition: Analyses based on anthropometry and skinfolds. *American Journal of Physical Anthropology* 147(2):169–86. [JCKW]

- Wells, J. C. (2012d) Ecological volatility and human evolution: a novel perspective on life history and reproductive strategy. *Evolutionary Anthropology* 201(21): 277–288. [JCKW]
- Wells, J. C. (2012e) The evolution of human adiposity and obesity: where did it all go wrong? *Disease Models and Mechanisms* 5(5):595–607. [JCKW]
- Wells, J. C. (2012f) Obesity as malnutrition: The role of capitalism in the obesity epidemic. *American Journal of Human Biology* 24(3):261–76. [JCKW]
- Wells, J. C. (2012g) Sexual dimorphism in body composition across human populations: Associations with climate and proxies for short- and long-term energy supply. *American Journal of Human Biology* 24(4):411–19. [JCKW]
- Wells, J. C. (2016) *The metabolic ghetto: An evolutionary perspective on nutrition, power relations and chronic disease*. Cambridge University Press. [JCKW]
- Wells, J. C. & Cortina-Borja, M. (2013) Different associations of subscapular and triceps skinfold thicknesses with pathogen load: An ecogeographical analysis. *American Journal of Human Biology* 25(5):594–605. [JCKW]
- Wells, J. C. & Siervo, M. (2011) Obesity and energy balance: Is the tail wagging the dog? *European Journal of Clinical Nutrition* 65:1173–89. [JCKW]
- Wells, J. C., Chomtho, S. & Fewtrell, M. S. (2007) Programming of body composition by early growth and nutrition. *Proceedings of the Nutrition Society* 66:423–34. [JCKW]
- Wells, J. C., Griffin, L. & Treleaven, P. (2010) Independent changes in female body shape with parity and age: A life-history approach to female adiposity. *American Journal of Human Biology* 22(4):456–62. [JCKW]