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From individual variation in energy intakes . . . to variations in energy requirements and adaptations to them

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Dr Widdowson and Professor McCance always expressed a great deal of interest in the inter-individual variability in their scientific data considering that extreme values often provided the most revealing results. Their interest developed as a result of Dr Widdowson's studies of the individual diets of men, women and children conducted in the 1930s; she later used the phrase 'nutritional individuality' to describe between-individual variability in intake and expenditure (Widdowson, 1962). This paper continues Dr Widdowson's theme of individual variability. It focuses on recent data which describe between-individual differences in daily energy expenditure, particularly the extremes, and also on the insights these have given into the measurements of energy intake (EI).

INDIVIDUAL VARIATION IN ENERGY INTAKES

Dr Widdowson's studies of energy intakes

In the first part of this century the methods used to assess diets had a number of disadvantages. Whole families were surveyed by examining household accounts and food stores. There was little or no allowance for waste, food fed to animals, or food preparation and a number of assumptions were made about the distribution of food within a household. Per capita food consumption was calculated assuming that the food eaten by women and children was some definite proportion of the food eaten by men. Many different 'man-values' and scales of family coefficients could be used and therefore the same diets could seem both adequate and inadequate (Widdowson, 1936; Davidson & Passmore, 1963). Using these methods it was impossible to measure the actual food consumption of individuals or to relate this to their health, growth or requirements, and there was no indication of the extent to which individuals might differ in food intake. The studies that Dr Widdowson conducted in the 1930s were the first attempts to make accurate dietary assessments of free-living individuals (Widdowson, 1936, 1947; Widdowson & McCance, 1936).

Sixty-three men (aged 18–69 years), sixty-three women (aged 19–62 years), 435 boys and 481 girls (at least twenty at each age from 1 to 18 years) were studied. The men and women and almost all the children were middle class and lived at home. They were deliberately selected so that food availability and choice would not be constrained by income. Dietary intakes were assessed using the 'individual method', familiar to us today as a 7 d weighed dietary record. The subjects were provided with a spring balance weighing up to 1 lb (2·2 kg) or 2 lb (4·4 kg) and accurate to ± $\frac{1}{4}$ oz (7 g), a plate and a record form. They were asked to weigh and describe all items of food and drink eaten in 1 week. Cooked, ready-to-eat food was weighed as it was served and edible leftovers were also weighed. Energy and nutrient intakes were calculated using the food composition tables recently compiled by McCance and Widdowson (Walker, 1997), and where necessary meals were specially cooked and analysed.

The publications resulting from these studies contain a wealth of detail, but only the EI will be discussed here. These averaged 3067 (SD 714) kcal/d (12·8 (SD 3·0) MJ/d) for men and 2187 (SD 388) kcal/d (9·2 (SD 1·6) MJ/d) for women. In her paper 'Nutritional individuality' Dr Widdowson wrote: 'I was at once struck by the wide variation in calorie intake from one person to another... in both sexes one person ate food which provided him or her with twice as many calories as another' (Widdowson, 1962). The frequency distributions of the adults' EI are illustrated in Fig. 1. Intakes ranged between 1772 and 4955 kcal/d (7–21 MJ/d) in the men and between 1453 and 3110 kcal/d (6–13 MJ/d) in the women. A similar degree of variability was observed in boys and girls of all ages and body weights. In 'Nutritional individuality' Dr Widdowson went on to write '...If calorie intakes are any measure of calorie requirements... then it must mean that some people require twice as many calories as others' (Widdowson, 1962).

Contemporary studies of individual energy intakes

Fig. 2 illustrates individuals' self-reported EI plotted against body weight in studies conducted in 1936 and 1996. Fig. 2(a) shows data from Widdowson's studies and Fig. 2(b) (Black, personal communication) indicates that nutritional individuality is apparent in contemporary data from similar subjects.

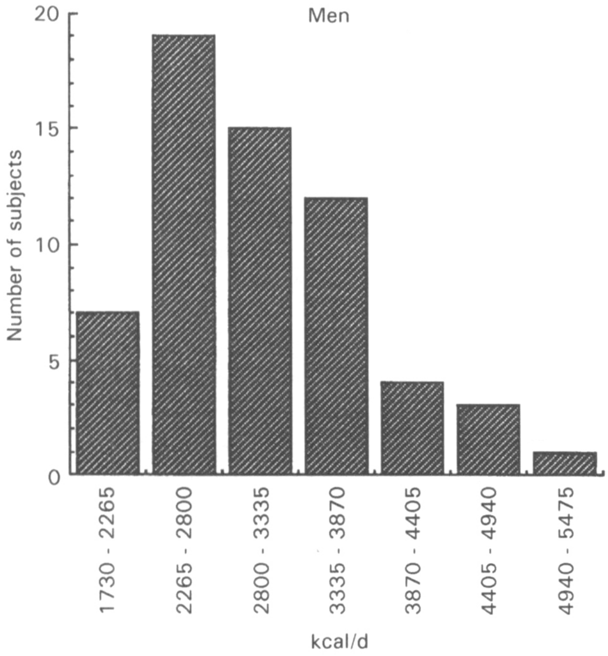
Individual dietary assessments are now routine and a variety of methods are used in a wide range of subjects and nutritional settings. The methods have been described and critically reviewed (Bingham, 1987; Borrelli, 1990). The 7 d weighed dietary record is often the method of choice since it seems to provide the best compromise between optimal precision, investigator workload and subject compliance. It is also the reference technique against which many others are compared. Until recently it was only possible to compare one form of dietary assessment with another without knowing which, if any, gave a valid result. In the 60 years since Dr Widdowson's studies, advances in methodology have been enormously hampered for lack of independent markers against which measurements could be validated.

INDIVIDUAL VARIATIONS IN ENERGY EXPENDITURE

Measurements of energy expenditure

In contrast to measurement of EI there have been major developments and improvements in methodology to measure energy expenditure (Murgatroyd *et al.* 1993). Two techniques in particular, whole-body indirect calorimetry and the doubly-labelled water method, have led to a much greater understanding of energy expenditure under various physiological and experimentally imposed conditions (International Dietary Energy Consultancy Group, 1990; Prentice *et al.* 1991; Prentice & Coward, 1992). Furthermore, because these techniques measure daily energy expenditure very accurately (±1 % and ±3 % respectively) insights have finally been obtained into the validity and interpretation of EI measurements (Black *et al.* 1993).

Whole-body indirect calorimetry. Whole-body indirect calorimetry is not a new technique (Nichols, 1994) but although the principles are the same, modern chambers bear little resemblance to those used in the first part of this century. Today, calorimeters provide subjects with a comfortable environment where they can be studied for many days. Minute-by-minute changes can be measured, enabling 24 h energy expenditure (24 h EE) to be



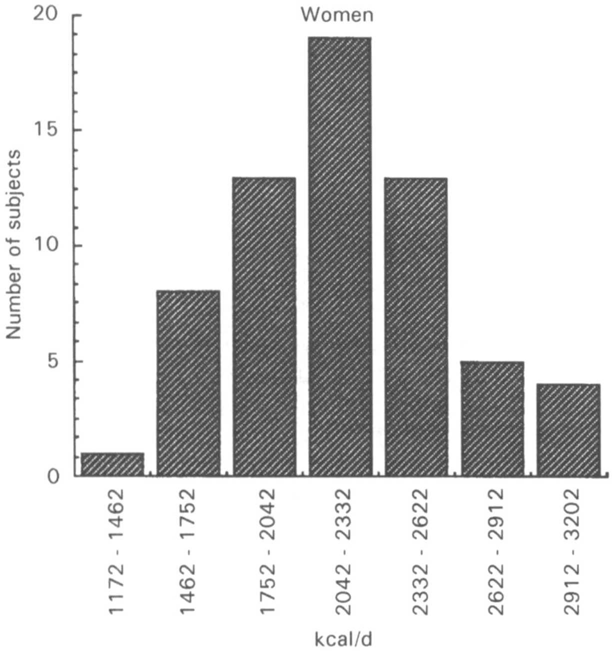


Fig. 1. Frequency distribution of energy intakes measured in sixty-three men and sixty-three women. Redrawn from the original figures (Widdowson, 1936; Widdowson & McCance, 1936).

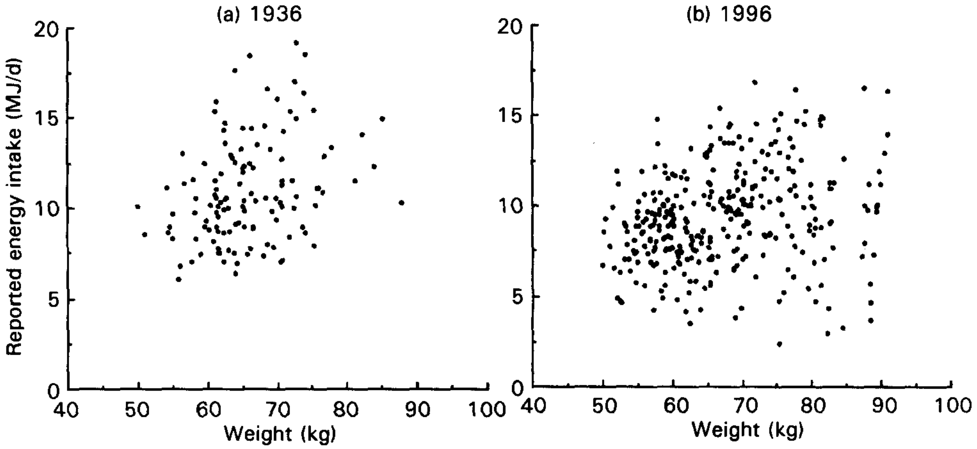


Fig. 2. Distribution of adults' self-reported energy intakes according to weight. (a) The 1936 data are from sixty-three men and sixty-three women (Widdowson, 1936; Widdowson & McCance, 1936); (b) the 1996 data are from 162 men and 233 women (A. E. Black, personal communication).

broken down into its major components (BMR; diet-induced thermogenesis, DIT; physical activity). If rigorous protocols are employed, the underlying physiology can be studied unconfounded by behavioural noise. There are about twenty whole-body calorimeters currently in use worldwide and in recent years they have been used in detailed studies of people of different ages (Bitar *et al.* 1995; Pannemans *et al.* 1995), physiological states (Ravussin *et al.* 1982; Prentice *et al.* 1989*b*; Pullicino *et al.* 1991) and/or imposed experimental conditions (de Boer *et al.* 1986; Garby *et al.* 1988; van Dale *et al.* 1989; Buemann *et al.* 1992*a,b*; Jebb *et al.* 1996). However, calorimeters are artificial environments and 24 h measurements are unlikely to represent habitual levels of energy expenditure in most healthy individuals.

Doubly-labelled water. The doubly-labelled water (DLW, $^2H_2{}^{18}O$) method for measuring energy expenditure was developed in the 1940s (Lifson *et al.* 1955; Lifson & McClintock, 1966), but for many years it was only used in small animals because ^{18}O was prohibitively expensive. Improvements in mass spectrometry in the early 1980s meant that smaller amounts of isotope could be given and the application of DLW in human studies became feasible. In contrast to whole-body calorimetry, DLW provides a measure of total energy expenditure (TEE) in free-living conditions integrated over 10–15 d. In the vast majority of subjects, therefore, this measurement is likely to be representative of their habitual energy expenditure and energy requirements. The DLW method has revolutionized studies of human energy expenditure, and over the past 15 years it has been used throughout the world by many investigators in a wide variety of subjects and circumstances (Black *et al.* 1996). Some individual data from healthy adults measured under normally active free-living conditions are illustrated in Fig. 3.

Extremes of daily energy expenditure measured in individuals

Whole-body calorimetry and DLW have been used to measure 24 h EE in a large number of individuals under a variety of conditions. So we are now in a position to use the data obtained not only to establish the range of physical activity levels (PAL) in normal healthy

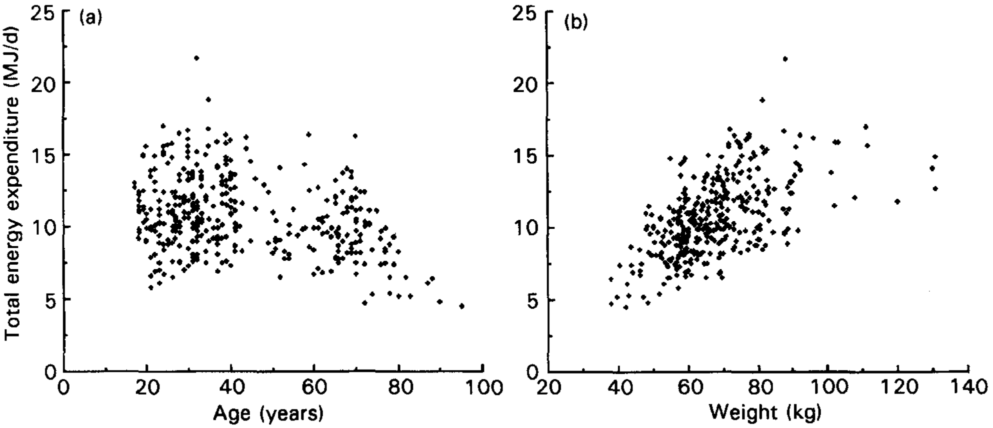


Fig. 3. Distribution of total energy expenditure measured by doubly-labelled water according to (a) age and (b) weight in 129 men and 237 women. The data are a subset of those used in a meta-analysis by Black *et al.* (1996).

people, but also the extremes of the range. The upper and lower limits of energy expenditure have been derived using data from DLW and calorimeter studies respectively.

Establishing the minimum level of energy expenditure compatible with normal life. The lower limits of 24 h EE compatible with normal life have been derived using individual data from whole-body calorimetry studies conducted in a number of different laboratories (Goldberg *et al.* 1991). In all the studies a sedentary protocol was imposed, measurements were made in the thermoneutral range (to exclude thermoregulatory thermogenesis) and EI was maintained close to energy balance (to exclude excess DIT). These protocols therefore yielded energy expenditures at or below the minimum which would be expected in healthy, free-living people.

Fig. 4(a) illustrates the close positive relationship between body weight and 24 h EE in very sedentary subjects. Although there is vertical scatter due to differences in the amount of activity imposed or allowed there is a lower limit of energy expenditure below which, regardless of body weight, 24 h EE never falls.

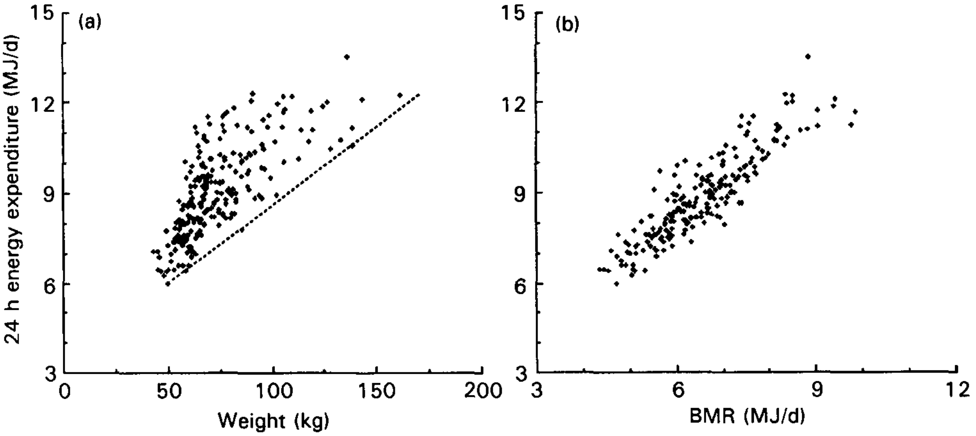


Fig. 4. Whole-body calorimeter measurements of 24 h energy expenditure plotted (a) against body weight in 241 men and women and (b) against BMR in 207 men and women (Goldberg *et al.* 1991).

PAL (24 h EE/BMR), provide a means by which the activity levels of individuals can be compared directly. Because BMR is the denominator, most of the inter-individual variability resulting from differences in weight, height, age and sex is removed. Fig. 4(b) shows the close part–whole correlation between BMR and 24 h EE from 207 measurements from a number of different calorimeter studies. The mean PAL derived from these data is 1·35 × BMR. Because of the constraints of being in a calorimeter, with respect to normal patterns of physical activity, it is highly unlikely that a healthy free-living person would have a habitual PAL lower than 1·35.

Establishing the average levels of energy expenditure compatible with normal life. Under imposed sedentary protocols in calorimeters the primary determinants of 24 h EE are body weight and BMR. In contrast, although free-living individuals may have the same weight and/or BMR, their TEE and hence PAL, will depend to a large extent on their particular occupations and discretionary activities. Free-living PAL values derived from DLW measurements of TEE and measured or predicted BMR have shown that energy expenditure can range from 1·2 to > 2·2 × BMR (Black, 1996; Black *et al.* 1996). Average PAL (derived from measured BMR) from over 400 adults measured under normal free-living conditions are illustrated in Fig. 5. In both men and women, in all age groups except > 75 years, the mean PAL is greater than 1·55, the value used by the World Health Organization to define sedentary adults.

Establishing the maximum level of energy expenditure compatible with normal life. Under free-living conditions at the upper levels of physical activity, distinctions must be made between the maximum achievable PAL over a defined period and the maximum sustainable habitual PAL assuming physical fitness and adequate food intake. The analysis of Black *et al.* (1996) suggested that a PAL of 2·5 was indicative of an extremely physically active lifestyle (for example during extended periods of training in athletes and soldiers and during peak harvest activities in subsistence farmers) and is probably the

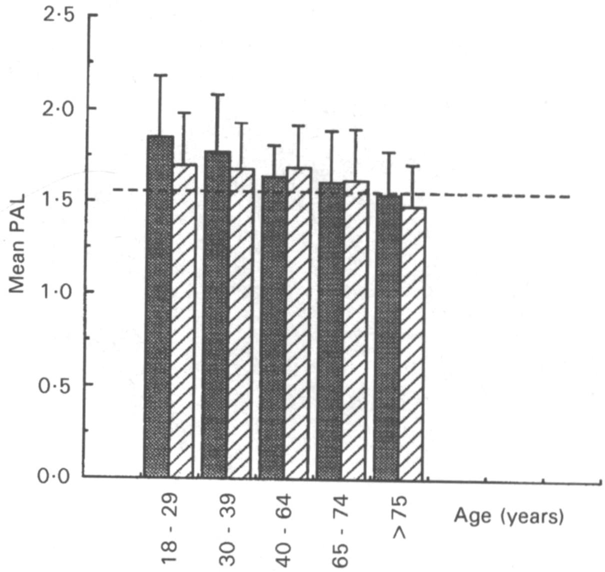


Fig. 5. Distribution of physical activity levels (PAL) derived from doubly-labelled water measurements according to age in 163 men (■) and 248 women (▨) (data from Black *et al.* 1996). The dotted line indicates the assumed PAL for sedentary adults (Food and Agriculture Organization/World Health Organization/United Nations University, 1985).

maximum sustainable in the long term. DLW measurements have also been conducted in subjects and under conditions which elicited extremely high levels of energy expenditure over relatively short periods of time. Data from some of these studies conducted in Polar explorers, mountaineers and elite athletes in competition are illustrated in Fig. 6. Under such conditions PAL were as high as 5·0 × BMR.

Critical evaluation of reported energy intakes using fundamental principles of energy physiology

Whole-body calorimetry and DLW studies have provided information on human energy expenditure at both extremes of physical activity. The limits of energy expenditure can be used as independent points of reference for critically examining EI data.

In the past 10 years a number of studies have shown that mean EI measurements are lower than simultaneous measurements of TEE (Prentice *et al.* 1986; Bandini *et al.* 1990; Livingstone *et al.* 1990; Schoeller *et al.* 1990; Lichtman *et al.* 1992; Black *et al.* 1993). DLW is too expensive and technically demanding to use routinely to validate measurements of food intake. However, on close inspection, almost all sets of EI data include results at the lower end of the range which seem patently implausible when judged against a knowledge of minimal energy requirements.

Goldberg *et al.* (1991) have proposed a method for evaluating EI data. It compares reported EI with presumed energy requirements, both expressed as multiples of BMR. Thus EI : BMR is compared with the presumed PAL of the population or individual being

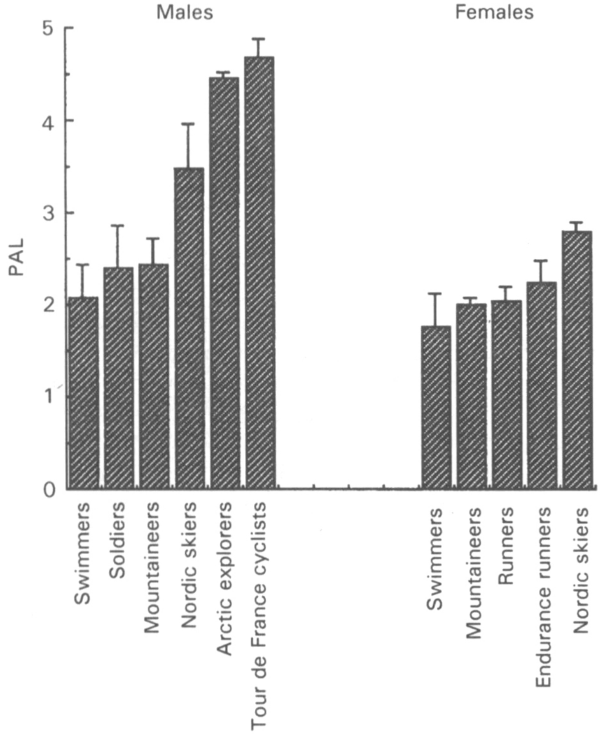


Fig. 6. Physical activity levels (PAL) derived from doubly-labelled water measurements in seventy-four men and twenty-one women with extremely high levels of physical activity (Black *et al.* 1996).

evaluated. For EI to be representative of habitual or average intake over the long term the reported intake should be greater than 1·35 × BMR. To assess whether the reported intake is a valid estimate of the actual intake as measured over a short time requires that a number of variables need to be considered (sample size, duration of assessment, intra- and inter-individual variance in EI and BMR and the expected PAL). Goldberg *et al.* (1991) derived a formula which calculates the 95 % confidence limits of agreement between EI : BMR and PAL taking all these variables into account. If reported EI : BMR falls below the lower 95 % confidence limits or cut-off points, then statistically it is highly improbable that the reported intake could represent genuinely low intakes obtained by chance.

Black *et al.* (1991) examined mean and individual EI data from a number of published studies and for each calculated the study specific cut-off limit. They used 1·55 × BMR as the 'yardstick' PAL; the value defined by the World Health Organization as a sedentary level of energy expenditure (Food and Agriculture Organization/World Health Organization/United Nations University, 1985). Their analyses showed conclusively that underreporting of habitual and actual EI is both widespread and serious even in the most carefully conducted studies. In many instances mean or individual reported EI were less than BMR. Furthermore, since mean PAL are greater than 1·55 at all ages except over 75 years (Fig. 5), the extent of underreporting has probably been underestimated.

The critical evaluation of EI data has so far been concentrated on underreporting for two reasons. First, there is a bias towards underreporting. When entire data-sets are examined, improbably low intakes from individuals are not balanced by high intakes at the upper end of the distribution and thus even mean intake data are not valid. Second, although any PAL can be assumed, until very recently the data illustrated in Fig. 6 were not available. Hence it was difficult to define an appropriate PAL for calculating upper 95 % confidence limits or cut-off points and thus identifying overreporters.

An obvious, if impertinent, question is how much of the between-individual variability in the adults studied by Dr Widdowson would now be attributed to over- or underreporting?! All individuals' absolute EI, EI/kg body weight and ages were tabulated in the original papers. It was therefore possible to derive estimated BMR values (Schofield *et al.* 1985). The distributions of EI : BMR for the sixty-three men and sixty-three women are illustrated in Fig. 7.

Nineteen women and ten men reported EI less than 1·35 × BMR. We have the benefit of hindsight and now know that 7 d are insufficient to measure the habitual EI of individuals (Bingham, 1987; Basiotis *et al.* 1989; Tarasuk & Beaton, 1991). None of the women and only one of the men reported an EI too low to have been the likely actual intake during the 7 d measurement (i.e. less than the cut-off value of 1·10 × BMR, assuming a PAL of 1·55 × BMR). Four men reported EI greater than 2·5 × BMR, the maximum likely habitual PAL of an individual.

Black (1996) has calculated the mean PAL in each third of the distribution of DLW data from almost 600 measurements. This can be used as a guide to evaluating EI when a survey has information to classify subjects into those with low, medium and high energy expenditures. The mean PAL values were 1·4, 1·65 and 1·95–2·0 respectively (Black, personal communication). For PAL of 1·55 and 2·0 the upper cut-off limits for 7 d EI measurements, calculated using the formula derived by Goldberg *et al.* (1991), are 2·2 × BMR and 2·82 × BMR respectively. A reported EI : BMR greater than 2·82 × BMR would therefore certainly represent overreporting of actual food intake. In fact none of the subjects reported EI greater than 2·9 × BMR.

After closer examination of Dr Widdowson's data it is probably reasonable to conclude that the highest and lowest reported EI were unlikely to have been habitual. However, with

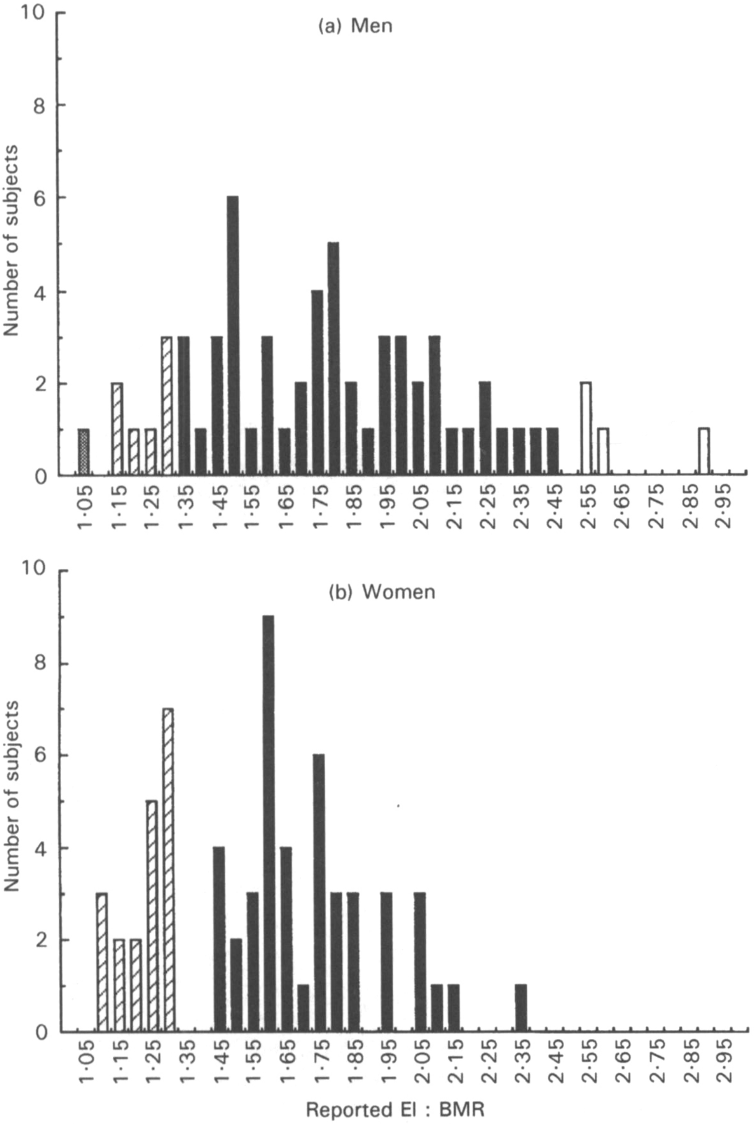


Fig. 7. Distribution of reported energy intake : BMR (EI : BMR) in (a) sixty-three men and (b) sixty-three women derived using data from Widdowson (1936), Widdowson & McCance (1936) and evaluated according to Goldberg *et al.* (1991). (▩), Reported intake which is implausible as measurement of actual intake during period of measurement (< 1·10 × BMR); (▨), reported intakes too low to be habitual (< 1·35 × BMR); (■), intakes likely to have been habitual (> 1·35 × BMR and < 2·5 × BMR); (□) intakes too high to be habitual (> 2·5 × BMR) but plausible as actual values during the period of measurement.

only one exception, they were entirely plausible as actual intakes during the period of investigation. Furthermore, there were both under- and probable overreporters and therefore the average intakes were likely to be valid. The reported EI : BMR averaged 1·81 (SD 0·41) and 1·60 (SD 0·29) for men and women respectively. It is interesting to note that crude calculations based on the subjects' occupations and associated values of energy expenditure compiled by Durnin & Passmore (1967) suggest that the mean PAL were probably about 1·80 for men and 1·65 for the women.

ADAPTATIONS TO VARIATIONS IN ENERGY REQUIREMENTS

One of McCance and Widdowson's pieces of advice to a young scientist was 'Treasure your exceptions', and 'If you get a result that does not fit in with all the others, or your results show wide variations, think about the extremes. Don't just regard them as a nuisance because they increase your standard error. They may be the most interesting part of your study' (Ashwell, 1993). A perfect example of how apt this advice is can be found in longitudinal studies of changes in BMR during pregnancy (Prentice *et al.* 1989*b*). In well-nourished women from England mean values were very close to theoretical calculations and data from cross-sectional studies. However, the standard deviation was very high, and although wide variability had been noted by other workers it had not been followed up. Closer inspection of individuals' results revealed, not noisy data, but distinct groups of 'energy-sparing' and 'energy profligate' individuals. The different metabolic responses, which were correlated to pre-pregnant body fatness, led to a very wide range in the metabolic cost and therefore energy requirements of pregnancy. This between-individual variability helped to provide an explanation for differences in mean values in the energy costs of pregnancy between different populations measured by a number of different investigators. Energy-profligate women tend to be those who are well nourished and from affluent countries, whilst energy-sparing women tend to be those who are marginally nourished and from developing countries. In the latter, energy-sparing adaptations may help to protect fetal growth (Poppitt *et al.* 1994). In the final paragraph of 'Nutritional individuality' Dr Widdowson wrote: 'Nutritional individuality as regards requirement for calories... has many important practical applications. All may be well in times of plenty,... but in times of food shortage and famine the person with the high energy requirement... must come off badly... The wide variation from one person to another in intake and expenditure of energy... makes it futile to attempt to give one single figure for requirement' (Widdowson, 1962).

THE FUTURE

A few years ago Dr Widdowson and Professor McCance expressed concern that individual variation had become a neglected issue. Whereas they had always been interested in the extremes as well as the means of the range, they felt that current researchers considered that only mean values were important (Ashwell, 1993). With respect to energy metabolism this was indeed the case in the 1980s and early 1990s and particularly so in studies which aimed to establish energy requirements or test their applicability in different conditions. Now, however, many investigators are concentrating on the sources of individual variability in intake and expenditure, from differences at a whole-body level (Hill *et al.* 1995; Prentice & Jebb, 1995; Stubbs *et al.* 1995; Lissner, 1996) to differences at the tissue and molecular levels (Ravussin & Bogardus, 1987; Bouchard *et al.* 1989; Ravussin & Swinburn, 1993; Astrup *et al.* 1994; Schneiter *et al.* 1995).

The dietary assessment of individuals, pioneered by Widdowson and McCance, is a central component of many areas of clinical research and epidemiological studies and provides vital background information when formulating allowances and making food policies. However, as Garrow (1974) stated more than 20 years ago: 'The measurement of the habitual food intake of an individual must be among the most difficult tasks a physiologist can undertake'. Black (1996) has recommended that in order for EI to be evaluated properly, dietary studies should routinely include measurements of height and weight (to estimate BMR) and some assessment of subjects' occupation and leisure activities so that an informed choice of PAL is used for comparison.

It is now generally accepted that under-reporting is a problem and researchers are examining and interpreting their data more critically (Mertz *et al.* 1991; Mertz, 1992). Whilst cut-off limits have heightened awareness about the prevalence of patently incorrect estimates of energy (and hence nutrient) intakes this must not be interpreted as suggesting that dietary surveys are a waste of time. Rather, the focus of future research should be the identification of the sources of bias which will then lead to better study designs and strategies for interpreting data. The reasons that individuals may misreport their habitual or actual EI have been discussed (Bingham, 1987; Black *et al.* 1991, 1993) but the prevalence of under- and overreporting in randomly selected populations still needs to be determined. It remains to be established if there is an observer effect which operates on everyone; if bias can be attributed to particular groups of individuals; if there is a continuum of good to poor reporters of EI and if particular meals or certain foods are misreported (Black *et al.* 1993; Lissner & Lindroos, 1994; Heitmann & Lissner, 1995).

Before Dr Widdowson's studies in the 1930s there was no indication, or indeed expectation, of between- or within-individual variability in food intake. The importance of the sources of variability which influence an individual's food intake, from meal to meal and from day to day, is now recognized and studies of the energy and nutrient intakes of individuals are returning to the fore, with an emphasis on the identification of regulatory mechanisms (de Castro *et al.* 1990; Lee *et al.* 1993; Stubbs, 1993; Hill *et al.* 1995). This is because researchers have spent many years seeking defects in the regulation of energy expenditure, i.e. hypo- and hyper-metabolism, to explain human obesity and wasting (due to disease or trauma) respectively. However, studies in which all the components of energy balance have been measured have shown that major defects in the regulation of human energy balance are more likely to be on the intake side of the energy balance equation (Prentice *et al.* 1989*a,c*; Macallan *et al.* 1995).

It has become increasingly important to conduct studies which cover a range of disciplines. In many circumstances the regulation of energy and macronutrient intake and expenditure have to be investigated simultaneously (Prentice *et al.* 1992) and such studies should also be accompanied by assessments of body composition. This is necessary both to determine the best way of expressing expenditure data and because changes in body energy stores are the end result of the differences between energy and macronutrient intake and expenditure (Jebb, 1997). The identification of leptin, the protein product of the *ob* gene, has opened up a whole new area of research in less than 2 years (Bray, 1996). Studies that integrate the regulation of intake and expenditure with genetics and molecular biology are already in progress.

The advent of the next millennium of nutrition research is only 3 years away. The mechanisms that regulate human energy balance will doubtless continue to challenge scientists for a long time beyond that.

I had many useful discussions with Alison Black and also thank her for giving me access to individual energy intake and total energy expenditure data.

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