REVIEW ARTICLE

Role of Nutritional Factors in Weight Management

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SUMMARY

Obesity has become one of the most serious public health problems currently affecting both developed and developing countries. Obesity develops as the result of a positive energy balance. Strategies in obesity prevention and management have therefore focused on the energy balance. Dietary weight management should be based especially on reduction of fat intake; of the three macronutrients, fat exhibits the highest energy density, low satiating properties as well as low diet-induced thermogenesis. Although carbohydrate does not play such an important role in the pathogenesis of obesity as fat, the intake of simple carbohydrate should be reduced during the treatment of obesity and of the metabolic syndrome. Different metabolic consequences of the intake of individual fatty acids (polyunsaturated and n-3 fatty acids vs. saturated fatty acids), individual carbohydrates (low vs. high glycemic index carbohydrates) and fiber should be considered in weight management. Dietary protein has a positive effect on the outcome of weight management through enhancement of postprandial satiety and thermogenesis. The role of calcium, phosphate and vitamin A intake in body weight regulation and obesity management has also been a topic of recent studies.
Key words: obesity, weight management, macronutrients, calcium, phosphate, vitamin A.

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Obesity – a disease neglected in the past, today classified as a disease bearing all the signs of a worldwide epidemic. The most alarming phenomenon is the increasing prevalence of overweight and obesity among children.

Obesity is characterized by the accumulation of body fat. Overweight and obesity in clinical practice is defined on the basis of the Body Mass Index /BMI = weight (kg)/height (m^2)/. However, BMI need not to reflect the body fat stores, i. e. the fat to fat-free mass ratio. The percentage of body fat can be approximately determined by anthropometry or by bioelectric impedance (BIA = measurement of the resistance of the body to the passage of low amplitude and high frequency current; three body components are measured – fat, non-fat tissue and water).

A number of factors contribute to the pathogenesis of obesity, ranging from metabolic causes, which are often genetically determined, to central regulatory disturbances, and to psychological and environmental influences including socio-economic factors. Focus on environmental factors reveals that the main role in the development of obesity is played by a positive energy balance, i. e. lack of physical activity and simultaneous intake of a high-energy density food. Energy intake affects the proportion of basic nutrients and, possibly, also certain micronutrients and alcohol in the diet (1). The main objective of dietary management of obesity is the reduction of total energy intake. Clinical and epidemiological studies have shown, however, that an important role in long-term weight reduction is played not only by reduction of energy intake but also by an appropriate intake of individual nutrients in the low energy diet (1).

FAT

Increased energy intake is mainly due to excessive consumption of dietary fat, as has been confirmed by Astrup's meta-analysis of dietary intervention studies (2). Fat has, simultaneously, a high energy density (38 kJ/g compared to 17 kJ/g in the case of protein and carbohydrate) and the lowest satiating properties of all the three macronutrients; fat also induces the lowest diet-induced thermogenesis. It means that to achieve satiety the consumption of greater amounts of fat than protein or carbohydrate is required (1, 3). There is no doubt that the ability to burn fats depends on genetic predisposition (4, 5). According to Heitmann et al., higher dietary fat intake was associated with body mass increase only in overweight women with a history of obesity in parents (5). This finding corresponds with a study conducted at our center, which demonstrated that obese individuals who reported parental obesity had a significantly higher fasting respiratory quotient (RQ) than obese individuals with a negative history of parental obesity (4). The higher fasting RQ reflects lower fat oxidation and is associated with the inability to maintain weight loss and with tendency to weight cycling (4).

Preferences for consumption of fatty items are caused in particular by the sensory properties of fat. Fat provides food a characteristic fullness due to its texture. Choice of food with a high fat and sugar content presents a high risk – especially for patients with a genetic predisposition to accumulation of fat; sweets often being the favorite for the obese individuals. The consumption of such foods does indeed induce pleasant, hedonic feelings due to the organoleptic properties of fat (texture) and sugar (sweetness), but it also contributes significantly to a positive energy balance. Fat intake is often underestimated, because people do not include into the calculation the intake of "hidden fats" from meat and dairy products (6). A low-fat diet (less than 30 % of the total energy intake covered by fats) is the best prevention of obesity, and in overweight people this leads to body weight loss (7).

Dietary guidelines emphasize, however, that it is not enough to monitor just the total fat intake, but that a very important factor is

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the type of fatty acids (FA) consumed. FA are classified according to the number of double bonds into saturated, monounsaturated and polyunsaturated (8). Saturated FA have a hypercholesterolemic effect and stimulate hyperplasia of adipose cells more than unsaturated FA. Unsaturated FA, on the other hand, stimulate oxidation of lipids in the muscles, liver and apparently also within the white adipose tissue (1). Positive metabolic effects are most expressed with intake of n-3 FA. n-3 FA play an important role in the prevention and treatment of cardiovascular diseases, hyperinsulinemia and type 2 diabetes mellitus. N-3 FA prevent coagulation, possess vasodilatory, antiinflammatory and antiarrhythmogenic properties and they lower serum triacyglycerols, especially their postprandial levels (9–12).

A reasonable consumption of fat is necessary, however, even during a low energy diet. Ingested fat inhibits synthesis of fatty acids in adipose tissue cells; insufficient intake of fats thus causes increased synthesis of fatty acids. The consequence is a change of the spectrum of fatty acids in plasma triacylglycerols – the saturated fatty acid content rises at the cost of reduction of the unsaturated fatty acids, which can have an adverse effect on the cardiovascular system (1).

It is a paradox that in ketogenic diets, where the contribution of fat in total energy intake is sometimes as high as 60%, but where the intake of carbohydrate is significantly reduced, both weight loss and fat loss is even higher than in the case of standard weight reduction diets. Short-term studies failed to demonstrate that the increased intake of fat, especially of saturated fatty acids, would cause an elevation of blood lipids, insulin resistance and rise of blood pressure (13–15).

CARBOHYDRATE

Excessive intake of carbohydrate in the diet does not play such an important role in the pathogenesis of obesity as excessive intake of fat. Unlike fat, however, enhanced intake of carbohydrate leads to an increase of their oxidation due to adaptation; there may be a twofold increase in carbohydrate oxidation in response to increased carbohydrate intake. Only after prolonged excessive intake of carbohydrate does the organism start transforming them into fat stores. However, the transformation of carbohydrates into fat stores is not very efficient – only $^3/_4$ of the received energy is deposited as fat stores – whereas in the case of fat the efficiency of incorporation into fat stores is 95%. The capacity of deposition of carbohydrates as a reserve is limited by the amount of liver and muscle glycogen; the capacity to create fat stores from dietary fat, however, is practically unlimited (1).

Carbohydrates play a unique role in weight reducing diets. They are a ready source of energy, and their adequate intake prevents the decline of resting energy expenditure. Low intake of dietary carbohydrate usually negatively affects the long-term prognosis of weight reduction regimes. Intake of dietary carbohydrates prevents the reduction of the sympathetic nervous activity and thus also the decline of blood pressure (prevention of orthostatic hypotension) during strict reduction regimes (6).

On the other hand, there is the Atkins diet, which has now been popular for quite a number of years. During this diet, carbohydrate intake is lowered to less than 30 g/day, but there is no restriction on the consumption of fat meat, butter and high-fat dairy products, and only certain types of vegetables are allowed (lettuce, spinach, cucumber, broccoli). All types of food containing carbohydrate are prohibited: cakes and biscuits, bread, pasta, rice and all other grains, potatoes and fruit. Lack of carbohydrate in the diet leads to the exhaustion of glycogen supplies, the body becomes dehydrated and, formation of ketone bodies decreases appetite. To this is added the satiating effect of protein, which intake is, of course, also higher and the result is reduced food intake and weight loss (15, 16).

Although the harmful effect of this diet in short-term reduction regimes has not been proven, there are some hazards – high fat intake is associated with the incidence of certain tumors (especially colorectal cancer, breast cancer, endometrial and ovarian cancer). This diet also contains insufficient amount of fiber and calcium. Although some specialists consider Atkins diet a feasible therapeutic strategy for obesity management, it cannot be recommended for long-term use and is unsuitable for people suffering from hyperlipidemia, diabetes mellitus and other metabolic diseases (16). A considerable disadvantage of these diets is the induction of enhanced energetic efficiency, which is associated with the earlier-mentioned suppression of sympathetic nervous activity. Moreover, significant restriction of energy intake and especially reduction of carbohydrate intake leads to induction of the low T3 syndrome.

Studies comparing the effect of a low-carbohydrate diet and conventional reduction diet have shown that after 6 months a low-carbohydrate diet leads to a larger reduction of body weight, but after one year the differences between the two diets are no longer significant. Surprisingly, some studies have recorded a more marked reduction of serum triacyglycerols and elevation of HDL cholesterol (15, 17, 18).

In recent years, the dietary glycemic index (GI) has often been discussed in relation to carbohydrate. The index indicates the ability of different types of foods that contain carbohydrate to raise postprandial blood glucose levels. The GI of individual foods is established experimentally and is defined by the ratio between the area under the incremental curve of the test food, and the area under the glycemic curve of glucose, which has a referential value of 100%. Foods with a low GI lead to lower elevation of the postprandial blood glucose and insulin levels, they induce a prolonged feeling of satiety and smaller feeling of hunger. On the other hand, foodstuffs with a high GI lead to a greater elevation of insulin with a more marked tendency to deposit nutrients in fat stores, which is associated with the risk of weight gain (1, 19–21).

The GI value is not invariable; much depends on the way in which food is processed, on the fiber, fat and protein content and on the presence of acid (e. g. wine vinegar, lemon juice, sour fruit), which are the factors influencing the speed of stomach emptying, and thus also the speed of digestion and absorption of carbohydrates.

Various epidemiological studies show that a lower GI is associated with lower levels of triacyglycerol and free fatty acids, with an elevated level of HDL-cholesterol and a favorable effect on insulin resistance. Another favorable feature is the improved adaptation of the body to a low-energy diet and greater body weight decrease, although in many studies the results have not been entirely unequivocal (22, 23).

An interesting phenomenon is the relation between fructose metabolism and changes in body weight. Fructose, present in syrups used mainly in soft drinks, pastries, desserts, etc. is considered one of the main causes of the rise in child obesity in the U. S. (24). The main cause is, on the one hand, excessive consumption of these foods, and on the other hand the effect on levels of certain hormones, which are usually directly associated with food intake. Fructose has a low GI (20), therefore digestion of fructose causes no rise in insulin levels; leptin levels are reduced and there is no suppression of the orexigenic gastrointestinal hormone ghrelin, as in the case of glucose. In general, leptin levels drop in response to fasting and rise after the food intake, and high levels of leptin suppress appetite. Insulin and leptin are transported to the brain where they modulate the effect of hypothalamic neuropeptides, which regulate eating behavior and body weight. Reduced production of insulin and leptin thus leads to enhanced energy intake and increase

of body weight (1, 24). Ghrelin is the food trigger and, unlike leptin, increases appetite and the feeling of hunger. It is evident therefore that fructose can increase the total energy intake because it reduces the feeling of satiety through the effect of the above-mentioned hormones.

The metabolic effect of fructose is very different from glucose. A smaller amount of transporter Glut-5 for fructose in the pancreatic beta cells leads to lower stimulation of insulin secretion, compared to glucose. Moreover, fructose promotes lipogenesis in the liver, which is associated with higher plasma triacylglycerol levels.

Animal studies have shown the relation between fructose intake and the metabolic syndrome, which is based on insulin resistance. One hypothesis of the origin of insulin resistance is a decreased adiponectin level. Adiponectin is a peptide hormone produced by adipocytes, which improves sensitivity to insulin in the muscles, stimulates glucose metabolism and simultaneously increases fat oxidation. Excessive fructose intake is associated with a rise in the levels of circulating non-esterified FA. The increased supply of non-esterified FA to the liver is thus one of the main causes of disturbance in carbohydrate metabolism, which lead to the development of the insulin resistance and metabolic syndrome (1, 21, 24, 25).

Fiber influences the energy balance by its effect on both the process of satiation and satiety, and the absorption of fats and carbohydrates. Weight reducing diets recommend a higher intake of vegetables, fruit, pulses and whole-grain foods essentially because of the fiber content of these foods (1).

PROTEIN

Protein plays a key role in regulation of body weight and composition of the human body.

Enhanced intake of protein does not lead to their transformation into fat, because enhanced intake of protein is accompanied by accelerated oxidation and, moreover, the capacity to store protein is limited. Compared to fat and carbohydrate, protein has the highest satiating value, not only postprandially, but also during food intake (1). Skov et al. (26) compared high-protein diet (25% protein, 45% carbohydrate, 30% fat) with a control diet (12% protein, 58% carbohydrate, 30% fat) over a course of 27 weeks with *ad libitum* energy intake.

Significantly better results were achieved in the case of high-protein diet, both as far as both weight decrease (8.9 kg *versus* 5.1 kg) and fat reduction (7.6 kg *versus* 4.3 kg), and the amount of energy intake (5.0 MJ *versus* 6.2 MJ/day) are concerned.

There is also a marked influence of protein on diet-induced thermogenesis, which is stimulated by their intake. The ability to influence thermogenesis is more marked in animal protein (27).

Compared to high-fat and high-carbohydrate diets, a high-protein diet is associated with a smaller feeling of hunger and, consequently, also with a lower energy intake. The inhibitory effect of protein on food intake is caused both by the stimulation of cholecystokinin, glucagon and glucagon-like peptide 1 (GLP1) secretion, and by the direct effect on food intake regulation in the hypothalamus of certain amino acids, e. g. tryptofan as a serotonin precursor (1, 28).

The protective effect of a high-protein diet has also been established in the "post-reduction" period when patients on a diet with 18% of the energy supplied by proteins gained only 1 kg compared with 2 kg in the control group where the protein intake was 15% of the total energy intake (29).

Some studies indicate that excessive consumption of protein in early childhood may potentially lead to the development of obesity later in life (30). The study carried out at our center monitored two groups of pre-term born infants (breast-fed and formula fed) from birth until the age of ten years. Energy, especially protein, intake was significantly higher in the first months of life in the formula-fed children. However, pre-term adiposity rebound was not observed in these children, nor was there any significant correlation of postnatal protein intake with higher BMI, anthropological parameters and serum leptin levels at the age of 7 and 10 years (31).

A study carried out last year on mice lead to interesting conclusions; it demonstrated that low-protein diet in the prenatal period is associated with food preferences at a later age. Mice whose mothers received a low-protein diet during pregnancy preferred food with a higher fat content than the controls in older age (32).

The discussion on the effect of higher protein intake on renal functions has been going on since the last century; according to recent studies by Poortmans and Dellalieux no negative effect on renal function has been established in protein intakes from 1.2 to 2.0 g/kg/day (33).

MICRONUTRIENTS

The influence of certain micronutrients, especially calcium, phosphates and vitamin A has been considered in relation to obesity.

It is probable that the amount of phosphate in the diet can influence the energy mechanism. Phosphate is used in some countries as a food supplement that prevents the drop of energy output during a reduction regime (34).

The mechanism of calcium effects is complex and affects several levels. The most important route is its influence on circulating 1.25-dihydroxyvitamin D levels, which stimulates the entry of Ca^{2+} into adipose cells. Intracellular Ca^{2+} is a key regulator of lipid metabolism; its elevated values stimulate the expression and activity of lipogenic enzymes and reduce lipolysis with the consequence of increased accumulation of fat in adipocytes. The suppression of 1.25-dihydroxyvitamin D by a diet with a high calcium content leads to a smaller penetration of Ca^{2+} into the cells and thus also to a smaller accumulation of fat in adipocytes. Since intracellular Ca^{2+} also has a relation to hypertension, insulin resistance and hyperinsulinemia, calcium intake is an important factor in the risks of metabolic diseases (35–40).

Another effect of calcium is increased fecal fat excretion. This effect is not very marked in common diet, but it could play an important role in individuals with an excessive fat intake (41).

Calcium increases also UCP2 expression (UCP2 = uncoupling protein2 which facilitates heat generation in mitochondria; it is found mostly in white adipose tissue), thus stimulating thermogenesis (1). Studies have been carried out comparing the influence of a high-fat diet with varying calcium content on UCP3 expression (UCP3 affects fatty acid oxidation; it is expressed mainly in the skeletal muscle and brown adipose tissue). The results show that calcium increases UCP3 expression in the skeletal muscle through the elevation of serum leptin and free T3 levels (1, 43).

The first studies on the influence of calcium on body weight regulation were carried out on transgenic mice that express agouti protein in the adipose tissue. Under ordinary circumstances the weight of these mice is normal, but induced hyperinsulinemia (caused by insulin itself or by a high dietary carbohydrate intake) makes them fat. Also a high fat and high carbohydrate diet with low calcium intake induced wight gain while $[Ca^{2+}]i$ rose . The switch to a calcium-enriched diet led to a decrease of weight; the decrease was more marked when the calcium supplied was of dairy origin. A similar situation has been described in experiments with a weight reducing diet; a higher calcium diet led to a greater decrease of weight, fat mass and also normalization of $[Ca^{2+}]i$ (36).

However, the studies on the effect of calcium on weight reduc-

Tab. 1. Correlation of body mass changes with changes in nutrient intake in obese patients followed for 3-6 months.

	r	P
fat intake	0.220	0.002
phosphorus intake	0.195	0.006
protein intake	-0.289	0.000
calcium intake	-2.210	0.003

tion in people are not so unequivocal. Some studies have provided evidence of a negative correlation between calcium intake and both BMI and the amount of body fat (44, 45). Another studies investigated the relation between calcium intake and fat oxidation. The real calcium intake correlated positively with fat oxidation during the course of 24 hours, both in sleep and during moderate physical activity. In this case, dairy product calcium was not more effective than calcium of other origin (46).

In a recent pilot study including 208 obese individuals (BMI: 40.0±7.6, weight: 112.8±25.6, age: 46.7±12.3) we found, over a 3- to 6-month weight reducing regime, a positive correlation between body weight changes and change of fat and phosphate intake, and a negative correlation between body weight changes and change of protein and calcium intake (Tab. 1) (47). On the other hand, the preliminary results of our intervention study, which took place over a period of three weeks, did not show any differences in weight decrease in dependence on calcium intake. The patients received a low calorie, calcium deficient (351 mg Ca/day) diet combined either with placebo or calcium at a dose of 500 mg/day. The calcium was provided in the form of calcium carbonate or of Lactoval, which is a calcium of dairy origin. The groups substituted with calcium showed greater preservation of lean body mass during the weight reduction regime.

Vitamin A and its derivatives (retinoid) are another factor that probably influences body weight. These substances are indispensable for embryonic development, reproduction, hematopoiesis, vision and differentiation of epithelial and mesenchymal cells. The studies show that they also play a role in the regulation of fat stores due to their effect on the differentiation of adipocytes, thermogenesis and fat oxidation.

In the case of vision, the main retinoid is retinol, other functions are facilitated by retinoic acid (RA), which occurs in two biologically active isomers, all-trans RA and 9-cis RA. RA is associated with the regulation of the energy metabolism which is caused by its ability to induce gene expression for UCP 1–3. RA also inhibits adipocyte differentiation (48).

The study, which was performed at our center in 2003, monitored the relationship between energy metabolism and vitamin A intake. Indirect calorimetry was carried out in 239 obese patients; vitamin A intake was evaluated from one-week dietary records by the Nutrition software. However, the association between vitamin A intake and resting energy expenditure and the respiratory quotient has not been revealed (49).

FINAL RECOMMENDATIONS

The optimal low energy diet for weight reduction should include a varied selection of foods; it should not be monotonous and should meet the following criteria:

- reduced energy intake compared to current intake or to the calculated energy expenditure by about 2.5 MJ;
- reduced fat intake (20 - 30% of the total energy intake);
- higher content of monounsaturated and polyunsaturated fats:
  - monounsaturated fats 15 or more %,
  - the n-6/n-3 ratio should be 4–5:1,
  - unsaturated fats below 6–7 %;
- cholesterol intake less than 300 mg/day;
- increased consumption of vegetables, pulses and fruit. An adequate intake of whole-grain flour and bakery products should ensure the recommended intake of fiber (approx. 25 g/day);
- preferred intake of foods containing carbohydrate with a low glycemic index;
- reduced salt intake (less than 4–6 g/day).

The diet regime should always take into account the patient's age, BMI, eating habits, the aim of the treatment, concomittant diseases, and must be designed individually for each patient. The composition of meals should be varied and well balanced. The energy content of prescribed diet depends on the pre-treatment energy content; lower values are prescribed for patients with an originally low energy intake, and for individuals with a low energy expenditure (1). In conclusion, it must be emphasized that the essential requirement for a successful weight reduction is a change of lifestyle and appropriate patient@s motivation.

Abbreviations

BMI	- body mass index
$[Ca^{2+}]i$	- intracellular calcium
GI	- glycemic index
GLP	- glucagon-like peptide
HDL-cholesterol	- high-density lipoprotein cholesterol
LDL-cholesterol	- low-density lipoprotein cholesterol
FA	- fatty acid
RA	- retinoic acid
RQ	- respiratory quotient
T3 - triiodothyronine	
UCP	- uncoupling protein

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COMMENTARY

Comment on Kabrnová K., Hainer V.: "Role of Nutritional Factors in Weight Management"

The metabolism of basic energy substrates and their mutual transformations have been developing for almost 3 billion years, during the whole process of evolution, i. e. ever since the appearance of the first unicellular organisms on Earth. Approximately 4 million years ago the first ancestor of man appeared on the surface of the Earth and lived for almost 2.5 million years as a hunter. The estimated energy intake at that time was composed mainly of animal proteins and fats; sugars accounted for approximately a mere 40 per cent. The high protein intake at that period is usually put into context with the accelerated development of the brain. Fiber (up to 40 g a day) played a significant role in the nutrition of Stone Age people (1).

Dietary proteins are employed for the synthesis of autogenous proteins or they may degrade and oxidize. The organism has no reserve form of protein and the amount of muscle mass is always bound to the amount of physical activity. Unlike proteins, dietary fat is deposited very easily as an energy reserve of the organism. Following oral intake, triacylglyceroles formed by the reesterification of fatty acids in the bowel are transported by lymph into adipose tissue, where they are deposited. Fat taken in with food thus circumvents the liver and is deposited directly in adipose tissue as a supply for periods of hunger. Carbohydrates in food can be deposited directly only in glycogen; supplies of this are limited, however, and bound to the liver and muscular tissue. It seems that the formation of fatty acids from glucose is not significant in a varied diet.

During the greater part of human evolution, periods of food intake were followed by periods of hunger; fat reserves were thus obviously very important for survival. Intake of fats (usually together with proteins) had probably been given preference during spontaneous food intake. This may be the root of the enduring fondness for fats – fat has a relatively low satiating ability and its intake is associated with feelings of bliss. Dietary preference for fat and proteins seems to have had a favorable influence on the survival of the human being as an individual (especially survival during periods of food shortage).

It was not until 10 thousand years ago that man started farming. And it was probably at that time that he also started storing larger amounts of agricultural products. But even then, food was probably in short supply.

It may be claimed therefore that a surplus of food has become an attainment of the last century. Our adaptation mechanisms had thus adjusted during evolution to periods of surplus and periods of hunger, to relatively intensive physical activity (3000 kcal per day) and to a hostile environment. It is therefore no surprise that at present, when we live in a comfortable environment, have enough food and less exercise yet continue to maintain an appetite for fat salty or sweet foods, obesity is a problem. Moreover, it is evident that a genotype that prefers oxidation of sugars to fats presents more advantage from the point of view of long-term survival. The tendency towards obesity is usually accompanied by a stronger tendency to oxidize carbohydrates, as Kabrnová and Hainer have shown in their recapitulative article. In spite of having been described more than 15 years ago, this fact is still not common knowledge. This is also due to the fact that that once obesity is established, fats are the first to oxidize. Observation of the enhanced oxidation of fats in obese individuals actually resulted in the "Randel cycle" being for a long time considered the cause of insulin resistance and type 2 diabetes.

The issue of obesity and its increasing incidence not only in Europe and North America but also in the developing countries of Asia will certainly not be resolved in a simple way, as it is the consequence of the pleasant sensations associated with food intake, deeply rooted in evolution; it is the consequence, especially, of the intake of fast food (usually fat and salty, or fat and sweet) often accompanied by a natural distaste for physical activity. The treatment of obesity will therefore continue to offer many amazing and "guaranteed" therapeutic methods. Some of them (Atkins, drastic diet, bariatric surgery) reappear again and again. However, a lasting result can be achieved only by a long-term change in behavior and the adjustment of the eating habits of obese patients. Mechanisms rooted in evolution, which had probably contributed to the survival of man as a species, will continue to put up effective resistance to our efforts.

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