

Energy Metabolism in Human Obesity

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The regulation of body weight in an adult man is the result of a precise adjustment of energy intake to the level of energy expenditure (Fig. 1). If energy intake was to exceed energy output by 5% each day during one year, a daily gain of about 125 kcal/day would result which corresponds to a weight gain of 7 kg over one year. This example is given to emphasize the fact that small differences between energy intake and energy expenditure can lead to obesity.

Abnormalities in the regulatory control of appetite are certainly involved in the development of human obesity. It is surprising that the proof which supports this statement has not been supported by studies on energy intake, since these studies have reported inconclusive results and have brought much confusion in this field. The proof, that obese individuals need more energy to maintain constant their body weight and body composition than sedentary lean persons, has been obtained by accurate measurement of energy expenditure in individuals of various body weights. By using a respiration chamber [1], a technique which allows to measure

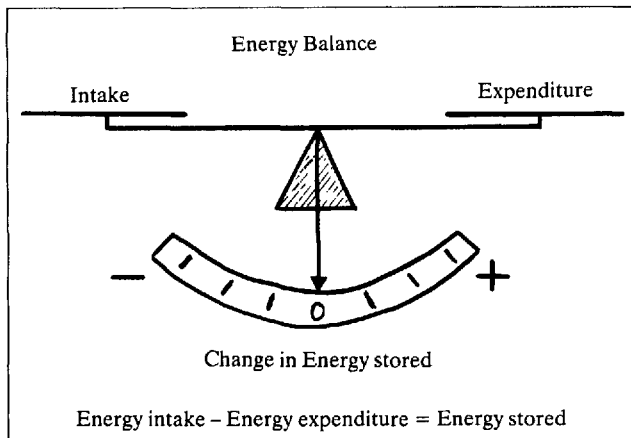


Fig. 1. Energy balance: intake of energy represents the metabolizable energy (i.e. gross energy minus losses in feces and urine); expenditure of energy represents the energy spent for basal metabolic rate, thermogenesis (i.e. diet-induced thermogenesis), and energy used for physical activity. Energy stored can be either positive when energy intake is larger than energy expenditure, or negative, when energy intake is smaller than energy expenditure.

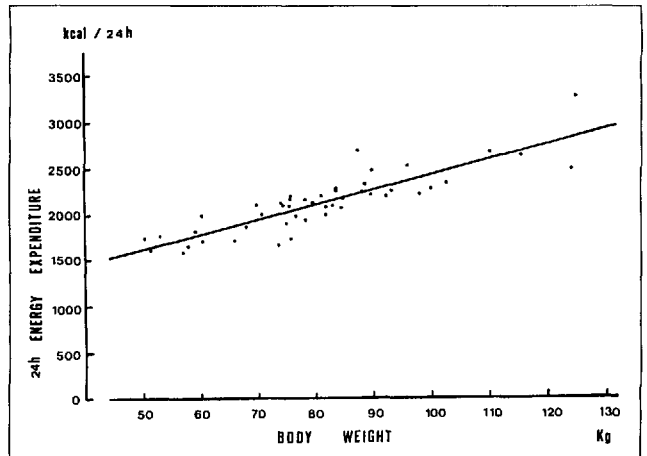


Fig. 2. 24-hour energy expenditure of 48 subjects measured in a respiration chamber plotted against body weight. A linear relationship is obtained showing that the greater the body weight, the larger the energy expenditure. Body weight is therefore a good predictor of total energy expenditure in sedentary subjects.

the energy expenditure of a subject who is free to move and whose physical activity is ad libitum, we have clearly shown that the overall energy expended over 24 hours is proportional to body weight, i.e. the more severe the obesity, the greater the energy expenditure [2] (Fig. 2). According to the first principle of thermodynamics, if body weight and body composition are stable, energy intake must match the level of energy expenditure; therefore obese individuals must eat more food energy than lean sedentary control subjects to maintain their body weight.

The elevated energy expenditure of obese subjects is partially due to their greater fat free mass than that of nonobese individuals. Numerous studies have shown that the basal metabolic rate (BMR) predominantly depends on the size of the fat mass. Since obese patients not only have an increased fat mass but also an enlarged lean body mass (due to an increase in muscle mass and other tissues (Fig. 3), their BMR is larger than that of lean controls (Fig. 4). Another factor which contributes to a large total energy expenditure in obese subjects is the energy cost of weight bearing activities such as walking and standing, since this cost is related to body weight.

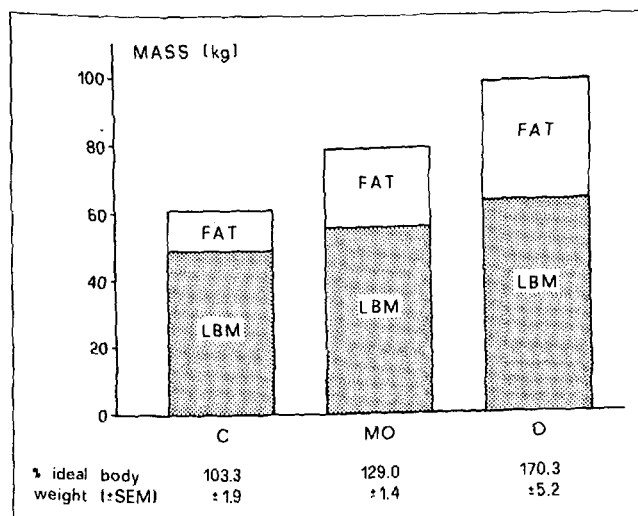


Fig. 3. Composition of body weight in three groups of women: C = control women with mean body weight 103% of ideal body weight; MO = moderately obese women (129% of ideal body weight); O = obese women (170% of ideal body weight). LBM = lean body mass. Note that the increase in the fat mass in MO and O women is accompanied a concomitant increase (but less pronounced) in lean body mass.

Dietary-induced Thermogenesis

The fact that obese subjects expend and need more food energy than lean sedentary individuals does not rule out the possibility that an alteration of the thermogenic response to food ingestion may favour energy gain and the development of obesity. After a meal, there is a rise in energy expenditure which has been called the thermic effect of food, the diet-induced thermogenesis or the thermogenic response to a meal. The thermogenic response to meals or to single nutrient loads have been extensively studied in control, obese and noninsulin-dependent diabetic patients. The possible contribution of a thermogenic defect in the etiology of obesity is a controversial issue [2]. It is therefore germane to summarize our present knowledge about the mechanisms of dietary thermogenesis in control subjects, before discussing the arguments in favour or against an involvement of thermogenic defect in the development of obesity.

Dietary thermogenesis includes two components: the "obligatory" costs of digesting, absorbing, processing and storing the nutrients, and a "facultative" component which involves the activation of the sympathetic nervous system [3]. The mean overall cost to synthesize one mole of ATP is about 20 kcal. Depending upon the number of moles of ATP used in the different obligatory processes of nutrient digestion, processing and storing, it is possible to calculate the theoretical cost for the thermogenic response to the administration of each single macronutrient. The cost of convert-

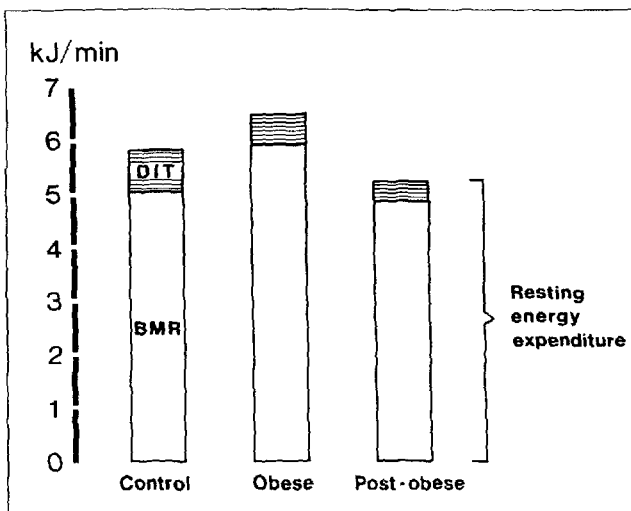


Fig. 4. Basal metabolic rate (open columns) and dietary-induced thermogenesis (DIT) (hatched columns) measured in kJ/min in a group of 17 control subjects (body weight 63 ± 2 kg) and a group of 12 obese subjects (body weight 83 ± 1 kg). The same obese individuals were studied after a mean weight loss of 15 ± 2 kg consecutive to a 17 \pm 3 week hypocaloric diet followed by 4 weeks of a maintenance diet (i.e. postobese). Dietary-induced thermogenesis was measured during three hours following a 100 g oral glucose load. The resting energy expenditure (BMR + DIT) was greater in the obese than in the control subjects ($p < 0.05$) but the resting energy expenditure was lower in the postobese group than in the control group ($p < 0.05$). These results show that the resting energy expenditure of obese subjects after weight loss is markedly reduced. They require less energy to maintain their new body weight than before, when they were obese.

ing glucose to glycogen corresponds to about 5% of the glucose energy content, whereas the cost of lipogenesis from glucose represents the equivalent of 24% of the energy content of glucose converted into lipid. The cost of digesting, absorbing and storing ingested fat corresponds to 2 to 4% of their energy content, the value depending upon the fraction of plasma free fatty acids removed by the liver and esterified in the form of lipoprotein triglycerides. Finally, protein ingestion induces the largest "obligatory" metabolic response amounting to about 25 to 30% of the ingested energy, due to the high cost of peptide bond synthesis, and to the cost of gluconeogenesis and ureogenesis.

The thermogenic response to meal ingestion that is in excess of the energetic cost of digesting, absorbing and storing the nutrients has been called "facultative" thermogenesis. Factors which are involved in "facultative" thermogenesis include recycling of three carbon compounds and stimulation of sympathetic activity. The

latter mechanism is supported by the increase in plasma norepinephrine plasma levels and the increase in the appearance rate of norepinephrine during hyperinsulinemic euglycemic clamps. The role of increased sympathetic activity in eliciting a part of the thermogenic response to glucose/insulin administration is further supported by recent reports showing that β -adrenergic blockade with propranolol induces a significant reduction in energy expenditure [4].

A low thermogenic response to glucose or to meal ingestion has been observed in most obese subjects, but conflicting results have also been published [5]. Glucose- and diet-induced thermogenesis are blunted in obese patients with insulin resistance [6]. Thus, in these patients, a lowered thermogenic response to a calorie excess can be an important mechanism which favours the storage of energy (Fig. 5).

The mechanisms that are responsible for a defective thermogenic response to meal ingestion in obese individuals include insulin resistance [6] and a blunted response of the sympathetic nervous system to food intake [7]. Insulin resistance is responsible for a decreased rate of tissular glucose uptake after a meal; this is accompanied by a reduced rate of glucose storage as glycogen in muscles with an economy of energy since glycogen synthesis is an energy-consuming process. Thus, a fraction of the absorbed glucose remains in the extracellular space and glycemia increases. This unstored glucose is available for further uptake and oxidation by various tissues, without the need of previous glycogen synthesis. A role for a defective response of the sympathetic nervous system is suggested by the fact that plasma norepinephrine flux failed to increase in obese subjects in response to ten-day periods of overeating whereas it increased in normal-weight subjects [7].

It is interesting to know whether there are mechanisms to oppose body weight gain in normal weight individuals under conditions of positive energy balance due to overfeeding. Most studies show that the "facultative" component to diet-induced thermogenesis may play a role to increase energy expenditure, especially when an excess carbohydrate load is chronically ingested [8]. This mechanism seems to be less efficient in some obese individuals with a reduced thermogenic response.

Energy Expenditure after Weight Loss

The major problem in the treatment of obesity is relapse and weight gain following weight loss: this occurs in the vast majority of patients [9]. Body weight loss, induced by a hypocaloric diet, is accompanied by a decrease in 24-hour energy expenditure; a diminution in body weight influences both the resting metabolic rate and the energy cost of physical activity. The composition of weight loss is approximately 75% fat and 25% fat-free mass, and the decrease in resting metabolic rate is related to the loss of fat-free mass. The total economy of energy induced by weight loss is

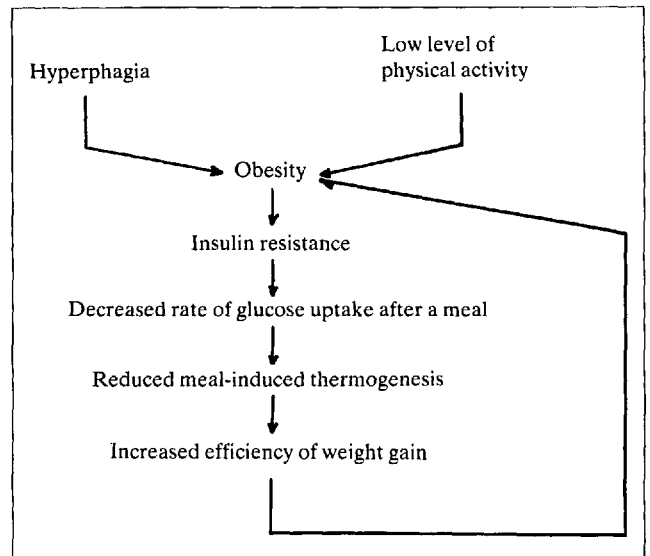


Fig. 5. Schematic representation of the consequence of a reduced meal-induced thermogenesis on body weight gain. Recent studies show that a certain degree of hyperphagia and a low level of physical activity are involved in the development of obesity (2, 5).

about 20 to 25 kcal/kg weight loss per day. This means that after a weight loss of 20 kg, the new maintenance energy requirements is 400 to 500 kcal/day less than before weight loss [2]. Failure to decrease the every day energy intake accordingly will necessarily result in relapse of body weight gain.

Figure 4 shows the decrease in resting energy expenditure in a group of twelve obese subjects after a mean weight loss of 15 ± 2 kg. This figure shows that the reduced thermogenic response to meals ingestion in obese subjects remains lower than normal in the same patients after weight loss [10]. Thus, the three components of energy expenditure, i.e., basal metabolic rate, the thermic effect of food and the energy cost of physical activity, contribute to an economy of the expended energy after weight loss [11]. In formerly obese women who have reached a normal body weight after a prolonged hypocaloric diet, the overall energy expenditure was found to be lower by 250 to 300 kcal/day than that of control female volunteers, of similar body weight [11]. If the formerly obese women were to eat the same amount of food energy as their matched lean controls, they would be in positive energy balance and gain weight until the rise in fat-free mass stimulates energy expenditure sufficiently to reach energy balance.

In conclusion, obese patients expend more energy than lean sedentary controls. A mild hyperphagia is therefore required to maintain body weight and body composition above normal values. However, many obese subjects exhibit thermogenic abnormalities which are

still present after weight loss and that may favour the relapse of body weight gain after cessation of hypocaloric therapy.

The practical implications of these findings can be summarized as follows:

1. The energy requirements of obese individuals needed to maintain their body weight and body composition constant are larger than that of sedentary lean individuals. Most obese patients expend more than 2000 kcal/day. Therefore, it can be predicted that all obese patients will lose weight under conditions of hypocaloric diets providing 1000 to 1200 kcal/day.
2. Insulin resistance is a factor that favours weight gain by decreasing the diet-induced thermogenesis.
3. The new energy requirements of obese patients after a period (or periods) of hypocaloric diet is much lower than the mean energy intake which was needed to maintain the obese state. Patients after weight loss have to change their previous eating behaviour by decreasing the amount of food consumed each day. The practical advice that can be given is a reduction of fat intake, whereas carbohydrates are to be reduced in a smaller proportion [12].
4. A high carbohydrate low-fat weight maintenance diet, after body weight loss, has the advantage of increasing the food induced thermogenic response. This diet can be useful to maintain the new body weight after a period of body weight loss [12].

Summary

Obesity results from a chronic imbalance between energy intake and expenditure. Accurate measurements of total energy expenditure of lean and obese individuals with a respiration chamber have clearly shown that obese individuals expend more energy than lean sedentary subjects. Studies on the body composition of obese individuals reveal that not only the fat mass is enlarged, but the fat-free mass is also increased as compared with that of lean subjects. Since basal metabolic rate is proportional to the fat-free mass, obese subjects have a greater basal metabolic rate than lean controls. The energy cost of weight bearing activities such as walking and standing is related to body weight, and is therefore increased in obese individuals.

The thermogenic response to food ingestion, the diet-induced thermogenesis, has been found to be reduced in some groups of obese people, but not in all obese individuals. The thermic effect of glucose or to meal ingestion is blunted in obese subjects with insulin resistance. Any alteration in thermogenic responses to a caloric excess can be important to store or to oxidize part of the excessive energy intake. After weight reduction in obese subjects due to a hypocaloric diet, the total 24-hour energy expenditure decreases by 20 to 25 kcal/day for each kilogram of weight loss. Failure to adapt the every day energy intake accordingly will result in body weight gain and relapse of obesity.

Résumé

Métabolisme énergétique dans l'obésité humaine

L'obésité résulte d'un déséquilibre chronique entre apports et dépenses d'énergie. Des mesures précises de la dépense énergétique de sujets normaux et obèses en utilisant une chambre calorimétrique ont clairement montré que les sujets obèses dépensent davantage

d'énergie que les sujets non obèses sédentaires. L'étude de la composition corporelle des obèses montre que non seulement la masse adipeuse est augmentée, mais que la masse de tissus maigres est aussi plus importante que celle de sujets non obèses. Le métabolisme basal étant proportionnel à la masse de tissus maigres, il s'ensuit que les obèses ont un métabolisme basal plus élevé que celui des sujets non obèses. Le coût énergétique de plusieurs activités physiques, telles que la marche, la station debout, est fonction du poids corporel; il est donc augmenté chez l'obèse.

La réponse thermogénique à la prise alimentaire est diminuée chez certains groupes de patients obèses, mais cette diminution n'est pas présente chez tous les obèses. La réponse thermogénique au glucose, ou à un repas, est diminuée chez les obèses qui se caractérisent par une résistance à l'insuline. Toute altération de la réponse thermogénique à un excès d'apports énergétiques peut influencer la part stockée ou oxydée de cet excès alimentaire. Après perte de poids chez les patients obèses consécutives à un régime hypocalorique, la dépense d'énergie totale de 24 heures diminue de 20 à 25 kcal par jour pour chaque kilogramme de poids perdu. Si l'apport alimentaire quotidien n'est pas adapté à cette diminution de la dépense, la reprise pondérale est inévitable, ce qui explique la récurrence fréquente de l'obésité après traitement.

Zusammenfassung

Energieumsatz bei Fettleibigen

Fettleibigkeit wird durch ein gestörtes Gleichgewicht zwischen Energiezufuhr und -verbrauch erzeugt. Exakte Messungen mit Hilfe einer kalometrischen Kammer haben deutlich ergeben, dass adipöse Personen einen höheren Energieverbrauch verzeichnen als normalgewichtige Personen mit passiven Lebensgewohnheiten.

Untersuchungen über die Körperzusammensetzung haben gezeigt, dass Fettleibige nicht nur mehr Fettgewebe besitzen, sondern auch mehr fettfreies Gewebe haben. Da sich der Grundenergieumsatz proportional zur Fettmasse verhält, haben adipöse Personen einen höheren Grundenergieumsatz. Der Energieverbrauch gewichtstragender Körperleistungen, wie Gehen und Stehen, steht in direktem Verhältnis zum Körpergewicht und ist somit bei Fettleibigen erhöht. Bei gewissen, jedoch nicht bei allen adipösen Personen wurde eine verringerte, auf die Mahlzeit folgende Wärmeerzeugung, diätinduzierte Thermogenese gefunden. Bei insulinresistenten Patienten konnte eine verminderte Wärmereaktion auf Glukose- oder Nahrungszufuhr nachgewiesen werden. Jede Änderung der Wärmereaktion auf eine übertriebene Kalorienzufuhr kann entweder die Ablagerung oder die Verbrennung eines Teils der überflüssigen Energiezufuhr beeinflussen. Nach Gewichtsverlust adipöser Personen durch kalorienarme Kost fällt der 24stündige Gesamtenergieverbrauch um 20 bis 25 kcal/Tag und pro verlorenes Kilogramm. Die Unfähigkeit, die Nahrungseinnahme dem neuen Zustand anzupassen, hat unvermeidlich eine Gewichtszunahme zur Folge und erklärt die häufigen Rückfälle zur Fettleibigkeit.

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