The ability to make accurate *in vivo* assessments of human energy balance lies at the core of much obesity research. It is now gaining even greater importance as it becomes necessary to integrate new genetic and molecular findings with the social and environmental conditions in which their influences are expressed. The energy balance equation has three primary components (energy intake, energy expenditure and energy stored) which can be measured using a range of techniques as shown in Table 1.

It is critical to select appropriate methods for a given experimental setting. None of the techniques are perfect but some of the imperfections can be minimised by simultaneous application of two or more methods, especially for body composition (Jebb & Elia 1995). Where this is not possible it is essential that investigators face up to the inherent limitations of the methodology. For instance, we have demonstrated that overweight and obese subjects tend to provide seriously biased under-estimates of habitual food intake and this problem also extends to post-obese subjects. Figure 1 shows the under-reporting of energy intake in relation to measured energy expenditure, corrected for changes in body weight during the measurement period (Black et al. 1993). On average the obese subjects underestimated intake by $-36\%$ and the post-obese by $-27\%$. We conclude that it is virtually impossible to obtain reliable estimates of energy intake in naturalistic behavioural studies. The discovery that obese people consume much more energy than previously acknowledged has had a profound influence on investigations of human obesity by steering the focus away from a search for energy-sparing metabolic defects and refocussing it on the dysregulation of food intake (Prentice et al. 1989).

The doubly-labelled water method, which derives accurate estimates of total free-living energy expenditure

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**Table 1** Techniques employed to measure the three primary components (energy intake, energy expenditure and energy stored) of the energy balance equation: energy intake – energy expenditure = body composition

<table>
<thead>
<tr>
<th>Energy intake</th>
<th>Energy expenditure</th>
<th>Body composition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weighed diary</td>
<td>Direct calorimetry</td>
<td>Densitometry</td>
</tr>
<tr>
<td>Diet history</td>
<td>Indirect calorimetry</td>
<td>Total body water</td>
</tr>
<tr>
<td>Food frequency</td>
<td>Whole-body</td>
<td>Total body potassium</td>
</tr>
<tr>
<td>24-h recall</td>
<td>Ventilated hood</td>
<td>Absorptiometry</td>
</tr>
<tr>
<td>Covert observation</td>
<td>Douglas bag</td>
<td>Neuron activation</td>
</tr>
<tr>
<td>Metabolic ward</td>
<td>Double-labelled water</td>
<td>Imaging (CT, MRI)</td>
</tr>
<tr>
<td></td>
<td>Labelled bicarbonate</td>
<td>Anthropometry</td>
</tr>
<tr>
<td></td>
<td>Heart-rate monitoring</td>
<td>Bioelectrical impedance</td>
</tr>
<tr>
<td></td>
<td>Actometers, pedometers</td>
<td>Ultrasound</td>
</tr>
</tbody>
</table>

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*OBESITY AND THE ADIPOCYTE*

Assessment of human energy balance

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from the disappearance rates of orally-dosed deuterium and oxygen-18, represents the most important methodological development in recent decades and has contributed to major conceptual advances in understanding energy balance in obesity (Coward 1988). A related technique, using constant subcutaneous infusions of labelled bicarbonate, can be used for shorter-term measurements (1–7 days) and is especially useful in a clinical setting (Elia et al. 1995). A recent analysis of the 319 measurements of total energy expenditure in healthy individuals in developed countries has confirmed our early observations of an increased energy expenditure in obese subjects compared with their lean counterparts (Prentice et al. 1986). Subjects with a body mass index (BMI) in excess of 35 kg/m² have a total energy expenditure of 13.51 ± 1.81 MJ/day and 17.54 ± 2.67 MJ/day for women and men respectively, whilst for those with a BMI less than 25 kg/m² total energy expenditure is 9.51 ± 1.57 MJ/day and 12.89 ± 2.59 MJ/day for women and men respectively (Prentice et al. 1996).

The most accurate way of assessing energy balance is by means of continuous whole-body indirect calorimetry over periods of 1–14 days. Calorimeter measurements inevitably represent an artificial situation, and are therefore used to test the underlying physiology in conditions where behavioural noise can be minimised. In this way it is possible to examine metabolic differences in energy expenditure between individuals, or in the same individual studied under two or more different conditions (e.g. pre- and post-weight loss (Jebb et al. 1991)). Figure 2 shows the energy expenditure of a lean and an obese subject measured during a 36-h period within a whole-body calorimeter. At all times of day and in all activities, including imposed periods of cycling and stepping, the obese subject has a higher energy expenditure than her lean counterpart.

Since subjects are captive within the chamber it is also possible to exert absolute control over energy intake or to make accurate estimates of self-selected intake in experiments where appetite is being assessed. We have studied the effect of changes in the macronutrient content of diets on intake available ad libitum (Stubbs et al. 1995a). This has shown clearly that high fat diets undermine the body’s physiological control systems, a phenomenon described as ‘passive over-consumption’. Parallel studies in free-living individuals where energy expenditure was measured by doubly-labelled water have shown that the increased level of physical activity outside the confines of the calorimeter may assist the regulatory processes, reducing the amount of fat which is stored in response to a high fat diet (Stubbs et al. 1995b).

In addition to assessing minute-by-minute energy expenditure, calorimeters allow the computation of substrate oxidation rates from the respiratory exchange ratio. The latest development, currently applied only in our Cambridge calorimeters, is the ability to assess cumulative changes in substrate balance with a precision of ± 9 g/day for the loss or gain of fat. It is now possible to consider the energy balance equation in terms of each of the individual macronutrients. We have measured the macronutrient flux in subjects who were continuously confined to the calorimeter over a 12-day period of over- or under-feeding (Jebb et al. 1996). This has demonstrated the precise oxidative auto-regulation of carbohydrate to match dietary intake, whereas fat takes a submissive role in the oxidative hierarchy of macronutrients. Fat oxidation can be predicted from the difference between the subject’s energy needs and the intake of other macronutrients. Substrate balance studies are the only method by which we can measure small changes in body composition. Even the best of the in vivo body composition methods have a precision of approximately 0.75 kg fat in an individual subject (Jebb et al. 1993).

The in vivo testing of the significance of newly discovered genetic defects putatively involved in the aetiology of human obesity can only be achieved using state-of-the-art techniques offering maximum precision and accuracy. However ultimately it will also be necessary to employ field techniques to account for the modulatory effects of the environment and individual patterns of behaviour. In these cases the precision of the technique will determine the sample size and the magnitude of the effect which can be measured.

References


