



Obesity should be accepted as a disease

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The prevalence of obesity is increasing world-wide and has reached epidemic proportions in both developed and developing countries. According to the recent data provided by The International Obesity Task Force 1.1 billion adults are overweight (BMI>25) and 312 million of them are obese (BMI>30). Within European countries 10-20 % of men and 15-25 % are obese and about 50 % of adults are overweight. In the United States almost 31% of adults meet the criterion for obesity and 64 % of American adults have BMI> 25kg/m². Weight excess is associated with increased risks of type 2 diabetes, hypertension, cardiovascular diseases, hyper/dyslipidaemia, non-alcoholic steatohepatitis, some types of cancers, sleep apnoea, gallbladder disease and osteoarthritis. Increasing body weight impairs quality of life and reduces life expectancy.

Accumulation of intraabdominal fat is associated with increased cardiometabolic health risks which are partly mediated by high portal flux of free fatty acids and cytokines. Abdominal obesity is the main feature of the metabolic syndrome which is frequently characterized by insulin resistance/type 2 diabetes, hypertension, dyslipidaemia, chronic low-grade inflammation, endothelial dysfunction and prothrombosis. Waist circumference is a simple anthropometric measure of intraabdominal fat. Cut-off points for optimum waist circumference should consider ethnic and gender differences. Limits as recently defined by the International Diabetes Federation for European white people are 94 cm for men and 80 cm for women...

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Obesity in animals

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More than twenty-five percent of dogs and cats are overweight. Many rodents and captive birds are obese too. Excessive weight is due to associated causes : genetics, hormonal disorders, neutering, decreased physical activity, aging, behavioural problems, self-service consumption of too much caloric or given in excess diets or treats (delicacies)... Many owners do not know what is the ideal weight of their pet despite of practical methods used by vets for assessing body condition (scoring). To reduce weight and body fat, many changes in owner's habits are prescribed : mainly an exercise plan and a feeding plan. It is important to assess the daily energy requirements of the pet. Equations are used to estimate the caloric restriction to produce weight loss...

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Brain regulation of energy metabolism

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The brain is responsible for regulating energy metabolism and, as a result, body weight (see Broberger, 2005). To accomplish this task, the central nervous system needs to inform itself about the metabolic state of the body, which it does via two main channels. In the arcuate nucleus of the hypothalamus, metabolically relevant hormones such as leptin and insulin relay information about the supply and demand of energy in the body, and act on two antagonistic populations of neurones: feeding-stimulatory neurones expressing neuropeptide Y (NPY) and feeding-inhibitory neurones expressing pro-opiomelanocortin (POMC). In the brainstem, the vagus nerve transmits sensory signals from the gastrointestinal tract in the nucleus tractus solitarii (nTS). In previous work, we have studied the ascending projections from the arcuate nucleus and found that NPY- and POMC-ergic neurones project in pathways parallel to each other and to cells originating in the nTS (e.g. Broberger et al., 1998). We are interested in defining the target neurones for this triple innervation to understand how higher brain regions are engaged in the initiation, organization and termination of feeding behaviour...

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Role of Circadian Clock in the Management of Obesity?

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The bHLH-PAS transcription factor, CLOCK, has emerged as a key component of the molecular circadian clock within pacemaker neurons of the hypothalamic suprachiasmatic nucleus. We have recently discovered that homozygous Clock mutant mice have a greatly attenuated diurnal feeding rhythm, are hyperphagic and obese, and develop a metabolic syndrome of hyperleptinemia, hyperlipidemia, hepatic steatosis and hyperglycemia, with insufficient compensatory insulin production, a hallmark of type 2 diabetes mellitus. In addition, the levels of expression of hypothalamic peptides associated with energy balance were greatly attenuated in the Clock mutant animals...

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Targeting the Lipid and Carbohydrate Metabolism

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Obesity is characterized by excessive accumulation of fat in adipose tissues. Consumption of Western diet enriched with animal fat has in part been attributed to the ongoing obesity epidemics. Major progresses have been achieved in recent years in our understanding of the regulatory roles of lipid metabolic enzymes in obesity and its related metabolic complications. These include identification of novel lipid metabolic enzymes as well as phenotypic characterization of mice with targeted deletion of these enzymes. The work has provided a rich source of novel drug targets for obesity drug development. Consequently, novel antiobesity drugs are currently been developed by major pharmaceutical companies by targeting enzymes involved in different stages of lipid metabolism — from digestion and absorption through synthesis and storage to mobilization and oxidation....

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Bariatric surgery

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Obesity has been described as worldwide epidemic. Obesity surgery (or “bariatric surgery”) has been criticized. As a matter of fact it deals with a small proportion of obese patients who are good candidates for this surgery – namely morbid obese patients. Nevertheless bariatric surgery has been recognized as an efficient method for treating morbid obesity. Dealing with a complex disease that is mixed up with many issues (social, behavioural factors, etc.) surgery cannot target all the potential patients it should.

Laparoscopic gastric banding is currently the reference for surgical treatment in Europe. Older techniques, like stapling gastroplasty (Mason) still deserve credit, but lap-banding took over rapidly at the end of the nineties.

More complex and risky procedures such as gastro-jejunal bypass or bilio-pancreatic diversion are presented as goldstandards in bariatric surgery. Indeed they are often performed through the laparoscopic approach nowadays. Yet one can see them as secondary options when a band has failed, and/or for very obese patients (BMI>50)...

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Dietary Calcium Intake, Dairy Products and Obesity

Dr. Michael B. Zemel

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Obesity is a complex genetic trait, with multiple genetic interacting to confer either resistance or susceptibility to overweight and obesity. Similarly, specific nutrients and dietary patterns act on the same metabolic pathways as these genetic factors and thereby modify our risk of this disease. This talk will focus on these dietary patterns, with an emphasis on new research demonstrating a pivotal role for dairy and calcium in controlling fat cell metabolism. This role provides the framework for dietary calcium playing an important part in preventing and treating obesity. High calcium diets cause reductions in body fat, work with calorie-restricted diets to increase the rate and amount of weight and fat loss and significantly attenuate the regain of body weight and body fat which commonly occurs following successful weight loss. Moreover, key evidence will be presented to demonstrate that dairy foods contain unique components which result in a much more profound effect in improving body composition, augmenting weight and fat loss and preventing obesity and obesity-related diseases compared to supplementary sources of calcium. Implications of these findings in combating the obesity epidemic and promoting healthy management will be discussed extensively...

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Beneficial effects of bile acids: a new way to treat obesity by food supplementation?

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While bile acids (BAs) have long been known to play an essential role in dietary lipid absorption and cholesterol catabolism, in recent years an important role for BAs as signaling molecules has emerged. BAs activate mitogen-activated protein kinase pathways, are ligands for the G-protein-coupled receptor (GPCR) TGR5, and activate nuclear hormone receptors such as farnesoid X receptor (FXR, NR1H4). FXR regulates the enterohepatic recycling and biosynthesis of BAs by controlling the expression of genes such as the short heterodimer partner (SHP, NR0B2) that inhibits the activity of other nuclear receptors. The FXR-mediated SHP induction also underlies the downregulation of SREBP-1c-mediated hepatic fatty acid and triglyceride biosynthesis and VLDL production. This suggests that BAs can function beyond the control of BA homeostasis as general metabolic integrators. Here we show that administration of BAs to mice increases energy expenditure in brown adipose tissue, preventing obesity and insulin resistance. This novel metabolic effect of BAs is critically dependent on induction of the cAMP-dependent thyroid hormone activating enzyme type 2 iodothyronine deiodinase (D2) since it is lost in D2^{-/-} mice. BA treatment of brown adipocytes and human skeletal myocytes increases D2 activity and oxygen consumption....

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Interesting Molecular Targets: the Peroxisome Proliferator-Activated Receptors (PPARs)

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Peroxisome proliferator-activated receptors (PPARs) play key roles in the regulation of energy homeostasis and inflammation, and agonists of PPAR α and PPAR γ are currently used therapeutically. Fibrates, first used in the 1970s for their lipid-modifying properties, were later shown to activate PPAR α . These agents lower plasma triglycerides and very low-density lipoprotein particles, and increase high-density lipoprotein cholesterol – effects that are associated with cardiovascular benefit. Thiazolidinediones, acting via PPAR γ , influence free fatty acid flux and thus reduce insulin resistance and blood glucose levels. PPAR γ agonists are therefore used to treat type 2 diabetes. PPAR α and γ agonists also affect inflammation, vascular function and vascular remodelling. As knowledge of the pleiotropic effects of these agents advances, further potential indications are being revealed, including roles in the management of cardiovascular disease and the metabolic syndrome...

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An RNAi-based Approach to Metabolic Disease

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Disruptions in insulin-sensitive pathways of metabolic flux in adipocytes are associated with obesity and can impair whole body glucose homeostasis and cause diabetes in mice. Thus, the identification and detailed characterization of novel regulators of adipocyte metabolism are fundamental objectives in the field. RNAi-based screens we performed have revealed two novel global regulators of adipocyte metabolism—the transcriptional corepressor RIP140 and the protein kinase Map4K4. Silencing either RIP140 or Map4K4 in cultured adipocytes: 1.) enhances expression of enzymes in carbohydrate and fatty acid oxidation as well as oxidative phosphorylation, 2.) enhances insulin-sensitive glucose uptake and glucose conversion to CO₂, and 3.) enhances mitochondrial biogenesis. Primary mouse adipose tissue also responds to RNAi-based depletion of RIP140 and MAP4K4. A subset of genes commonly regulated by both RIP140 and MAP4K4 are also PPAR γ -sensitive, consistent with PPAR γ being a target of their regulation...

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Inflammation, oxidative stress and obesity: a New Field for Therapy?

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Obesity is the most common and fastest growing nutritional disorder in occidentalized countries. Both morbidity and mortality increase with excessive body weight because of enhanced relative risk for developing diabetes, hypertension, insulin resistance, coronary heart disease... White adipose tissue is not only the physiological site of energy storage as lipids, it is also an active endocrine organ secreting a large variety of proteins termed adipokines including : cytokines, chemokines and hormone like factors, with multiple metabolic roles in regulating metabolism, inflammation and immunomodulatory functions. Obesity is considered as a state of low-grade chronic inflammation which can subsequently lead to insulin resistance, impaired glucose tolerance and even diabetes. In obesity, the production of numerous proinflammatory molecules is increased, which may affect not only adipose tissue but also other organs. Many of the proteins produced by adipose tissue have dual actions. Indeed, numerous adipokines are involved in inflammation (IL-1beta, IL-6, IL-8, TNF-alpha), while adiponectin is an insulin-sensitising effector and leptin is a regulator of metabolism and inflammation...

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Role of Mitochondria and Uncoupling Proteins in Obesity and Insulin Secretion

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Adaptive or diet-induced thermogenesis is an important component of energy expenditure that can help maintain body weight. Uncoupling protein-1 (UCP1), which exists predominantly in brown adipose tissue, induces thermogenesis by promoting uncoupling of oxidative phosphorylation from ATP synthesis, allowing increased heat production. However, the role of UCP1 in adult humans is minor. The existence of novel uncoupling proteins, named UCP2 and UCP3, gave rise to the hypothesis that these molecules could function as thermogenic proteins and might be manipulated to increase heat production and therefore induce weight loss. However, neither UCP2 nor UCP3 functions in thermogenesis...

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Dietary supplements and body weight reduction

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The aim of this systematic review is to critically assess the evidence from randomized controlled trials (RCTs) and systematic reviews of dietary supplements for reducing body weight. Literature searches were conducted on Medline, Embase, Amed, and the Cochrane Library until January 2004. Hand-searches were performed of relevant medical journals and bibliographies of identified articles. No restrictions regarding the language of publication were applied. Trial selection, quality assessment and data abstraction were performed systematically and independently by both authors. Data from RCTs and systematic reviews, which based their findings on the results of RCTs, were included. Four systematic reviews and 21 additional RCTs met our inclusion criteria and were reviewed. Except for Ephedra sinica and other ephedrine-containing dietary supplements the weight of the evidence was not convincing enough to suggest effectiveness. For these interventions, small effects compared with placebo were identified. In conclusion, our findings suggest that for most dietary supplements, the evidence for reducing body weight is not convincing. E. sinica and other ephedrine-containing dietary supplements may lead to small reductions in body weight...

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Natural Appetite Suppressants: Reducing caloric intake in the natural way

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Despite the wide recognition of the epidemic proportions, the prevalence of obesity is still increasing sharply among adults, adolescents, and children. There are now as many obese people in the world as there are people suffering from hunger. The deleterious effects of obesity on chronic disease risk, its high medical, psychological, and social costs, impact on quality of life, the paucity of successful treatment options call for increased attention to the prevention of excessive weight gain. The food industry has been busy for some time developing 'diet' or 'light' products to help people reduce their caloric intake, but these products often fail to offer a sense of fullness, which then leads to further unhealthy snacking behavior. Interesting products on the market are appetite suppressants which work on the very simple premise of 'What you don't eat now, you won't need to lose later!' In fact, these appetite suppressants influence the production of hormones that naturally tell our brain to stop eating, preventing weight gain at the source. Mechanisms of appetite control will be presented which form excellent targets for natural appetite suppressants. Appetite suppressants are quite popular nowadays to help control cravings and emotional hunger...

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Point of View of a Medical Doctor: Which Natural ingredients could be efficient treatments of Obesity in medical everyday practice?

Dr Paul Goetz

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Obesity, which is not induced by a precise disease, is the result of calorific food intake and energy output. Intake of fatty meat or hydrocarbonates is the first cause of putting on weight. Lack of physical exercise is the second element, which may upset the balance toward overweight. Output and intake is also under the strong influence of alimentary behaviour. Everyday treatment of obesity needs a complete treatment based on a good knowledge of alimentary habits of each patient. There are different methods to influence alimentary disorders. First of all, will be a diet accompanied by diet education. Then, if needed, psychological support should be considered...

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