For discussion:

Agenda Item: 5

Draft report chapter

I. Introduction

SACN Energy Requirements Working Group

Terms of reference

The Terms of Reference for the Energy Requirements Working Group are to:

- Review and agree on the interpretation of the methods, definitions and assumptions used by Committee on Medical Aspects of Food Policy (COMA) (Department of Health, 1991) and the FAO/WHO/UNU expert consultation (FAO, 2004) to agree energy requirements.

- Agree a framework by which to arrive at energy requirements for the UK population and its subgroups.

- Agree population based Dietary Reference Values for energy, and provide recommendations taking into account age, body size, levels of activity, gender and physiological state (i.e. growth, pregnancy and lactation).

- Consider the implications of these recommendations on the requirements for other nutrients.

Introduction

Background

1. The Dietary Reference Values (DRV) for food energy are used to provide guidance to consumers about how much energy they should consume to meet their needs, and, as a benchmark, to judge the adequacy of the food energy intake of the population. They are also used in clinical settings, by caterers and in food labelling (e.g. as a basis for Guideline Daily Amounts). Population targets for fat and sugar intakes are also expressed a percentage of the DRV for food energy. The DRV for food energy, therefore, needs to be as accurate as possible and any changes to the DRV would have implications for the delivery of Government policy, e.g. in relation to consumer guidance on energy and other macronutrients, fat and sugar targets, labelling and catering. .

2. The National Diet and Nutrition Survey (NDNS) series has consistently show average energy intakes to be below the DRV (Gregory *et al.*, 1995; Finch *et al.*, 1998; Gregory *et al.*, 2000; Henderson *et al.*, 2003; Ruston *et al.*, 2004). The NDNS, and other surveys of the UK population, have also show that the number of people classified as overweight or obese is increasing (data from NDNS series is given in Appendix 1). These data indicate that on average habitual energy intake is in fact above energy need. Although it is recognized that under-reporting of food intake is responsible for at least some of the discrepancy between measured energy intake and recommended energy intake, these observations have led the Food Standards Agency to question the robustness of the DRV for energy, which were last reviewed in 1991 (Department of Health, 1991).

3. The FAO/WHO/UNU has also published updated recommendations for energy intake and expenditure in the report Consultation on Human Energy Requirements (FAO, 2004). The Working Group was asked to review that FAO/WHO/UNU Energy Consultation, the evidence used in the report and its implications for UK energy recommendation.

Dietary reference values

Definition

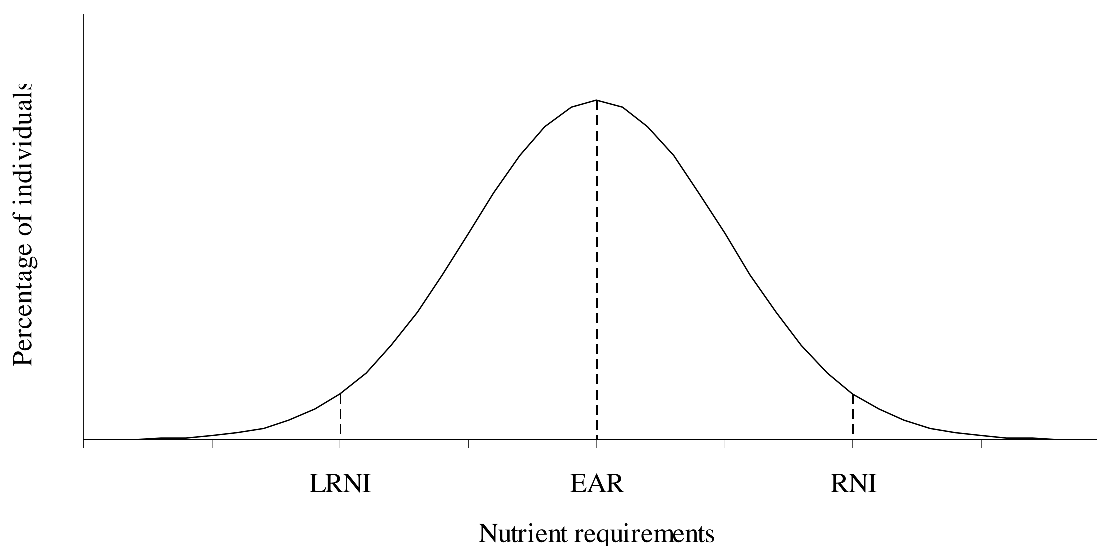
4. Information is usually inadequate to calculate the precise distribution of requirements in a group of individuals for a nutrient; however, it has been assumed to be normally distributed (Figure 1). This gives a notional mean requirement or Estimated Average Requirement (EAR) with the inter-individual variability in requirements illustrated in Figure 1. The EAR is the best statistical approximation of the nutrient requirement for any one individual in the population. The Reference Nutrient Intake (RNI) is defined as two notional standard deviations above the (EAR). Intakes above this amount will almost certainly be adequate. The Lower

Reference Nutrient Intake (LNRI) is defined as two notional standard deviations below the mean and represents the lowest intakes which will meet the needs of some individuals in the group. Intakes below this level are almost certainly inadequate for most individuals (Department of Health, 1991).

5. At higher levels of consumption there may be evidence of undesirable effects. The RNI is equivalent to the 1969 Recommended Daily Intake – that is the amount sufficient or more than sufficient to meet the nutritional needs of practically all healthy persons in a population, and therefore exceeds the requirements of most (Department of Health and Social Security, 1969). The revised nomenclature, however, emphasizes the true nature of what are estimates of reference values rather than recommendations for intakes by individuals or groups.

6. Setting the RNI at a notional two standard deviations above the EAR might, in theory, be perceived as leaving up to 2.5 per cent of the population inadequately provided for, but this is unlikely to be so in practice. In any population choosing spontaneous diets it is likely that, while the distribution stays roughly the same, the individuals comprising the extremes will vary, so that consistent intakes at the extremes are unlikely (Department of Health, 1991).

Figure 1. Assumed frequency distribution of individual nutrient requirements



Energy dietary reference values

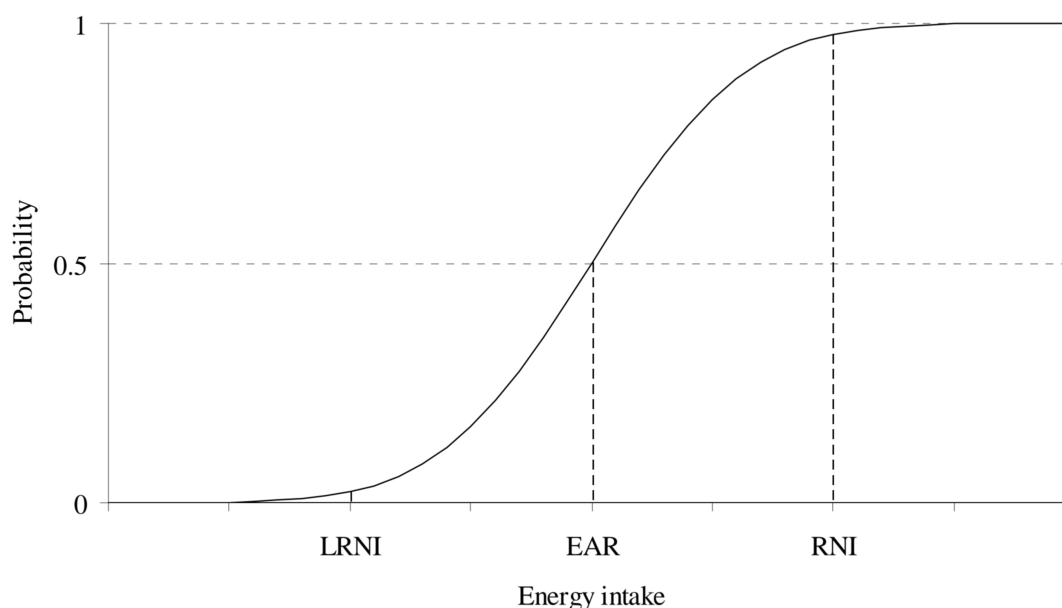
7. Energy requirements are affected by age, gender, body size and composition, pregnancy, lactation and physical activity. These characteristics are used to define population groups for whom Dietary Reference Values are given.

8. RNIs for most specific nutrients, except energy, can be set at the upper

end of the range of requirements because an intake moderately in excess of requirements has no adverse effects, but reduces the risk of deficiency in the population. For energy, however, this is not the case. Energy intakes that exceed requirements will produce a positive energy balance and could lead to obesity in the long term. An RNI for energy intakes would result in a high probability of energy excess and, hence, obesity (see Figure 2). The EAR is the point at which the probability of excessive energy intake is equal to the probability of insufficient energy intake, in a random individual within the population.

9. Recommendations for energy, therefore, have always been set as the average of energy requirements for any population group. The EARs for energy, but not LRNIs or RNIs, have been calculated (Department of Health, 1991).

Figure 2. Probability of excessive intake in a random individual at a given energy intake level



Food energy

10. Ingested food contains chemical energy – the maximum amount can be determined, by measuring the heat produced after complete combustion to carbon dioxide and water, in a bomb calorimeter. Not all combustible energy is available to human metabolism.

11. Incomplete digestion of food in the small intestine, in some cases accompanied by fermentation of unabsorbed carbohydrate in the colon, results in losses in gases (e.g. hydrogen and methane) and the faeces. Short-chain fatty acids are formed in the process, some of which are absorbed and available as energy. Most of the energy that is absorbed is

available to human metabolism; however, due to the incomplete catabolism of protein some is lost as urea in the urine. A small amount of energy is also lost from the body surface. The energy that is available to human metabolism is termed metabolizable energy and is the value quoted in the UK food composition tables (Food Standards Agency, 2002).

12. The body is able to capture some of the energy from food, through cytoplasmic glycolysis and mitochondrial respiration, resulting in the generation of an intermediary chemical form – the high energy pyrophosphate bond of adenosine triphosphate (ATP). Enzymatic hydrolysis of the high energy bond produces adenosine diphosphate (ADP), phosphate and releases energy, which when coupled to various chemical reactions drives them to completion. ATP, therefore, acts as an energy source for cellular processes and is regenerated from ADP using the energy in food. Cells require chemical energy for three general types of tasks: to drive metabolic reactions that would not occur automatically; the transport of substances across cell membranes; and mechanical work, e.g. muscle contraction. Energy is also released as heat in these metabolic processes, which maintains body temperature.

13. Not all metabolizable energy is available for the production of ATP. Some energy is utilized during the metabolic processes associated with digestion, absorption and intermediary metabolism of food and can be measured as heat production; this is referred to as dietary-induced thermogenesis, or the thermic effect of food, and varies with the type of food ingested. When the energy lost to microbial fermentation and dietary-induced thermogenesis are subtracted from metabolizable energy, the result is an expression of the ATP-producing capacity of foods, and has been termed the net metabolizable energy (FAO, 2003).

Energy yields from substrates

14. The unit of energy in the International System of Units (SI) is the joule (J) and is the energy expended when 1 kg is moved 1 m by a force of 1 Newton. Nutritionists, physiologists and food scientists are concerned with large amounts of energy and the convenient units are the kiloJoule (kJ = 10^3 J) and the megaJoule (MJ = 10^6 J). The calorie is a derived unit and a thermochemical calorie is equivalent to 4.184 J (1 kcal = 4.184 kJ).

15. The macronutrients, carbohydrate, fat, protein and alcohol, provide the energy supplied by foods. The metabolizable energy value of a food or diet is calculated by applying conversion factors for each macronutrient (see Table 1) to the amount of substrates determined by chemical analysis or estimated from food composition tables. These conversion factors are estimates of the energy content of each macronutrient and have been rounded-up for practical purposes.

Table 1. Metabolizable energy conversion factors (Food Standards Agency, 2002).

	kJ/g	kcal/g

Protein	17	4
Fat	37	9
Available carbohydrate expressed as monosaccharide	16	3.75
Alcohol	29	7

16. The amount (weight) of carbohydrate to yield a specific amount of energy differs depending on the molecular form of the carbohydrate, due to the water of hydration in different molecules. If expressed as monosaccharide equivalent, 100 g of glucose, 105 g of most disaccharides and 110 g of starch each contain 100 g of anhydrous glucose. Different energy conversion factors have to be used to convert carbohydrate expressed as weight (16.7 kJ/g, usually rounded to 17 kJ/g) and available carbohydrate expressed as monosaccharide equivalents (15.7 kJ/g, rounded to 16 kJ/g) in order to account for the weight difference between the values of these two expressions of carbohydrate.

17. Other carbohydrates may also provide energy. Non-starch polysaccharides that are fermented in the colon are an energy source. A conversion factor of 8 kJ/g (2 kcal/g) has been suggested (FAO, 2003), as have conversion factors for organic acids (13 kJ/g; 3 kcal/g), and polyols (10 kJ/g; 2.4 kcal/g). The UK food composition table energy values only include carbohydrate expressed as monosaccharide (Food Standards Agency, 2002). The COMA Dietary Reference Values report (Department of Health, 1991) noted that diets rich in non-starch polysaccharides were associated with a lower apparent digestibility of fat and protein and that this apparent loss in energy intake was similar to the net gain in energy intake from certain non-starch polysaccharides.

Energy balance and storage

18. Energy balance is the difference between metabolizable energy intake and total energy expenditure. A neutral energy balance means that energy intake is equal to energy expenditure; a positive energy balance is when energy intakes are in excess of energy expenditure; and a negative energy balance is when energy intakes are insufficient for energy expenditure.

19. Energy is stored in the body in the form of triglyceride and glycogen within adipose tissue, liver, and skeletal muscle. Triglyceride present within adipose tissue is the body's major fuel reserve. The amount of energy stored in the adipose tissue of a healthy adult of normal weight provides a large buffer capacity and is equivalent to over a month's energy requirements.

20. An individual in negative energy balance mobilizes stored energy from triglyceride and glycogen; energy is also mobilized from protein in muscle and viscera. An individual in positive energy balance stores excess food energy as triglyceride and glycogen. Muscle and liver glycogen stores are small and have a limited capacity; whereas, the capacity of the body to

store triglycerides in adipose tissue appears almost limitless.

21. Short-term, day to day energy imbalances are mostly accommodated by the deposition and mobilization of glycogen. Long-term energy imbalances are mostly accommodated by the deposition and mobilization of adipose tissue triglycerides (Schutz & Garrow, 2000). Substantial positive and negative energy balances occur in the short term in free living individuals, so it is important to consider the overall energy balance over a prolonged period of time.

Obesity

22. Problems relating to insufficient energy intakes are uncommon in the UK, and do not generally arise from insufficient food supplies, but from accompanying physical or psychological diseases. In contrast, there is a high prevalence of overweight and obesity in the population resulting from a chronic excess of dietary energy intake over energy expenditure. Overweight is defined as a Body Mass Index (BMI) in excess of 25.0 kg/m^2 and obesity is defined as a BMI in excess of 30 kg/m^2.

23. The prevalence of obesity in children aged under 11 in England increased from 9.9 % in 1995 to 13.7 % in 2003; 31.6% of boys and 30.7% of girls aged 2-15 years old were overweight or obese (Department of Health, 2004). If the current trends continue, 20% will be obese by 2010 – estimated at over 1 million children.

24. The 2004 Health Survey for England (Department of Health, 2005) estimates that 22% of men and 23.5% of women are obese; 67% of men and 57% of women are overweight. The prevalence of obesity has trebled since the 1980s, and almost 24 million adults are either overweight or obese. Obesity in both adults and children is more common among lower social groups.

25. Obesity is an important risk factor for a number of diseases (see Table 2 for an overview) and is responsible for more than 9,000 premature deaths per year in England alone. The Health Select Committee has estimated the costs of obesity at £3.3 - £3.7 billion per year and of obesity plus overweight at £6.6 - £7.4 Billion. The National Audit Office estimates that one million fewer obese people in this country could lead to around 15,000 fewer people with coronary heart disease, 34,000 fewer people developing type 2 diabetes, and 99,000 fewer people with high blood pressure (Department of Health, 2006).

Table 2. Summary of associations observed in prospective studies between obesity and subsequent ill health (Haslam et al., 2006).

Association for increased risk	Health outcome
Relative risk >3	Type 2 diabetes Hypertension Dyslipidaemia

	Breathlessness Sleep apnoea Gall bladder disease
Relative risk about 2-3	Coronary heart disease or heart failure Osteoarthritis (knees) Hyperuricaemia and gout Complications of pregnancy, e.g. pre-eclampsia
Relative risk about 1-2	Cancer, e.g. oesophagus (adenocarcinoma), colorectum, breast (postmenopausal), endometrium and kidney (Key *et al.*, 2004) Impaired fertility/polycystic ovary syndrome Low back pain Increased risk during anaesthesia Fetal defects arising from maternal obesity

Components of energy requirements

26. The energy requirement of an individual has been defined by the FAO/WHO/UNU as ‘the amount of food energy needed to balance energy expenditure in order to maintain body size, body composition and a level of necessary and desirable physical activity consistent with long-term good health. This includes the energy needed for the optimal growth and development of children, for the deposition of tissues during pregnancy, and for the secretion of milk during lactation consistent with the good health of mother and child’ (FAO, 2004).

27. The energy requirements of an individual can be divided into a number of discrete components, which can be determined separately.

Basal and resting metabolism

28. A measure of an individual’s metabolism in a basal state is termed the basal metabolic rate (BMR) and is the minimal energy requirement needed to sustain life in a resting state, e.g. for the cellular and tissue functions required for the functioning of the heart, lungs, nervous system, liver, kidneys, sex organs, muscles and skin. BMR is the energy expenditure of an individual at mental and physical rest in a temperate neutral environment, in a post-absorptive state (at least 12 hours after eating) and without having performed heavy physical exercise on the preceding day. If the measure is conducted at least 6 hours after eating or performing a rigorous physical activity, the energy expenditure is termed resting metabolic rate (RMR), as all the conditions for BMR have not been met. BMR is usually the largest component and ranges from 45 to 70% of energy requirements depending on age and lifestyle. BMR includes a small component associated with arousal, as compared to sleeping.

Dietary-induced thermogenesis

29. The metabolic processes associated with ingestion, digestion and absorption of food, and intermediary metabolism and deposition of nutrients increase heat production and oxygen consumption; this is referred to as dietary-induced thermogenesis, the thermic effect of food or postprandial thermogenesis. This leads to an increase in energy expenditure for several hour after the ingestion of food and is assumed to be about 10% of the energy requirements.

Physical activity

30. This is the most variable component of energy requirements and the energy expended depends on the type and duration of activities, but, in most individuals, accounts for 20-40% of energy requirements. Due to differences in body size and skill there is a large inter-individual variation in the energy expended for a given activity. The energy cost of different physical activities are often expressed a multiples of BMR or RMR to account for differences in body size. The metabolic equivalent (MET) values give multiples of RMR (defined as multiples of an individual's resting oxygen uptake) and are usually expressed per hour; the physical activity ratio (PAR) give multiples of BMR and are also usually expressed per hour.

Growth

31. During growth energy is deposited into new tissues and is required for the synthesis of growing tissues. The energy required for growth is highest in the first 3 months of life when it accounts for about 35% of energy requirements, by 12 months of age this has fallen to about 5% and by the second year is about 3%. Between 2 years of age and mid-adolescence 1-2% of energy requirements are required for growth, but by the late teens the amount is negligible.

Pregnancy and lactation

32. During pregnancy the energy requirements for placental and foetal growth are provided by the mother, as are the energy requirements for the growth of maternal tissues, e.g. uterus, breast and adipose tissue triglycerides. There are, therefore, increased energy costs from changes in maternal metabolism and a larger tissue mass, along with an increased energy cost of movement, particularly for weight bearing activities after 25 weeks.

33. During lactation energy is required for the energy content of secreted milk and the energy required producing the milk. Fat stores that accumulate during pregnancy provide part of this requirement.

Methodologies for estimating energy requirements

34. There are a variety of methods for estimating energy requirements. Problems of interpretation are inherent in all methods and there is a need for caution in reliance on any single method of measurement. In the 1991 DRV report (Department of Health, 1991), measures of total energy expenditure in infants and children were used to validate the use of dietary intake data in the formation of energy requirements for these groups.

Measurement of energy intake

35. In the absence of sufficient information on energy expenditure, measurements of energy intake, reported in surveys of healthy well-nourished subjects, have been used to estimate energy requirements, e.g. in infants and preschool children (Department of Health and Social Security, 1969; Department of Health and Social Security, 1979; WHO, 1985; Department of Health, 1991). The reported energy intakes of weight-stable subjects (i.e. those in neutral energy balance, where energy intake equals energy expenditure) could, in principle, be used to predict energy requirements for weight maintenance. This method is dependent on the accuracy of the dietary data.

36. A variety of dietary assessment instruments have been developed to assess dietary intake, including weighed food records, diet histories, 24-hour recalls and food-frequency questionnaires, each with many variations to suit particular investigative situations (Bingham *et al.*, 1994).

37. By comparing subjects' reported energy intake to their measured free-living total energy expenditure (TEE), the accuracy of food intake reporting has been assessed (Livingstone *et al.*, 1990; Goldberg *et al.*, 1991; Black *et al.*, 1991; Schoeller, 2002). Studies examining the accuracy of reported energy intakes, where TEE has been measured, have consistently shown under-reporting of energy intakes (Black *et al.*, 1993; Schoeller, 1995; Black & Cole, 2001; Livingstone & Black, 2003). The majority of self-reported dietary intakes are systematically biased toward the underestimation of energy intakes (Livingstone & Black, 2003).

38. Under-reporting tends to increase as children grow older (Livingstone *et al.*, 1992; Livingstone & Robson, 2000); for younger children, reporting is the responsibility of a parent or carer, and there is likely to be less access to unsupervised eating. Under-reporting is more pronounced among overweight and obese, than among lean, adults and children (Prentice *et al.*, 1986; Bandini *et al.*, 1990; Lichtman *et al.*, 1992; Buhl *et al.*, 1995; Champagne *et al.*, 1998; Goris *et al.*, 2000). Low socioeconomic status has also been shown to increase the tendency to underreport energy intakes (Stallone *et al.*, 1997; Price *et al.*, 1997), as has subject-specific bias to dietary assessment (Livingstone & Black, 2003). There also exists a small element of over-reporting within study populations (Livingstone & Black, 2003). These issues complicate the interpretation of self-reported food consumption data for the determination of estimated energy requirements.

39. Determining the energy intake of breast-fed and formula-fed infants is also not straightforward (Davies, 1998). Test weighing in breast-fed infants can be time consuming, invasive in relation to the mother and infant, and is based assumptions about the energy content of breast milk that may be inaccurate. The calculation of energy intake in formula-fed infants is easier if the child is being fed ready-to-feed formula, but if the formula is being made up by the mother or carer, large variations in energy density can be produced.

Measurement of energy expenditure

40. There are three components to TEE in humans: basal metabolic rate (BMR), dietary-induced thermogenesis and the energy expenditure of activity (physical activity). There are three approaches used to measure energy expenditure. In indirect calorimetry, oxygen consumption and/or carbon dioxide production is measured and converted to energy expenditure using formulae. In direct calorimetry, the rate of heat loss from the subject to the calorimeter is measured. A number of non-calorimetric techniques have been used to predict the energy expenditure by extrapolation from physiological measurements, e.g. heart rate, and observations (Levine, 2005).

41. There are two variants on indirect calorimetry, closed-circuit spirometry and open–circuit spirometry. Open-circuit systems comprise components to collect and mix expired air, measure flow rate, analyse gas concentrations and pump air through the system; whereas, closed-circuit systems consist of a sealed respiratory gas circuit in which gaseous concentrations are measured over a short time. The closed circuit method was widely used during the first half of the 20th century, but has been shown to overestimate measures of BMR, relative to the open circuit method (Henry, 2005). Chamber-based systems are the most accurate open circuit method for the long-term measurement of specified activity patterns, but behaviour constraints mean they do not reflect real life.

42. The components of TEE can be measured separately using direct and indirect calorimetry, but not by using non-calorimetric methods. Although TEE can be measured by some calorimetric methods it is usually only in confined subjects or, in the case of open-circuit expiratory collection, measures may be imprecise. Non-calorimetric methods allow TEE to be estimated in free-living subjects. The use of the stable isotope technique, doubly labelled water (DLW), enables TEE to be measured accurately in free-living subjects – other non-calorimetric methods, e.g. heart rate monitoring, are less accurate (Levine, 2005). Calorimetric methods are less applicable to large scale studies over periods of several days. The use of DLW techniques provides an indirect measure of energy expenditure in free living individuals integrated over days and weeks.

43. In the doubly labelled water technique, the subject consumes water containing a known concentration of the stable isotopes of hydrogen (^{2}H) and oxygen (^{18}O), based on their body weight. The isotopes mix with

normal hydrogen and oxygen in body water within about 5 hours. As energy is expended in the body, CO_2 and H_2O are released. Labelled hydrogen leaves the body as water (^2H_2O) in sweat, urine, and evaporation from the lung, while labelled oxygen leaves as both water ($H_2{}^{18}O$) and carbon dioxide ($C^{18}O_2$). The isotope concentration of subject's urine or saliva is determined by isotope ratio mass spectrometry. The difference between the elimination rates of the two isotopes relative to the baseline levels reflects the rate at which CO_2 is produced from metabolism. Oxygen consumption, and energy expenditure, can be estimated based on an assumed (or measured) respiratory quotient value (ratio of CO_2 produced to the O_2 consumed), which is determined by substrate oxidation.

44. The technique is based on the assumptions about the amount of water lost from the body by evaporation and the extent of incorporation of ^2H and ^{18}O into body tissues, especially during growth. This technique, however, provides a direct measure of TEE and is the most accurate available measure in free-living subjects. The TEE is the energy expended during a time period and, therefore, does not include the energy content of tissue laid down (growth, pregnancy, weight gain) or milk produced during lactation; these are estimated from analysis of tissue deposition and milk secretion. The TEE does include the energy required for tissue synthesis during a time period.

Calculation of energy requirements

45. As discussed above, estimates of energy requirements can be based on energy intake data. If sufficient data is available, however, energy requirements are based on measures of energy expenditure, as these provide a more direct basis for estimating energy requirements than energy intake data (Department of Health, 1991). Energy requirements have previously employed a factorial approach based on calorimetric measures of the components of TEE: BMR, dietary-induced thermogenesis and the energy expended in specific physical activities. Dietary-induced thermogenesis is normally included in any measurement or estimation of energy expenditure and is not assessed separately.

46. The compilation of calorimetric measures of BMR values and anthropometric data led to a series of predictive equations being developed for BMR based on body weight, age and gender (James, 1985; Schofield, 1985a; Schofield, 1985b). The BMR is predicted using these equations and used, in conjunction with an assessment of energy expended through physical activity, to obtain an estimate of energy requirements. The predicted BMR is multiplied by a factor that reflects the physical activity level (PAL) of the individual or group to give an estimate of energy requirements.

47. PAL is the ratio of TEE to BMR and is characterized by a description of lifestyle, e.g. non-active, moderately active, and very active. PAL is calculated from the duration of the various work and leisure activities,

which are each assigned a specific energy cost (a PAR value; a multiple of BMR for a given activity), e.g. 4 x BMR for walking on the level at an average pace. The activities are multiplied by their corresponding PAR values to give total PAR hours of activity per day and the PAL. Tables of the energy costs of different physical activities given in PAR values have been complied (Vaz *et al.*, 2005).

48. The main reason for using the BMR multiple approach to calculate energy requirements is that it is assumed to compensate for differences in body weight between individuals; however, energy expenditure in programmed work activities has been shown to influenced by body weight and body fatness, suggesting that the assumed constancy of BMR multiples across a wide range of body weights might not be valid (Haggarty *et al.*, 1997; Rosetta *et al.*, 2005). The accuracy of the MET values to estimate the energy cost of physical activity, may also be affected by adiposity (Leenders *et al.*, 2001; Byrne *et al.*, 2005; Forsum *et al.*, 2006). Energy requirements derived from factorial approaches may, therefore, be biased with respect to the body fatness of subjects, as it assumes that physical activity energy expenditure is dependent entirely on BMR or RMR.

49. The dataset upon which the predictive equations for BMR were based was mostly obtained from results in West European and North American subjects, with almost half being Italian subjects in whom BMR was estimated using a closed circuit method in the 1930s and 1940s. Questions have been raised about the universal applicability of these equations (Henry, 2005). The predictive equations proposed in 1985 (James, 1985; Schofield, 1985a; Schofield, 1985b) form the basis for the FAO/WHO/UNU energy requirements for adults (FAO, 2004) and modified versions were used for the previous UK DRV for energy in children aged 3-18 years and adults (Department of Health, 1991).

50. The factorial approach only includes discrete conscious activities in the assessment of PAL and the energy costs of all activities may not be available, which may lead to underestimation. Measures of free-living TEE do include all activities, but do not give a direct measure of the energy expenditure of physical activity or BMR. It has been suggested that the factorial approach is not based on a sound physiological model of TEE, which should be the sum of its components and not multiples of one component (Goran, 2005).

51. A more recent approach to estimating energy requirements uses multiple regression techniques to develop prediction models of total energy expenditure as a function of measured predictor variables, such as body weight, age, height etc. This approach has been developed by the compilation of measures of free-living TEE and their potential predictor variables (Goran, 2005).

52. The development of predictive equations from studies measuring TEE forms the basis of FAO/WHO/UNU energy requirements for infants, children and adolescents (FAO, 2004). For infants, DLW studies were

used, and for children and adolescents DLW and heart rate monitoring studies were used to develop datasets on which the equations were derived. The USA Dietary Reference Intakes for energy were based on datasets of DLW measures of TEE (normal weight and overweight/obese datasets) for all age/gender groups; the TEE results were presented in units of PAL (Institute of Medicine, 2005). The USA energy requirements are based on a dataset of DLW measures comprising individual TEE and ancillary data obtained directly from investigators of each study; whereas, the FAO/WHO/UNU dataset of TEE studies used mean values from each study, and weighted the results on the number of subjects, to derive the predictive equations.

Methodologies used to determine the Dietary Reference Values for energy

To be determined

Infants

Children and adolescents

Adults

Pregnancy and lactation

Factors affected energy expenditure

Body composition and size

53. Body size and weight exert marked effects on energy expenditure. The metabolically active tissue mass of the body, termed fat-free mass (FFM), comprises the organs (e.g. digestive tract, kidney, lungs, heart, liver, brain), which together constitute about 5% of body weight and contribute around 60% to the energy expended by FFM, and muscle, which constitutes about 35% of body weight and is responsible for the remaining 40% (Illner *et al.*, 2000; Muller *et al.*, 2002).

54. FFM is the principal determinant of BMR and RMR and the inter-individual variation in BMR and RMR (Nelson *et al.*, 1992; Weinsier *et al.*, 1992; Illner *et al.*, 2000; Wang *et al.*, 2000; Heymsfield *et al.*, 2002; Byrne *et al.*, 2003; Muller *et al.*, 2004; Johnstone *et al.*, 2005). Fat mass (FM), which is less metabolically active than FFM, has been observed to account for a small amount of the inter-individual variation in BMR and RMR in most studies (Fukagawa *et al.*, 1990; Cunningham, 1991; Nelson *et al.*, 1992; Weinsier *et al.*, 1992; Ferraro & Ravussin, 1992; Svendsen *et al.*, 1993; Karhunen *et al.*, 1997; Muller *et al.*, 2004; Johnstone *et al.*, 2005), but not all (Bogardus *et al.*, 1986; Segal *et al.*, 1987).

55. Metabolically, FFM is a heterogeneous compartment. Organ size, as determined by magnetic response imaging, explains a greater proportion of the variation in RMR than total FFM (Illner *et al.*, 2000). Resting energy expenditure per kg FFM is, therefore, not constant; resting energy expenditure per kg FFM decreases with increasing body weight because of a disproportional increase of muscle mass (Weinsier *et al.*, 1992). Variation in the composition of FFM may account for a small amount of the inter-individual variation in BMR and RMR (Garby & Lammert, 1994; Sparti *et al.*, 1997; Gallagher *et al.*, 1998; Illner *et al.*, 2000; Heymsfield *et al.*, 2002).

56. It has been suggested that, on a population basis and up to a moderate level of fatness (BMI < 30 kg/m^2), the relative proportions of FFM and of FM are unlikely to influence energy metabolism at rest or while physically active in ways other than through their impact on body weight (Durnin, 1996). In adults with higher percentages of body fat composition, an effect on the mechanical efficiency of movement can increase the energy expenditure associated with certain types of activity. The energy expenditures for weight-bearing activities have been observed to be affected by body mass (Prentice *et al.*, 1996b). Physical activity-related energy expenditure (PAEE) and its relation to body mass and composition depend on whether the activity is weight-bearing or not; different activities have different weight-bearing impacts on PAEE.

57. Body mass and body composition have been shown to be related to PAEE and TEE in children (Johnson *et al.*, 1998; Ekelund *et al.*, 2004) and adults

(Goran *et al.*, 1993; Schulz & Schoeller, 1994; Carpenter *et al.*, 1995; Black *et al.*, 1996; Roberts & Dallal, 1998; Rush *et al.*, 1999; Butte *et al.*, 2003; Mâsse *et al.*, 2004; Plasqui *et al.*, 2005).

58. Gains in body weight and percent fat mass are the consequence of a positive energy balance over time. Overweight and obese individuals have been shown to have higher absolute TEE than normal weight individuals, because of the effect of a higher BMR associated with increased body size, both FM and FFM (Prentice *et al.*, 1996a; Das *et al.*, 2004). This observed increase in energy expenditure was not in direct proportion to body weight since, when expressed per kg, both TEE and PAEE declined significantly with increasing BMI (Prentice *et al.*, 1996a).

Physical activity

59. Physical activity in relation to energy balance and chronic disease risk is discussed in Chapter 8. PAEE is the most variable component of TEE. Analysis of energy expenditure measures has established the extremes of human daily energy expenditure: from a TEE of about 1.2 x BMR (PAL value of 1.2) in non-ambulant subjects to a TEE of about 4.5 x BMR (PAL value of 4.5) in elite endurance athletes (Black *et al.*, 1996).

60. Occupational, leisure and home activities are major determinants of PAEE (Ainsworth *et al.*, 1993). The role of planned exercise in raising TEE depends on the intensity and duration of the physical activity undertaken and whether this affects the degree to which other physical activities are performed, i.e. an increase in one component in PAEE may be balanced by a decrease in another. Planned exercise has been observed to raise TEE in children and adults (Westerterp *et al.*, 1992; Goran *et al.*, 1994a; Eliakim *et al.*, 1996; Van Etten *et al.*, 1997; Withers *et al.*, 1998; Hunter *et al.*, 2000a; Eliakim *et al.*, 2001; Ades *et al.*, 2005), but some studies, especially where the exercise was of a relatively low intensity, have not observed planned exercise to raise TEE despite improving physical fitness (Goran & Poehlman, 1992; Treuth *et al.*, 1998; Poehlman *et al.*, 2002).

Gender

61. Variation in energy expenditure among individuals is primarily determined by differences in FFM. Women have a lower percentage FFM than men, i.e. they have a higher percentage FM, so absolute energy expenditure is lower in women. After adjustment for body size and composition, BMR and TEE have been observed, in most studies, to be lower in girls (Goran *et al.*, 1994b; Goran *et al.*, 1995; Kirkby *et al.*, 2004) and women (Ferraro *et al.*, 1992; Arciero *et al.*, 1993; Poehlman *et al.*, 1997; Carpenter *et al.*, 1998; Dionne *et al.*, 1999); however, some studies have observed no differences in energy expenditure between sexes after adjustment for FFM in children (Ekelund *et al.*, 2004) and adults (Klausen *et al.*, 1997; Blanc *et al.*, 2004).

62. In premenopausal women, a small increase in BMR/RMR, sleeping

metabolic rate and TEE during the luteal phase of the menstrual cycle, has been observed in several studies (Solomon *et al.*, 1982; Hessemer & Bruck, 1985; Webb, 1986; Bisdee *et al.*, 1989; Ferraro *et al.*, 1992; Meijer *et al.*, 1992; Howe *et al.*, 1993; Lariviere *et al.*, 1994; Melanson *et al.*, 1996; Pelkman *et al.*, 2001; Day *et al.*, 2005; Reimer *et al.*, 2005), although not all (Piers *et al.*, 1995; Diffey *et al.*, 1997; Li *et al.*, 1999; Kimm *et al.*, 2002). This suggests regulation of energy expenditure by sex hormones; in premenopausal women, pharmacological suppression of oestrogen and progesterone release has been observed to reduce RMR (Day *et al.*, 2005). There have been no longitudinal studies of energy expenditure in women across the menopausal transition to determine whether the natural withdrawal of sex hormones influences energy expenditure. It has been speculated that suppression of ovulation with contraceptives could prevent the increase in energy expenditure observed in the luteal phase (Bisdee *et al.*, 1989), but results from studies investigating the effect of contraceptive drug use on energy expenditure have been equivocal (Diffey *et al.*, 1997; Eck *et al.*, 1997; Pelkman *et al.*, 2001; Kimm *et al.*, 2002).

Age

63. BMR and RMR decline with older age and this is mainly attributable to the progressive loss of FFM observed with aging (Kyle *et al.*, 2001); however, a small decline in BMR with age, independent of any age-related changes in body composition, has been observed (Poehlman *et al.*, 1991; Vaughan *et al.*, 1991; Pannemans & Westerterp, 1995; Roberts *et al.*, 1995; Visser *et al.*, 1995; Klausen *et al.*, 1997; Piers *et al.*, 1998; Kim *et al.*, 2002; Johnstone *et al.*, 2005).

64. When the decline in body cell mass (the total mass of cells comprising the metabolically active tissue of the body) with age was measured, using the total body potassium technique, it was observed to fully account for the age-related decrease in RMR (Calloway & Zanni, 1980; Roubenoff *et al.*, 2000), whereas other measures of FFM did not (Roubenoff *et al.*, 2000). This suggests that elderly subjects may not have slower organ metabolic rates compared to younger subjects; however, one study applying an RMR-prediction model based on seven organ/tissue components to calculation of RMR in older men and women, reported that factors other than organ atrophy contributed to the lower metabolic rate of older persons (i.e. lower organ metabolic rates) (Gallagher *et al.*, 2000). In another study in healthy subjects, the age-related decline in resting energy expenditure was not associated with decreasing organ metabolic rate and was fully accounted for by both a reduction in FFM and proportional changes in its metabolically active components (Bosy-Westphal *et al.*, 2003).

65. It is unclear, therefore, whether changes in the energy expenditure with age are entirely a result of changes in body composition or whether this is related to other factors, e.g. a decline in sodium-potassium ATPase activity, decreased muscle protein turnover, and changes in mitochondrial membrane protein permeability (Wilson & Morley, 2003). A difficulty

encountered in studies of the effects of aging on the decline in BMR and RMR is the differentiation of the aging process itself from common age-associated diseases and the subsequent effects on organ metabolic rates, e.g. left ventricular hypertrophy (Bosy-Westphal *et al.*, 2003).

66. Physical activity energy expenditure has been shown to decline with aging (Wilson & Morley, 2003; Roberts & Rosenberg, 2006), but the results from studies investigating an effect of aging on diet-induced thermogenesis have been inconsistent (Melanson *et al.*, 1998; Kunz *et al.*, 2000).

Genetics

67. Genetic inheritance potentially influences all factors affecting inter-individual variation in energy expenditure, e.g. body size and composition, differences in BMR independent of body composition, ethnicity. A familial influence on RMR, independent of FFM, age, and sex, has been reported (Bogardus *et al.*, 1986; Bouchard *et al.*, 1989).

68. Studies have investigated the association between different genotypes and variation in energy expenditure. Several have investigated the role of the Trp64Arg polymorphism in the β_3-adrenoceptor gene (*ADRB3*). Although one study observed a lower RMR, adjusted for lean body mass and age, in subjects with the *ADRB3* Trp64Arg genotype relative to Trp64Trp homozygotes (Sipilainen *et al.*, 1997a), most have reported no association between the *ADRB3* Trp64Arg genotype and RMR (Gagnon *et al.*, 1996; Rissanen *et al.*, 1997; Tchernof *et al.*, 1999; Dionne *et al.*, 2001; Shiwaku *et al.*, 2003; Hojlund *et al.*, 2006), post-prandial energy expenditure (Rawson *et al.*, 2002; Hojlund *et al.*, 2006) and TEE (Tchernof *et al.*, 1999; Rawson *et al.*, 2002).

69. A polymorphism that leads to a three-amino acid deletion in the α_{2b}-adrenoceptor was associated with a lower BMR in subjects homozygous for the short allele (Heinonen *et al.*, 1999), but in a subsequent study no association was observed (Dionne *et al.*, 2001).

70. A polymorphism in the β_1-adrenoceptor (Gly389Arg *ADRB1*) was not observed to be associated with RMR (Dionne *et al.*, 2002) and no independent contribution of the Gly16Arg polymorphism of the β_2-adrenoceptor gene (*ADRB2*) to the variation in thermogenic response to a high-carbohydrate meal was demonstrated either (Oomen *et al.*, 2005).

71. Other studies have investigated the role of genetic variation in the leptin receptor gene (*LEPR*) on energy expenditure. The *LEPR* Gln223Arg polymorphism was observed to be associated with TEE and PAL in one study – homozygotes for Arg223Arg had a lower TEE and PAL (Stefan *et al.*, 2002) – but other studies failed to observe an association (Wauters *et al.*, 2002; Loos *et al.*, 2006). RMR has been associated with the *LEPR* Lys656Asn polymorphism, with the Asn656Asn homozygotes having a higher RMR compared to the other two genotypes (Loos *et al.*, 2006), but no association was observed in another study (Wauters *et al.*, 2002).

72. Several studies have investigated the association between the mitochondrial uncoupling protein gene (*UCP*) variants and energy expenditure. A polymorphism in *UCP1* gene (*-3826A>G*) was identified, but no association with RMR was observed (Oppert *et al.*, 1994). Other studies have also failed to observe an association between this polymorphism and energy expenditure (Valve *et al.*, 1998; Ukkola *et al.*, 2001), however, in subjects with both the *UCP1 -3826A>G* and the *ADRB3* Trp64Arg genotypes a lower BMR, adjusted for FFM, age and sex, was observed relative to the subjects without these polymorphisms. A lower thermic effect of food after the high fat, but not a high carbohydrate, meal was observed in subjects with the *UCP1 -3826A>G* genotype relative to the other genotypes (Nagai *et al.*, 2003).

73. A study of the linkage relationships between 3 microsatellite markers that encompass the *UCP2* gene location on 11q13 with RMR, concluded that they were linked to RMR (Bouchard *et al.*, 1997). One study identified three polymorphisms, informative for association studies, in the *UCP2-UCP3* gene cluster (Walder *et al.*, 1998). Heterozygotes for two *UCP2* gene variants (Ala55Val and a 45 base pair insertion/deletion in the 3'-untranslated region of exon 8) had higher sleeping metabolic rates, adjusted for fat-free mass, fat mass and sex, than homozygotes; the UCP3 variant (*C>T* silent polymorphism, Tyr99Tyr) was not associated with metabolic rate.

74. In subsequent studies, the *UCP2* Ala55Val polymorphism was not associated with BMR or RMR (Klannemark *et al.*, 1998; Yanovski *et al.*, 2000; Ukkola *et al.*, 2001; Kimm *et al.*, 2002; Maestrini *et al.*, 2003); however, a lower sedentary TEE, adjusted for fat-free mass, fat mass, and spontaneous physical activity, was observed in the Val55Val homozygotes relative to the other genotypes (Astrup *et al.*, 1999). In a study of energy expenditure during bicycling, subjects with the Val55Val *UCP2* genotype had higher exercise efficiency across the three different work levels than subjects with the Ala55Ala genotype (Buemann *et al.*, 2001).

75. The 45-base pair deletion/insertion in 3'-untranslated region of *UCP2* was not observed to be associated with RMR in other studies (Yanovski *et al.*, 2000; Ukkola *et al.*, 2001; Kimm *et al.*, 2002; Maestrini *et al.*, 2003), but was associated with sedentary TEE, adjusted for age, sex, family membership, FFM and FM (Kovacs *et al.*, 2005), as was the *UCP2* variant *-866G>A* in the 5' upstream region.

76. RMR was observed to be lower in subjects with the *CC* genotype of the *UCP3 -55C>T* polymorphism in one study (Ukkola *et al.*, 2001), but another study found no association with this genotype(Kimm *et al.*, 2002); however, a *C>T* silent polymorphism (Tyr210Tyr) in exon 5 of *UCP3* was observed to be associated with RMR in African American, but not white, women; *CC* homozygotes had a lower RMR, adjusted for FFM, FM, and smoking status, than those with the *CT* or *TT* genotype. This may reflect linkage disequilibrium for a functional variant elsewhere in the *UCP2* and

UCP3 gene regions in African Americans but not in whites.

77. Genetic variants of other genes have been investigated with regard to a role in energy expenditure. Several have found associations. A higher RMR was observed in women, but not men, who were heterozygotes for the Asn363Ser polymorphism in the glucocorticoid receptor gene (*GCCR*) relative to homozygotes (Di Blasio *et al.*, 2003). Subjects heterozygous for the interleukin-6 (*IL6*) gene -174C>G promoter polymorphism were found to have a lower RMR than homozygous subjects (Kubaszek *et al.*, 2003). The melanocortin-4 receptor (*MC4R*) Val103Ile genotype was associated with a higher RMR, adjusted for age, sex, and BMI, compared to the subjects with the Val103Val genotype (Rutanen *et al.*, 2004).

78. Other studies have reported no association between RMR and genetic variants of the sodium-potassium ATPase genes (*ATP1A1*, *ATP1BL1*) (Deriaz *et al.*, 1994) or the Ala54Thr substitution in the intestinal fatty acid binding protein 2 (*FABP2*) gene (Sipilainen *et al.*, 1997b; Kim *et al.*, 2001).

79. There have, as yet, been no clearly established relationships between specific gene variants and energy expenditure, although potentially genetic inheritance is an important factor.

Ethnicity

80. Differences in body composition and FFM composition have been observed between different ethnic groups, e.g. between whites and blacks (Jones, Jr. *et al.*, 2004) and whites and South Asians (Soares *et al.*, 1998). RMR, BMR and sleeping metabolic rate, adjusted for differences in FFM and FM, have been reported to be lower in black subjects than white subjects in most studies (Chitwood *et al.*, 1996; Kaplan *et al.*, 1996; Morrison *et al.*, 1996; Albu *et al.*, 1997; Foster *et al.*, 1997; Yanovski *et al.*, 1997; Carpenter *et al.*, 1998; Forman *et al.*, 1998; Jakicic & Wing, 1998; Weyer *et al.*, 1999; Wong *et al.*, 1999; Foster *et al.*, 1999; Gannon *et al.*, 2000; Treuth *et al.*, 2000; Weinsier *et al.*, 2000; Sun *et al.*, 2001; Lovejoy *et al.*, 2001; Kimm *et al.*, 2002; Sharp *et al.*, 2002; Blanc *et al.*, 2004), but not all (Lawrence *et al.*, 1988; Kushner *et al.*, 1995; Nicklas *et al.*, 1997; Sun *et al.*, 1998; Blanc *et al.*, 2004). In one study a lower RMR and TEE was observed in African Americans after adjustment for FFM, but not trunk lean tissue (Hunter *et al.*, 2000b); equally, another study found a lower RMR, adjusted for FFM and FM, in African American subjects, but these differences were no longer evident after adjustment for regional FFM distribution (Byrne *et al.*, 2003). A racial difference in RMR, after adjustment for trunk lean tissue, was observed in one study, although this was decreased from the association observed with adjustment for FFM (Tershakovec *et al.*, 2002). The racial differences in RMR, apparent after adjustment for FFM, sex and age, were no longer significant in studies that adjusted for the mass of specific high-metabolic-rate organs (Jones, Jr. *et al.*, 2004; Gallagher *et al.*, 2006).

81. A lower TEE, adjusted for differences in FFM and FM, in African American

subjects relative to whites has been reported (Carpenter *et al.*, 1998; Treuth *et al.*, 2000) although other studies have observed no association with TEE (Kushner *et al.*, 1995; Sun *et al.*, 1998; Weyer *et al.*, 1999). As mentioned above, one study that observed a lower and TEE in African Americans relative to whites, after adjustment for FFM, found this became non significant after adjustment for trunk lean tissue (Hunter *et al.*, 2000b).

82. Differences have been observed between the BMR, adjusted for body weight, of South Asians and whites, but these became insignificant when BMR was adjusted for FFM and FM (Soares *et al.*, 1998). Differences in body composition may, therefore, be mainly responsible for the reported differences in energy expenditure between ethnic groups.

83. Because of the lack of available evidence, it is not possible to make specific allowances for different ethnicities in the energy requirements.

Endocrine state

84. As discussed above sex hormones may affect energy expenditure. Other hormones have also been implicated in energy balance.

85. Thyroid status is a major determinant of metabolic rate. Hyperthyroidism increases while hypothroidism decreases RMR (Danforth E Jr & Burger, 1984). Physiological variations in plasma concentration of the thyroid hormone, tri-iodothyronine (T_3), have been associated with between- and within-subject variations in BMR or RMR, independently of FFM, in some studies (Muller *et al.*, 1989; Astrup *et al.*, 1992; Svendsen *et al.*, 1993; Toubro *et al.*, 1996; Al Adsani *et al.*, 1997), but not all (Bernstein *et al.*, 1983; Welle *et al.*, 1990; Johnstone *et al.*, 2005). Serum concentration of thyroid hormones, RMR and TEE have been observed to decrease in some studies during energy restriction and weight loss (Vagenakis *et al.*, 1977; Jung *et al.*, 1980b; Danforth E Jr & Burger, 1984; Weyer *et al.*, 2000; Heilbronn *et al.*, 2006) and, during weight regain, increases in T_3 have been associated with increases in RMR, independently of FFM, in some studies (Rosenbaum *et al.*, 2000; Onur *et al.*, 2005), but not all (Obarzanek *et al.*, 1994; Van Wymelbeke *et al.*, 2004).

86. Plasma noradrenaline concentration has been observed to be associated with RMR, adjusted for FFM (Toubro *et al.*, 1996; Rosenbaum *et al.*, 2000), but not all studies have found this association (Obarzanek *et al.*, 1994).

87. The hormone leptin is involved in energy balance and is produced primarily in white adipose tissue; it is subject to acute regulation, particularly by the sympathetic nervous system (Trayhurn, 2001). Plasma leptin concentration is related to adiposity, but other factors also affect the inter-individual variability, e.g. women have higher plasma leptin concentrations, adjusted for FM, than men (Jequier, 2002).

88. Some studies have found positive associations between plasma leptin

concentrations and RMR, adjusted for FFM and FM (Nicklas *et al.*, 1997; Toth *et al.*, 1997; Jorgensen *et al.*, 1998), others have found negative associations (Bobbioni-Harsch *et al.*, 1999; Wauters *et al.*, 2002) or no significant association (Salbe *et al.*, 1997; Kennedy *et al.*, 1997; Roberts *et al.*, 1997; Nagy *et al.*, 1997; Filozof *et al.*, 2000; Neuhauser-Berthold *et al.*, 2000; Johnstone *et al.*, 2005; Haas *et al.*, 2005). Some of these differences may reflect problems accounting for the confounding effects of FM on plasma leptin concentrations (Neuhauser-Berthold *et al.*, 2000). Plasma leptin concentrations were positively associated with TEE, adjusted for FM, in one study (Salbe *et al.*, 1997), but no association was found in other studies (Roberts *et al.*, 1997; Nagy *et al.*, 1997).

89. Plasma leptin concentration has been observed to decrease with acute starvation, disproportionately to changes in FM (Ahima *et al.*, 1996; Boden *et al.*, 1996; Weigle *et al.*, 1997; Chan *et al.*, 2003) and increase with subsequent weight gain (Grinspoon *et al.*, 1996; Hebebrand *et al.*, 1997; Eckert *et al.*, 1998).

90. Longitudinal studies of leptin secretion during nutritional rehabilitation in anorexia nervosa patients have not observed serum leptin concentration to be associated with RMR, adjusted for FFM, during weight gain (Pauly *et al.*, 2000; Satoh *et al.*, 2003; Haas *et al.*, 2005).

91. Metabolic stress and fever have also been observed to increase BMR; this is discussed in more detail in Chapter 6 (the energy requirements for Illness).

Pharmacological agents

92. Adminstration of pharmacological doses of leptin to overweight and normal subjects was observed to have no effect on RMR (Hukshorn *et al.*, 2000; Mackintosh & Hirsch, 2001) and did not reverse fasting-induced decreases in the thyroid hormones, cortisol, growth hormone, insulin-like growth factor-1 and RMR (Hukshorn *et al.*, 2003a; Hukshorn *et al.*, 2003b); subsequently, it was suggested that leptin predominantly influences the human energy balance through appetite, but does not appear to be involved in regulating energy expenditure (Hukshorn & Saris, 2004).

93. In subjects undergoing dietary energy restriction, low-dose leptin administration (restoration of circulating concentrations to levels that were present prior to weight reduction) was observed to have no effect on RMR, but the observed reduction in TEE after weight loss was attenuated in subjects receiving leptin (Rosenbaum *et al.*, 2002; Rosenbaum *et al.*, 2005). Low-dose leptin administration was also observed to reduce the decline in plasma T_3 concentration observed with dietary energy restriction and weight reduction (Rosenbaum *et al.*, 2002). The effect observed on TEE in response to energy restriction was due predominantly to a reduction in the energy expended in physical activity, which may reflect an increased work efficiency of skeletal muscle in response to energy restriction (Rosenbaum *et al.*, 2003). Low-dose leptin administration has

been observed to reverse the decline in TEE and the increased work efficiency of muscle in response to energy restriction (Rosenbaum *et al.*, 2005). The role of leptin on energy expenditure is, therefore, unclear.

94. Smoking has been shown to increase energy expenditure to a small extent; sympathoadrenal activation by nicotine is thought to be primarily responsible for this effect (Perkins, 1992; Collins *et al.*, 1994; Kimm *et al.*, 2002). Caffeine has also been shown to increase energy expenditure to a small extent (Astrup *et al.*, 1990; Arciero *et al.*, 1995) and to have an additive thermogenic effect to nicotine (Collins *et al.*, 1994; Perkins *et al.*, 1994; Arciero *et al.*, 1995; Jessen *et al.*, 2003). Administration of alcohol was not observed to have an acute effect on energy expenditure in one study (Perkins *et al.*, 1996), but chronic alcoholics have been observed to have a higher RMR, adjusted for FFM, than healthy social drinking controls (Addolorato *et al.*, 1998a) and abstinence from alcohol reduced the alcoholics' RMR (Addolorato *et al.*, 1998b; Levine *et al.*, 2000).

95. Administration of glucocorticoids (Chong *et al.*, 1994; Tataranni *et al.*, 1996), adrenaline (Astrup *et al.*, 1991), amphetamines and novel anti-obesity drugs (Heal *et al.*, 1998) have all been shown to increase energy expenditure. Growth hormone administration may also increase energy expenditure (Wallace *et al.*, 2002), but this may be partly explained by increased FFM (Hansen *et al.*, 2005). β-blockers (β-adrenergic antagonists) have been shown to reduce RMR (Jung *et al.*, 1980a).

Environment

96. In cold-exposed adult humans, decreases in body temperature are delayed by reducing heat loss via peripheral vasoconstriction and by increasing energy expenditure by shivering thermogenesis and increased muscular activity (Haman, 2006). The maintenance of indoor temperatures to within 20-25℃ and the use of clothes to control body heat loss, however, mean that ambient temperature remains relatively constant for most people in the UK and shivering thermogenesis is not a significant contributor to energy expenditure.

97. Most studies in adult subjects in the UK and Holland suggest that short-term variation (1-3 days) in ambient temperatures of between 16-28℃ is inversely associated with energy expenditure. During the studies subjects are asked to execute the same daily activities protocol at different ambient temperatures.

98. The short-term exposure to mild cold (20-22℃ relative to 26-28℃) has been shown to produce a small increase in BMR or sleeping metabolic rate in some studies (Dauncey, 1981; Lean *et al.*, 1988), although most observe no significant increase (Blaza & Garrow, 1983; Warwick & Busby, 1990; Valencia *et al.*, 1992; van Marken Lichtenbelt *et al.*, 2001). The short-term exposure to 16℃ relative to 22-24℃ was shown to produce a small increase in sleeping metabolic rate in one study (Westerterp-Plantenga *et al.*, 2002), but not in others (Buemann *et al.*, 1992; van

Marken Lichtenbelt *et al.*, 2002).

99. An increase in sedentary TEE has been observed after the short-term exposure to mild cold: both for 16°C relative to 22 -24°C (Buemann *et al.*, 1992; Westerterp-Plantenga *et al.*, 2002; van Marken Lichtenbelt *et al.*, 2002) and for 20-22°C relative to 26-28°C (Dauncey, 1981; Blaza & Garrow, 1983; Warwick & Busby, 1990; van Marken Lichtenbelt *et al.*, 2001). Skin and core temperatures where also observed to decrease in response to mild cold (van Marken Lichtenbelt *et al.*, 2001; Westerterp-Plantenga *et al.*, 2002; van Marken Lichtenbelt *et al.*, 2002). One study, however, in the UK, observed at increased sedentary TEE at both 20°C and 30°C relative to 23°C and 26°C (Valencia *et al.*, 1992).

100. Overall, these studies suggest that the variation in energy expenditure due to differences in environmental temperature is about 2-5 per cent TEE.

101. Two studies in the USA have observed higher sedentary (Bitar *et al.*, 1999) and free-living (Goran *et al.*, 1998) TEE and sleeping metabolic rate, adjusted for fat-free mass, in spring than in autumn. A study in Dutch adults reported seasonal changes in sleeping metabolic rate that could not be explained by changes in body composition, thyroid activity, or plasma leptin concentration (Plasqui *et al.*, 2003). Sleeping metabolic rate was at it highest in the winter and lowest in the summer. No changes in TEE between season were reported (Plasqui & Westerterp, 2004).

102. It is not possible to make specific allowances for changes in ambient temperature, e.g. seasonal variation, in the energy requirements.

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