Energy expenditure in disease: time to revisit?

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Knowledge of energy expenditure is especially important in disease, and may in fact help in the understanding of the pathophysiology of wasting associated with disease. Energy requirements in a clinical setting are often 'prescribed' by health professionals, either directly through enteral or parenteral feeding, or perhaps controlled through a hospital diet. Studies initially suggested an increase in energy expenditure, and thus energy requirements, as a direct result of an increase in basal metabolic rate often seen in disease. However, many problems exist in the measurement of BMR in a disease situation, due to the effects of drugs, clinical practice, feeding or possibly anxiety either as a cause of the disease or the measurement itself. These problems could in themselves contribute to the rise in metabolism seen in disease. More recently, however, with the use of tracer techniques such as doubly-labelled water and the bicarbonate–urea method, more accurate estimates of energy expenditure, and thus energy requirements, have been made. Some such measurements have in fact shown that even with an elevated BMR, free-living total energy expenditure can in fact be reduced in many disease situations, suggesting a reduced rather than an increased energy requirement. The present review investigates measurements of total energy expenditure in disease to explore the hypothesis that energy expenditure in disease, even with an elevated BMR, can in fact be reduced due to a concurrent reduction in physical activity.

Energy expenditure: Resting metabolic rate: Disease: Energy requirements

Measurement of energy expenditure (EE) in both healthy individuals and different groups of patients is fundamental in the establishment of accurate estimates of energy requirements in both health and disease, and also provides an insight into the mechanism of the wasting process associated with disease (Nelson *et al*. 1994; Elia, 1995). Such information is clinically useful for the prescription of energy and protein nutrition, both of which aim to avoid the detrimental effects of overfeeding and underfeeding (Long *et al*. 1979; McClave *et al*. 1998).

Total EE (TEE) in its simplest form is comprised of three components, the sum of which determines the energy requirement for any individual:

1. BMR;
2. thermogenesis, usually dietary-induced thermogenesis (DIT);
3. physical activity (PA).

Previously, energy requirements in disease had been thought to be elevated due to a measured increase in BMR often observed with disease. Estimates of EE and energy intake provided by different health organizations (Department of Health, 1991) are usually given as a multiple of BMR, either measured using indirect calorimetry or estimated using standard equations (Schofield *et al*. 1985). However, prediction of TEE from BMR is liable to errors, particularly when BMR is elevated. The use of tracer techniques have shown that even when BMR is increased TEE can actually be reduced (Goran *et al*. 1994; Gibney *et al*. 1996) due to a concurrent reduction in PA (Fig. 1). Since the energy cost of PA is the most variable component of TEE, and is affected in many different ways by various diseases, TEE in clinical practice can be very variable.

Interpretation of measurements of BMR

An individual's true BMR can only be accurately measured under the strict conditions indicated in Table 1. Such conditions can be difficult to meet with patients in a clinical setting. The effects of continuous or intermittent feeding, drug administration and the stress of trauma are difficult to

Abbreviations: AIDS, acquired immune deficiency syndrome; DIT, diet-induced thermogenesis; EE, energy expenditure; HIV, human immunodeficiency virus; PA, physical activity; RMR, resting metabolic rate; TEE, total energy expenditure.

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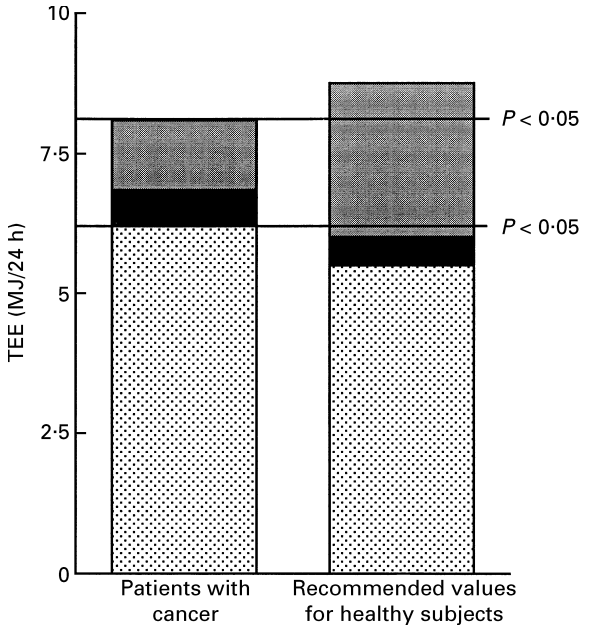

Fig. 1. Total energy expenditure (TEE) in patients with lung cancer (Gibney *et al.* 1996) compared with recommended values (Department of Health, 1991; Table 5). (▤), BMR; (▬), dietary-induced thermogenesis; (▨), physical activity. BMR was significantly increased ($P<0·05$) and TEE significantly reduced ($P<0·05$) in patients with lung cancer compared with recommended values for healthy subjects.

Table 1. Standardized conditions for measurement of BMR

Postprandial state, 12–14 h after eating
Completely relaxed and still, usually shortly after waking
Thermoneutral environment
Free from the thermic effect of drugs
20–30 min of stable measurements

Table 2. Problems associated with measurements of BMR in disease

Variations in BMR, both with respect to time of day and course of disease (ebb and flow phases)
Effect of pretest conditions on subsequent measurements
Unknown and/or unreported regimen of drugs
Unknown and/or unreported feeding regimen
Blood transfusion
Anxiety due to measurement
Spastic disorders

control, although they are known to influence BMR. As true measurements of BMR may be difficult to obtain, an alternative, i.e. resting metabolic rate (RMR), can be measured more easily, e.g. in the fed state, after drug administration or blood transfusion. It is important to note however that BMR and RMR differ by about 10–15 % (Garrow & James, 1993).

In disease BMR can deviate from normal for a number of reasons (Table 2), many of which are difficult to avoid. Berke *et al*. (1992) showed that even pretesting conditions had an effect on subsequent measurements of metabolic rate. They demonstrated that when measurements of RMR were taken under 'out patient' conditions (i.e. when individuals made their way to the test centre on the morning of the measurement), measurements of RMR were overestimated by an average of 8 %.

It is well known that ingestion of food can cause an increase in basal metabolism (Romon *et al*. 1993; Reed & Hill, 1996). The term 'DIT' encompasses the full physical response to the ingestion of food (Garrow & James, 1993). DIT is typically assumed to correspond to approximately 10 % of the energy content of a normal meal or 10 % of TEE in a weight-stable individual. Often, in clinical situations patients are maintained on strict dietary regimens, including parenteral or enteral feeding (24 h, overnight and bolus regimens). Measurements taken without proper interruption of feeding for an appropriate length of time will give a misleadingly high estimation of BMR which could be misinterpreted as being due to the hypermetabolism of disease.

Drugs can produce either an increase or a decrease in BMR and/or PA (Demark-Wahnefried *et al*. 1997; Diffey *et al*. 1997). Dempsey *et al*. (1985) investigated the effect of sedative dosage on EE in critically-ill ventilated patients. They found that as the dosage of sedative increased, EE decreased, with some individuals reaching only 60 % of predicted EE on the high doses of sedative. The same conclusion was drawn by Fried *et al*. (1989), who also showed a significant ($P<0·05$) decrease in measured EE in their sedated group.

It is a well documented fact that BMR, even in healthy individuals, can vary throughout the course of the day (Cunningham, 1980; Soares & Shetty, 1986). It is also important to note that BMR can vary not only during the day, but also considerably from day-to-day, especially in the early phases of infectious disease and trauma. Cuthbertson's (1942) classic work during the 1940s described the ebb and flow phases of injury, and the associated changes in O_2 consumption. He noted that after an initial decrease in O_2 consumption (ebb phase) individuals showed a marked increase in O_2 consumption (flow phase) which slowly returned to normal. More recently, Young *et al*. (1985) assessed repeated measurements of BMR in hospitalized patients suffering from severe trauma. Measurements of metabolic rate were initially found to be 1·5 times that of predicted BMR, only returning to approximately normal levels at 22 d after the initial trauma.

If recommendations for energy requirements are to be based on measurements of BMR, then when should the measurements be made? If a measurement is taken at the peak of metabolism, and recommendations of energy intake are based on this measurement, then for the majority of the duration of the trauma, an individual will receive an energy intake that is in excess of requirements. Conversely, if a measurement is taken at a point of reduced metabolism, then an individual may become more malnourished during the course of the illness. What must be stressed is the need to estimate the provision of energy requirements over a period of time. In essence, what we really need to know is the

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pattern of BMR in any given disease, and so should not base recommendations on single estimates of BMR, since recommendations based on single estimates of BMR are more likely to be in error.

Measurements of total energy expenditure

TEE can be measured using a number of different methods (for review, see Murgatroyd *et al*. 1993):

1. 24 h respiratory gas exchange (indirect calorimetry);
2. doubly-labelled water;
3. bicarbonate–urea method;
4. heart-rate monitoring.

Indirect calorimetry

Indirect calorimeters measure CO_2 production and O_2 consumption, which are used in the calculation of EE, in the context of TEE. To make full estimates of TEE using indirect calorimetry, subjects must be confined to a whole-body chamber to ensure a complete 24 h measurement. Measurements in such chambers give important information about EE under controlled conditions, but do not necessarily reproduce conditions in free-living circumstances. One circumstance in clinical practice, i.e. continuous ventilation in critically-ill patients, allows the measurement of 24 h TEE outside a respiratory chamber; details of such studies will be discussed later (p. 202).

Doubly-labelled water method

The doubly-labelled water method allows measurement of free-living TEE through oral administration of stable isotopes of water, ^2H_2O and $H_2{}^{18}O$ (Lifson & McClintock, 1956; Coward, 1988). The technique is based on the principle that after mixing with total body water, the ^2H is lost from the body only as water and the ^{18}O is lost both as water and CO_2. Thus, the difference in the rates of loss of isotopes from the body is due to CO_2 production, from which an estimate of TEE can be made. The disappearance from the body is typically measured over two half-lives of the isotope, about 12–14 d in adults. Although the method is non-invasive and widely used, it only gives an average daily estimate of TEE over the 14 d period and is unable to assess day-to-day variation. Validation studies against whole-body indirect calorimetry have shown the method to be accurate to within a mean (SD 10 %) (Ravussin *et al*. 1991; Klein *et al*. 1984; Schoeller *et al*. 1986; Schoeller & Webb, 1984; Westerterp *et al*. 1988; Parkinson, 1990).

Bicarbonate–urea method

The bicarbonate–urea method is a relatively novel method for measuring TEE in free-living human subjects. Like the doubly-labelled water technique it is essentially an isotopic-dilution technique, measuring endogenous CO_2 production. Labelled CO_2, given subcutaneously as $H^{14}CO_3^-$, is diluted by the CO_2 produced in the body. The extent of this dilution, measured through the specific activity of urinary urea, allows the calculation of CO_2 production in the body. Using an appropriate value for the energy equivalent of CO_2 (Elia, 1991), EE can then be estimated. Unlike the doubly-labelled water technique, the bicarbonate–urea method can make measurements over periods of 24 h, allowing the study of day-to-day variation in free-living conditions. Such day-to-day measurements may be important in a clinical setting as EE may vary from day-to-day during the course of a disease or trauma. This method has been validated in both healthy individuals (Elia *et al*. 1995) and those with disease (Gibney *et al*. 1997*b*; E Gibney, J Jennings, SA Jebb, PR Murgatroyd, A Wright and M Elia, unpublished results).

Heart-rate monitoring

Heart-rate monitoring is a simple and inexpensive method of measuring free-living TEE. There are a number of different heart-rate monitoring and recording devices that allow minute-to-minute recording of a heart rate over a set period of time. By measuring heart rate at different levels of PA and creating individual calibration curves, an estimation of EE can be made from such recordings of heart rate. This method has been extensively validated against a number of different methods (e.g. doubly-labelled water and indirect calorimetry) in both adults and children (Dauncey & James, 1979; Spurr *et al*. 1988; Ceesay *et al*. 1989). This method is not typically used in a disease population, as the physical limitations of the population group that inhibit the ability to obtain a proper calibration curve (bedridden, fatigue and injuries), and also the multiple clinical factors that affect heart rate.

Interpretation of measurements of total energy expenditure

The second part of the present review investigates the hypothesis, that, although an elevated BMR is seen in many disease situations, the increase in BMR is counteracted or more than counteracted by a decrease in PA. This hypothesis was examined by comparing results obtained in studies measuring energy expenditure in disease with values obtained in healthy individuals. The theory that energy requirements may in fact be reduced is in contrast with the physical wasting seen in disease, which may be due to a number of reasons, including negative energy balance (Hellerstein *et al*. 1990; Elia, 1995), immobility (Deitrick *et al*. 1948) or high protein requirements compared with a standard diet (Long *et al*. 1979). The present paper, however, will only attempt to discuss the overall energy requirements, and does not investigate the macronutrient composition of any given diet.

Methods

All studies measuring free-living TEE in different inflammatory disease states were examined. These studies included those using the doubly-labelled water method, bicarbonate–urea method, heart-rate monitoring and indirect calorimetry. Studies that did not contain a true 24 h measurement of TEE and used only partial measurements as an estimate were excluded. Studies of stable congenital

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disease conditions (heart defects, ventricular septal defects, etc.) were also excluded.

The following information was obtained from the literature review: age; weight; height; BMI; sample size; method of measurement of EE; duration of study; location of study; measured BMR; predicted BMR; TEE. Results from individual patients were included whenever possible, otherwise the group mean data was used. To allow for different comparisons, results were expressed in a number of different ways: TEE per kg; PA level; predicted PA level (Schofield *et al*. 1985); energy expended in PA plus thermogenesis (PA + DIT); energy expended in PA + DIT per kg; energy expended in PA; energy expended in PA per kg; disease factor.

In studies where indirect calorimetry was carried out during feeding (resting EE) it was assumed that DIT was 10 % of the TEE. In studies where BMR was actually measured DIT was again assumed to be 10 % of the EE. The energy cost of PA was calculated as being equal to TEE − BMR − DIT. This calculation does not take into account thermogenesis due to other causes (e.g. drugs, coldness), but the value probably gives a good approximation of PA.

The data of Black *et al*. (1996) for measurements of EE, obtained using doubly-labelled water, were used to compare the results of TEE in disease with those of healthy individuals. Dietary reference values (Department of Health, 1991) were used for comparison with recommended intakes for healthy individuals. The studies were separated into two categories: those carried out in hospital; those carried out at home. Mean values for each study are given in Tables 3 and 4 with values for healthy individuals and recommended reference values shown in Table 5.

Results

As hypothesized, many studies demonstrated a reduced TEE in comparison with reference values for healthy individuals. This reduction was evident in the study of Gibney *et al*. (1996) in patients with small-cell lung cancer (Fig. 1). Whole-body indirect calorimetry indicated that values for BMR were significantly ($P < 0{\cdot}05$) elevated in the lung-cancer group by a mean of 6 % when compared with predicted values (Schofield *et al*. 1985). These results are close to those found in a similar but larger group of patients (Jebb *et al*. 1994). It is important to note, however, that TEE, measured under free-living conditions using the bicarbonate–urea technique in patients with lung cancer, was significantly reduced (8·9 MJ/d) compared with reference control values (9·6 MJ/d). Furthermore, PA accounted for 21 % of the TEE in the patients with cancer compared with 31 % in reference controls (Department of Health, 1991; $P < 0{\cdot}05$). Such results apply to a variety of clinical conditions, demonstrated by the fact that TEE per kg was reduced in the majority of studies when compared with age-matched controls (see Table 5). Studies were conducted both in hospital (Table 4) and at home (Table 3).

Measurement of EE in critically-ill patients is, as mentioned previously, of particular importance as energy intake is controlled by the clinician either through parenteral or enteral feeding (Weissman *et al*. 1986; Bruder *et al*. 1994). Weekes & Elia (1996) measured 24 h EE by indirect calorimetry in critically-ill head-injured patients whilst they were being maintained on continuous ventilation. This study highlighted several interesting points. First, as there was very little voluntary movement in these individuals, EE was stable throughout the day, thus the measurement of TEE was similar if not equal to any measurement of RMR. This value was 35 % above BMR of study controls of the same age, weight and height, but irrespective of whether measurements of TEE were expressed in absolute terms, in relation to body weight or as multiples of BMR, TEE was reduced in this group. The results mirror those obtained by Pullicino (1991) in a similar cohort of patients. Second, Weekes & Elia (1996) demonstrated that EE decreased significantly ($P < 0{\cdot}05$) as time progressed, returning to normal a full 12–19 d after initial injury.

Patients with burns are well known to be hypermetabolic as a result of the 'injury response' (heat loss across the damaged skin; Long *et al*. 1979; Goran *et al*. 1991). Royall *et al*. (1994) measured EE in a group of twenty adults with severe burns (severe burn area > 30 %) whilst being maintained on continuous ventilation. Although RMR was 37 % higher than that in controls, PA was virtually non-existent, which more than compensated for this substantial increase in RMR. This finding would then suggest that the energy requirement in this particular group should perhaps be reduced, even though an extremely high metabolic rate was recorded. Several formulas have been used to estimate energy requirements in these patients (Long, 1979; Wolfe, 1982; Cunningham *et al*. 1989; Goran *et al*. 1991), with some equations prescribing up to 200 % of predicted BMR (Mildreth & Carvajal, 1982; Guzman *et al*. 1994). In their study of stable patients with a severe burn area of 37 %, Royall *et al*. (1994) recommended that an activity factor of 20 % should be added to the measured resting EE to account for daily requirements. However, caution should be used in generally accepting this recommendation because of the considerable variability and changes over time in patients.

Human immunodeficiency virus (HIV) is responsible for the acquired immunodeficiency syndrome (AIDS). AIDS is in itself diagnosed using criteria advocated by the Centers for Disease Control, Center for Infectious Diseases (1987) classification as a greater than 10 % weight loss together with more than 30 d of constitutional symptoms in individuals with HIV (Hellerstein *et al*. 1990). Thus, measurement and understanding of such wasting associated with AIDS is of considerable importance. Schwenk *et al*. (1996) reviewed measurements of RMR in HIV patients, and concluded that it is unlikely that hypermetabolism by itself is the major cause of weight loss in HIV-infected patients. They suggested that weight loss is seen only in combination with another disorder such as anorexia or malabsorption. These thoughts were mirrored by Hellerstein *et al*. (1990), who suggested that malnutrition is not only a result of the HIV infection, but may also be a contributing cofactor to the onset of AIDS, due to the reduced cellular immunity seen with malnutrition. Two studies discussed in the present review which measured free-living TEE in HIV patients (Paton *et al*. 1996; Heijligenberg *et al*. 1997) reported an increase in RMR (a mean increase of 10 % in the study by Heijligenberg *et al*. 1997), but no difference in

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Table 3. Studies measuring free-living total energy expenditure at home
(Values are means and standard deviations)

		Age (years)		Weight (kg)		Height (m)		BMI (kg/m^2)			Duration	BMR (MJ/24 h)		Predicted BMR (MJ/24 h)		TEE (MJ/24 h)		PAL (TEE: BMR)		PA + DIT (MJ/24 h)		PA (MJ/24 h)		TEE per kg (MJ/24 h per kg)		PA + DIT per kg (MJ/ 24 h per kg)		PA per kg (MJ/24 h per kg)	
Study	Disease	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Method	(d)	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Gibney *et al.* (1996)	Cancer	67·8	11·9	68·5	10·4	1·65	0·10	25·2	4·42	BU	2	6·39	1·04	5·95	0·66	7·96	1·56	1·23	0·07	2·62	1·89	1·72	1·65	0·13	0·03	0·04	0·03	0·03	0·02
Paton *et al.* (1997)	AIDS	34·9	3·61	70·5	15·9	1·78	0·08	22·1	3·95	BU	2	7·46	0·09	7·08	0·83	10·92	1·68	1·43	0·14	3·23	1·19	2·16	0·01	0·15	0·02	0·05	0·01	0·03	0·01
Shepherd *et al.* (1988)	Cystic fibrosis	1·48	0·48	9·79	1·12	—		—		DLW	12	—		2·28	0·27	3·98	0·48	—		—		—		0·41	0·07	—		—	
Bandini *et al.* (1991)	Cerebral palsy	18·1	1·61	41·2	13·6	1·49	0·14	18·3	4·86	DLW	14	5·16	0·55	5·09	0·70	7·62	1·45	1·42	0·34	2·17	1·64	1·69	1·41	0·15	0·03	0·05	0·04	0·04	0·03
	Myelo-dysplasia	17·1	2·35	61·2	19·5	1·46	0·14	29·0	7·59	DLW	14	5·14	0·87	6·17	1·43	6·96	1·45	1·34	0·23	1·69	1·11	1·44	0·64	0·14	0·03	0·04	0·02	0·03	0·01
Taggart *et al.* (1991)	Surgery	40–62		77·7	11·9	—		—		DLW	12	—		7·36	0·55	9·62	2·34	—		—		—		0·13	0·03	—		—	
Molinger *et al.* (1985)	Spinal cord injury	33·6	7·27	71·4	12·9	1·79	0·07	22·2	1·66	HRM	3	5·76	0·82	4·50		7·61	0·08	1·32	0·31	3·28	1·96	3·17	0·69	0·11	0·03	0·05	0·03	0·04	0·01
Koea *et al.* (1995)	Sepsis	49·5	4·36	50·5	2·86	—		—		DLW	10	4·45	0·38	5·25	0·09	6·38	1·46	1·44	0·37	1·93	1·51	1·29		0·13	0·03	0·04	0·03	0·03	0·03
Tomesko *et al.* (1994)	Cystic fibrosis	7·70		23·9		1·23		15·8		DLW	9	4·99		4·37		8·42		1·68		3·43		2·59		0·35		0·14		0·11	
Pullicino *et al.* (1993)	IV-fed patients	39·2	7·56	47·3	8·51	—		18·2	2·92	DLW	14	5·44	0·89	5·54	0·34	7·23	1·81	1·32	0·17	1·79	1·05	1·39	0·69	0·15	0·02	0·04	0·02	0·02	0·02
Heijligenberg *et al.* (1997)	HIV	34·0		77·4		1·83		23·1		DLW	14	8·20		7·38		13·72		1·67		6·32		4·14		0·18		0·06		0·05	
Kushner & Schoeller (1991)	IBD	29		—		—		—		DLW	14	5·83		—		11·70		2·01		5·87		5·22		—		—		—	
Stallings *et al.* (1996)	Cerebral palsy	9·01	4·32	18·82	7·70	—		—		DLW	15	3·46	1·07	3·80		4·03	1·08	1·23	0·36	0·57		0·17		0·21	0·06	0·03		0·01	

AIDS, acquired immune deficiency syndrome; BU, bicarbonate–urea; DIT, dietary-induced thermogenesis; DLW, doubly-labelled water; HIV, human immunodeficiency virus; HRM, heart rate monitoring; IBD, inflammatory bowel disorder; IV, intravenously; PA, energy expended in physical activity; PAL, physical activity level; TEE, total energy expenditure.

Table 4. Studies measuring total energy expenditure in hospital
(Values are means and standard deviations)

		Age (years)		Weight (kg)		Height (m)		BMI (kg/m^2)				BMR (MJ/24 h)		Predicted BMR (MJ/24 h)		TEE (MJ/24 h)		PAL		PA + DIT (MJ/24 h)		PA (MJ/24 h)		TEE per kg (MJ/24 h per kg)		PA + DIT per kg (MJ/24 h per kg)		PA per kg (MJ/24 h per kg)	
Study	Disease	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Method	Duration	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Guzman *et al.* (1994)	Trauma	40·7	15·4	80·6	85·21	1·73	0·03	28·1	10·2	EB and RGE	1 d	9·40	1·72	7·04	1·03	12·7	3·46	1·35	0·26	3·32	2·67	2·74	2·23	0·16	0·03	0·04	0·03	0·03	0·02
Turner *et al.* (1985)	Burns	34·0	15·0	—		—		—		RGE	24 h	—		7·38	1·03	9·05	2·68	—		—		—		—		—		—	
Carlsson *et al.* (1984)	Critically-ill	54·0	4·00	70·0	5·00	1·72	0·02	23·6	6·75	RGE	24 h	—		6·49	1·18	8·14	0·34	—		—		—		0·12	0·02	—		—	
Royall *et al.* (1994)	Burns	44·4	3·30	—		—		—		RGE	19 h	8·99	0·43	6·55		10·43	0·50	1·16		1·47		0·39		—		—		—	
Pullicino (1991)	Head injury	41·2	17·1	68·4	13·0	1·77	0·08	21·6		RGE	24 h	5·69	1·18	6·67	0·76	5·69	1·18	1·00		0·57		0·00		0·08	0·02	0·01	0·00		
Weekes & Elia (1996)	Head injury	23·2	5·04	73·4		1·75	0·07	24·2	2·28	RGE	3–5 d	—		7·45	1·12	9·32	1·28	—		—		—		0·13	0·02	—		—	
Novick *et al.* (1988)	Crohns	34·0	6·00	53·0	2·00	1·64	0·03	19·7	1·89	DLW	4 d	5·49	0·44	5·59	0·08	6·72	0·63	1·22	0·27	1·23	0·44	0·56	0·31	0·13	0·02	0·02	0·02	0·01	0·01
	Surgery	34·0	6·00	53·0	2·00	1·64	0·03	19·6	1·89	DLW	4 d	6·14	0·44	5·59	0·08	7·83	0·74	1·36	0·12	2·10	1·24	1·47	0·48	0·15	0·02	0·02	0·01	0·04	0·02
Goran *et al.* (1991)	Burns	7·83	3·72	32·2	19·8	—		—		DLW	12 d	3·59	0·66	—		6·72	2·92	1·18	0·17	2·61	0·70	2·47	0·69	0·24	0·09	0·11	0·05	0·09	0·05
Pullicino *et al.* (1993)	IV-fed patients	35·1	9·43	49·5	13·3	—		18·0	2·29	DLW	14 d	5·28	0·92	5·92	0·87	7·18	1·69	1·36	0·19	1·92	1·01	1·22	0·81	0·15	0·02	0·04	0·02	0·03	0·01
Mitchell *et al.* (1994)	Surgery	1·41	0·73	9·25	2·87	—		—		DLW	7 d	—		2·14	0·69	3·46	1·66	—	—	—		—		0·36	0·09	—		—	
Baarends *et al.* (1997)	COPD	66·5	6·11	61·0	7·62	—		21·8	2·51	DLW	15 d	6·15	0·73	—		10·46	1·34	1·62	0·31	4·30	0·99	3·26		0·17		0·07		0·05	

COPD, chronic obstructive pulmonary disease; DIT, dietary-induced thermogenesis; DLW, doubly-labelled water; EB, energy balance; IV, intravenously; PA, energy expended in physical activity; PAL, physical activity level; RGE, respiratory gas exchange; TEE, total energy expenditure.

Table 5. Reference values for energy expenditure of healthy subjects (Black *et al.* 1996) and recommended reference values (Department of Health, 1991)

Reference		Age (years)	Weight (kg)	TEE (MJ/d)	BMR (MJ/d)	RMR (MJ/d)	PA + DIT (MJ/d)	PA (MJ/d)	TEE per kg (MJ/kg per d)	PA/kg (MJ/kg per d)	PA + DIT per kg (MJ/kg per d)
Black *et al.*(1996)	Males	3·50	19·7	6·10	3·80	4·41	22·2	1·69	0·31	0·09	0·11
		9·50	40·7	9·80	5·70	6·68	24·1	3·12	0·24	0·08	0·10
		15·0	72·0	14·1	8·10	9·51	46·0	4·59	0·19	0·06	0·08
		23·5	75·6	13·8	7·50	8·88	6·30	4·92	0·18	0·07	0·07
		34·5	86·1	14·3	8·20	9·63	6·10	4·67	0·17	0·05	0·06
		52·0	77·0	11·5	7·00	8·15	4·50	3·35	0·15	0·04	0·05
		69·5	76·4	11·0	6·90	8·00	4·10	3·00	0·14	0·03	0·04
		75·0	72·6	9·20	6·00	6·92	3·20	2·28	0·13	0·03	0·10
	Females	3·50	18·4	5·50	3·60	4·15	1·90	1·35	0·29	0·07	0.08
		9·50	33·3	8·00	4·80	5·60	3·20	2·40	0·24	0·07	0·09
		15·0	71·5	11·4	6·70	7·84	4·70	3·56	0·16	0·05	0·07
		23·5	69·2	10·4	6·20	7·24	4·20	3·16	0·15	0·05	0·06
		34·5	67·9	10·0	6·00	7·00	4·10	3·00	0·15	0·04	0·06
		52·0	70·0	9·80	5·80	6·78	4·00	3·02	0·14	0·04	0·06
		69·5	60·2	8·60	5·30	6·16	3·30	2·44	0·14	0·04	0·05
		75·0	48·3	6·10	4·10	4·71	1·90	1·39	0·13	0·03	0·04
Department of Health (1991)	Males	2·00	12·4	5·15	2·96	3·48	2·19	1·67	0·42	0·14	0·18
		5·00	19·3	7·16	3·94	4·66	3·22	2·50	0·37	0·13	0·17
		8·50	28·3	8·24	4·79	5·61	3·45	2·63	0·29	0·09	0·12
		12·5	40·5	9·27	5·94	6·87	3·33	2·40	0·14	0·06	0·08
		16·5	62·5	11·5	6·94	8·09	4·57	3·42	0·13	0·05	0·07
		34·0	74·0	11·5	7·21	8·36	4·32	3·17	0·16	0·04	0·06
		54·5	74·0	11·5	7·21	8·36	4·32	3·17	0·16	0·04	0·06
		62·0	74·0	9·93	7·21	8·36	4·32	3·17	0·16	0·04	0·06
		69·5	71·0	9·50	5·94	6·89	3·56	2·61	0·14	0·04	0·05
		75·0	69·0	9·34	5·84	6·77	3·50	2·57	0·13	0·03	0·05
	Females	2·00	11·8	4·86	2·75	3·24	2·11	1·62	0·41	0·14	0·18
		5·00	18·9	6·46	3·64	4·29	2·82	2·17	0·34	0·12	0·15
		8·50	28·2	7·28	4·43	5·21	2·85	2·07	0·26	0·08	0·10
		12·5	43·0	7·92	5·32	6·11	2·61	1·89	0·18	0·03	0·06
		16·5	56·5	8·83	6·07	6·95	2·77	1·88	0·16	0·02	0·05
		34·0	60·0	8·93	5·58	6·47	3·35	2·46	0·15	0·04	0·06
		54·5	63·0	9·09	5·68	6·59	3·41	2·50	0·14	0·04	0·05
		62·0	63·5	9·10	5·69	6·60	3·14	2·50	0·14	0·04	0·05
		69·5	63·0	8·24	5·15	5·97	3·09	2·27	0·14	0·04	0·05
		75·0	60·0	8·06	5·04	5·85	3·02	2·24	0·13	0·04	0·05

DIT, dietary-induced thermogenesis; PA, physical activity; RMR, resting metabolic rate; TEE, total energy expenditure.

TEE when compared with reference controls. These observations are consistent with a concurrent reduction in PA (Table 3). Such results do not help to explain the characteristic weight loss seen in this disease, and would suggest that the answer may be a combination of disorders, as previously suggested (Hellerstein *et al*. 1990).

Conclusions

The present paper confirms that EE is very variable in disease (Tables 3 and 4; Goran *et al*. 1985; Elia, 1995). Such variations are partly due to variable effects of disease on BMR and PA, the presence of variable nutritional status (undernutrition tends to reduce predicted BMR) and inconsistent or inappropriate procedures for measuring and interpreting measurements of EE. What became evident in researching this topic is the lack of reporting of any such deviations, i.e. measurements being made whilst feeding, or under an unknown or unreported influence of drugs. Reporting such deviations and also reporting the timing of the measurement with respect to the trauma or disease stage would allow other observers to fully evaluate the results obtained, and allow proper comparisons from group-to-group. General recommendations are given in Table 6.

The appropriate use of tracer techniques and indirect calorimetry in a wider range of disease states would allow a greater understanding of the pathophysiology of wasting, and at the same time provide a better basis for recommendations as to the energy requirement in disease. It is important to affirm that measurements of EE in disease will only allow the clinician to assess the energy requirement of an individual with respect to the initial body composition of the

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Table 6. Recommendations for the reporting of assessments of energy requirements in disease

Ensure most, if not all, conditions of BMR measurements are fulfilled
Report any deviations from strict conditions of BMR
Report time of measurement, both with respect to time of day and course of the disease
Document drug and feeding regimens regardless of whether measurement is taken free from thermic effects
Take note of initial body composition of individual

patient involved. Additional energy intake may be required for tissue repletion, especially during recovery from illness, and in individuals who are initially malnourished. Although the requirements of different patients vary widely, the principles of nutritional care remain very similar.

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