

The Obese Species: a special issue on obesity and metabolic disorders

Alessandro Bartolomucci^{1,*}, Stefano Parmigiani², R. John Rodgers³, Antonio Vidal-Puig⁴, Sarah E. Allan⁵ and Vivian Siegel^{5,6}

Current epidemiological data show a dramatic increase in obesity in industrialized countries over the past 20 years: its prevalence has trebled in both men and women (currently ~25-30%), with the largest increases seen in adolescents and young adults. Alarming, similar trends are also apparent in children, and the problem has also begun to affect the populations of developing countries. Obesity is not only associated with physical incapacity and psychological distress but also with a considerably increased risk of type 2 diabetes, cardiovascular disease, respiratory difficulties, certain cancers and premature mortality. Clearly, obesity is a major public health concern.

Remarkably, *Homo sapiens sapiens* seems to be the only species that consistently shows an obese phenotype. With the exception of hibernating and migrating animals (in which weight gain is a physiological adaptation linked to the absence of caloric intake during a defined period), only domesticated animals are known to display obesity-related problems. Why are we the only obese species on the planet? Answering this fundamental question would help us treat and ultimately prevent obesity.

The many aspects of obesity were the focus of a workshop entitled *The Obese Species*, hosted by the Ettore Majorana Foundation and Centre for Scientific Culture (President Prof. A. Zichichi), International School of Ethology (co-directors Prof. D. Mainardi and Prof. S. Parmigiani), in Erice, Italy, on October 21-26, 2011 (Fig. 1).

During this highly focused workshop, experts in endocrinology, physiology, neuroscience, psychology, nutrition and ethology addressed recent advances in our understanding of appetite and weight control. The workshop was organized to address the issue of why humans are an obese species, following the logic proposed by Nobel Laureate and founder of ethology, Nikolaas Tinbergen, who proposed that studies of animal behavior (Tinbergen, 1963) and human pathology (Tinbergen, 1974) should be addressed through questions related to proximate and ultimate mechanisms.

Thus, sessions that were focused on proximate explanations (mechanisms and ontogeny) discussed central, peripheral and unexpected routes to obesity, the contribution of stress to obesity, and how to screen for and counteract obesity. The concluding provocative session focused on evolutionary (ultimate) explanations for obesity. For a summary of the speakers' contributions, see Sukkar and Polidori (Sukkar and Polidori, 2011).

This Special Issue of *Disease Models & Mechanisms* (<http://dmm.biologists.org/content/5/5.toc>) aims to provide an authoritative update on obesity that embraces the multidisciplinary spirit of the workshop held in Erice. It is not intended to be a comprehensive account of the workshop's proceedings, and also includes contributions from authors from the wider obesity field.

The special issue comprises several invited review articles (two 'At a Glance' poster reviews, a Special Article and three Commentaries) written by participants of the workshop in Erice, as well as nine research papers. The issue also contains an interview with Jeffrey Friedman (see the Model for Life article on p. 576), a Journal Club piece authored by graduate student Piya Ghose (p. 574) and, sadly, an Obituary written by Bruce McEwen celebrating the late Zofia Zukowska^a (p. 580), to whom we dedicate this special issue.

We are pleased to open the issue with a provocative Editorial by John Speakman and Steve O'Rahilly (see p. 569), who discuss the central question of why a large number of us are in positive energy balance, and therefore obese. Their discussion touches on both proximate and ultimate explanations, and is thus an excellent summary of the key concepts discussed at the workshop held in Erice and an ideal opener for the remainder of the articles presented in this issue.

We then present two innovative and integrative 'At a Glance' poster reviews that we hope will become mainstays on the walls of laboratories near and far for years to come. The first, by Chun-Xia Yi and Matthias Tschöp, provides an updated summary of communication pathways between the brain, gut and adipose tissue that regulate energy balance (p. 583). This review also highlights the role of astrocytes in mediating hormonal signaling in the arcuate nucleus, and summarizes peptidergic signals regulating energy balance. In the second poster review, Saverio Cinti provides an authoritative overview of the anatomy and many functions of the adipose organ. This poster guides the reader through developmental aspects, as well as cytology, anatomy, pathology and the remarkable phenotypic plasticity of adipocytes (p. 588).

¹Department of Integrative Biology and Physiology, University of Minnesota, 321 Church Street SE Minneapolis, MN 55455, USA

²Department of Neuroscience, University of Parma, I-43100 Parma, Italy

³Institute of Psychological Sciences, University of Leeds, Leeds, LS2 9JT, UK

⁴Metabolic Research Laboratories, Institute of Metabolic Science, Addenbrooke's Hospital, University of Cambridge, Hills Road, Cambridge, CB2 0QQ, UK

⁵*Disease Models & Mechanisms*, The Company of Biologists Ltd, Bidder Building, Cambridge, CB4 0DL, UK

⁶The Broad Institute of MIT and Harvard, 7 Cambridge Center, Cambridge, MA 02142, USA

*Author for correspondence (abartolo@umn.edu)

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^aZofia Zukowska, MD, PhD, was a vibrant and passionate scientist who contributed immensely to our knowledge on neuropeptide Y and to the scientific success of the workshop in Erice. She brightened everyone's spirit with her joyful attitude to life. Her smile and red scarf will forever be remembered by everyone who had the privilege to meet her. This Special Issue is dedicated to the loving memory of our friend Zofia.



Fig. 1. Group photo taken following the final session of the workshop entitled “The Obese Species”, hosted by the Ettore Majorana Foundation and Centre for Scientific Culture, International School of Ethology, Erice, Italy, on October 21-26, 2011.

In his Special Article on p. 595, Jonathan Wells reviews current literature on the molecular and environmental determinants of adiposity, and conducts a detailed sociological analysis of obesity incidence worldwide. Wells discards the molecular credo that the only way to treat obesity is to oppose defective genetic or aberrant signal transduction and concludes with the provocative viewpoint that “socio-environmental cues, collectively orchestrated by our capitalist economic system [...] are the optimal target for obesity prevention”.

A key issue in obesity research – both of theoretical importance and relevant to the clinical management of obesity – is how energy expenditure regulates food intake. In their Commentary, John Blundell and colleagues review available data and outline a new formulation proposing that resting metabolic rate (i.e. energy burned during sleeping or complete rest) is an important driver of hunger and energy intake (see p. 608).

The identification of disease biomarkers is a crucial goal in obesity research and will advance our understanding of the disease, and help to define diagnostic and prognostic endpoints. In his Commentary, Matej Orešič (page 614) discusses how recent advances in metabolomics are moving forward our ability to diagnose obesity-associated disorders (including psychiatric comorbidities) at an earlier stage, and to identify underlying molecular mechanisms. The hope is that metabolomic approaches will be an important tool in improving personalized medicine for the obese population.

How good is our current pharmacological management of obesity and obesity-related complications? How can we combine efficacy and safety in an anti-obesity therapy? What’s next in the anti-obesity drug market? In their Commentary on p. 621, John Rodgers, Matthias Tschöp and John Wilding review the past, present and future of anti-obesity therapies, discussing new peptidergic candidates as well as

the rising hopes for drug polytherapies. They also consider current problems in this area and offer authoritative insights into the much debated issue of clinical trials.

The second half of the special issue includes peer-reviewed research received in response to a call for papers to the scientific and medical research community. This selection of papers nicely illustrates the remarkable diversity of approaches used in obesity research. The work covered here spans topics such as: animal models of obesity and diabetes; the role of inflammation; the link between obesity and pathology; and the characterization of new drugs.

It is beyond the scope of this special issue to provide a complete overview of our current knowledge on obesity. Nonetheless, we sincerely hope that readers will find the papers in this issue interesting and useful, and that some are encouraged to undertake further scientific studies on the disease that is rapidly becoming the most serious health problem in our society.

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