Basics in clinical nutrition: Energy metabolism.

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Basics in clinical nutrition: Energy metabolism

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Learning objectives

- To know the measurement of energy expenditure with indirect calorimetry.
- To be familiar with components of daily energy expenditure.
- To know the determinants of energy expenditure and its components.
- To be aware of disease related alterations in energy expenditure.

Calorimetry for the measurement of energy expenditure

Life can be regarded as a combustion process. The metabolism of an organism is a process of energy production by the combustion of fuel in the form of carbohydrate, protein, fat or alcohol. In this process oxygen is consumed and carbon dioxide produced. Measuring energy expenditure means measuring heat production or heat loss, which is called direct calorimetry. The measurement of heat production by measuring oxygen consumption and/or carbon dioxide production is called indirect calorimetry. The early calorimeters for the measurement of energy expenditure were direct calorimeters. Nowadays, energy expenditure is mostly measured with indirect calorimetry.

In indirect calorimetry heat production is calculated from chemical processes. Knowing for example that 1 mol glucose oxidizes with 6 mol oxygen (O_2) to 6 mol water and 6 mol carbon dioxide (CO_2) and produces 2.8 MJ heat, we can then calculate heat production from oxygen consumption or carbon dioxide production.

Glucose oxidation:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6H_2O + 6CO_2 - 2.8\,MJ$$

The energy equivalent of oxygen and carbon dioxide varies with the nutrient oxidized. Formulae for calculating the heat production and the quantities of carbohydrate (C), protein (P) and fat (F) oxidized are based on oxygen consumption, carbon dioxide production and urine-nitrogen loss. The principle of the calculation consists of three equations with the mentioned three measured variables:

- Oxygen consumption (VO_2) = 0.829 C + 0.967 P + 2.019 F
- Carbon dioxide production (VCO_2) = 0.829 C + 0.775 P + 1.427 F
- Heat production (MJ) = 21.10 C + 18.70 P + 19.60 F

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Protein oxidation (g) is calculated as 6.25 × urine-nitrogen (g), and subsequently oxygen consumption and carbon dioxide production can be corrected for protein oxidation to allow calculation of carbohydrate- and fat oxidation.

The general formula for the calculation of energy production (E) derived from these figures is:

$$E = 16.20VO_2 + 5.00VCO_2 - 0.95\ P$$

In this formula the contribution of P (protein oxidation) to E, the so-called protein correction, is small. In the case of a normal protein oxidation of 10—15% of the daily energy production, the protein correction for the calculation of E is about 1%. Usually one only measures urine-nitrogen when information on the contribution of C, P, and F to energy production is needed. For calculation of energy production the protein correction is often neglected.

Measuring separate components of daily energy expenditure with a ventilated hood and a respiration chamber

A ventilated hood and a respiration chamber are instruments to measure oxygen consumption and carbon dioxide production continuously. They allow accurate determination of energy production in subjects under controlled conditions. Measurements with a ventilated hood are usually performed over intervals of 1/2 to several hours to determine a subject's resting energy expenditure (REE) or diet induced energy expenditure (DEE). Measurements with a respiration chamber last several hours to several days and allow determination of a subject's REE, DEE, and energy expenditure for (standardized) physical activity (AEE).

A typical example of a ventilated hood system is an open canopy. The subject lies with his head enclosed in a transparent plastic canopy, sealed of by plastic straps around the neck (Fig. 1). Air is sucked through the canopy with a pump and blown into a mixing chamber where a sample is collected for analysis. Measurements consist of airflow and oxygen- and carbon dioxide concentration in inlet (outdoor) and outlet (respiratory) air. The most common device for the measurement of airflow is a dry gas meter comparable to the apparatus to measure calor gas consumption in homes. The most common device for the measurement of the oxygen- and carbon dioxide concentration is a paramagnetic oxygen analyser and an infrared carbon dioxide analyser, respectively. The airflow is adjusted to keep differences for oxygen- and carbon dioxide concentration between inlet- and outlet air in the range of 0.5—1.0%. This implies that for an adult airflow rates are between 25 L/min and 50 L/min.

Measuring average daily energy expenditure with doubly labelled water

The doubly labelled water method is an innovative method of indirect calorimetry that has only recently been validated for human use. The principle of the method is that after a loading dose of water labelled with the stable isotopes of ^2H and ^{18}O, ^2H is eliminated as water, while ^{18}O is eliminated as both water and carbon dioxide. The difference between the two elimination rates is therefore a measure of carbon dioxide production (Fig. 2). The deuterium (^2H) equilibrates throughout the body's water pool, and the ^{18}O equilibrates in both the water and the bicarbonate pool. The bicarbonate pool consists largely of dissolved carbon dioxide, which is an end product of metabolism and passes in the blood stream to the lungs for excretion. The rate constants for the disappearance of the two isotopes from the body are measured by mass spectrometric analysis of samples of a body fluid, blood, saliva or urine.

This method can be used to measure carbon dioxide production (VCO_2) and hence energy production in free-living subjects for periods of some days to several weeks. The optimal observation period is 1—3 biological half-lives of the isotopes. The biological half-life is a function of the level of the energy expenditure. The minimum observation interval is about 3 days in highly active subjects or prematures. The maximum interval is three times 9.8 days or about 4 weeks in elderly (sedentary) subjects.

An observation starts by collecting a baseline sample. Then, a weighed isotope dose is administered, usually a mixture of 10% ^{18}O and 5% 2H in, for a 70 kg adult, 100—150 cc water. Subsequently the isotopes equilibrate with the body water and the initial sample is collected. The equilibration time, depending on body size and metabolic rate, for adults is 4—8 h. During equilibration the subject usually does not consume any food or drink. After collecting the initial sample the subject resumes their

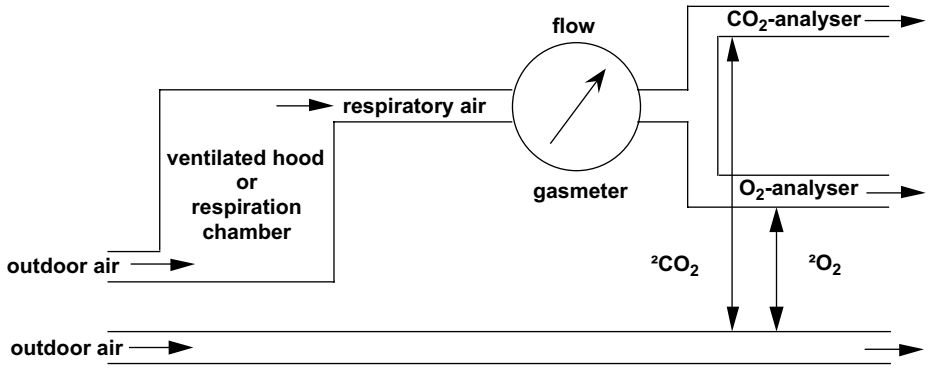

Figure 1 Schematic representation of an open-circuit system for the measurement of oxygen consumption and carbon dioxide production as applied in a ventilated hood and a respiration chamber.

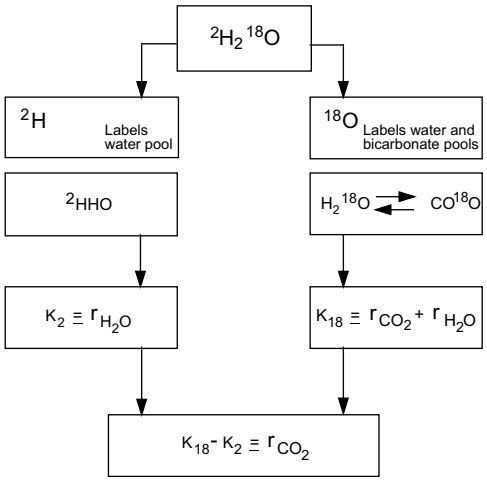

Figure 2 Principle of the doubly labelled water ($^2H_2^{18}O$) method for the measurement of carbon dioxide production (r_{CO_2}) from the elimination rates of ^{18}O (k_{18}) and ^2H (k_2). The elimination rate of ^2H is a function of water loss (r_{H_2O}) while k_{18} is a function of r_{CO_2} and r_{H_2O}.

routine according to the instructions of the experimenter and is asked to collect body water samples (blood, saliva or urine) at regular intervals until the end of the observation period. Validation studies in four laboratories resulted in an accuracy of 1–3% and a precision of 2–8%, comparing the method with respirometry.

The doubly labelled water method gives precise and accurate information on carbon dioxide production. Converting carbon dioxide production to energy expenditure needs information on the energy equivalent of CO_2, which can be calculated with additional information on the substrate mixture being oxidized. One option is the calculation of the energy equivalent from the macronutrient composition of the diet. The second possibility is to measure discrete values of respiratory quotient (RQ):

$$RQ = VCO_2/VO_2$$

Components of energy expenditure, measurement and determinants

Daily energy expenditure consists of four components, i.e. the sleeping metabolic rate (SMR), the energy cost of arousal, the thermic effect of food or diet induced energy expenditure (DEE), and the energy cost of physical activity or activity induced energy expenditure (AEE). Sometimes daily energy expenditure is divided into three components, taking sleeping metabolic rate and the energy cost of arousal together as energy expenditure for maintenance or basal metabolic rate (BMR) or resting energy expenditure (REE), which is usually the main component of average daily metabolic rate (ADMR).

- Sleeping metabolic rate (SMR) or resting energy expenditure (REE) can be compared between subjects by standardizing SMR or REE to an estimate of metabolic body size. Fat-free body mass seems to be the best predictor. However, energy expenditure should not be divided by the absolute FFM value as the relationship between energy expenditure and FFM has a *y* and *x* intercepts significantly different from zero. The smaller the FFM the higher the SMR/FFM ratio and thus the SMR per kg FFM is on average higher in women with on average a lower FFM compared with men. The reliable way of comparing SMR or REE data is by regression analysis. Covariates to be included are FFM, fat mass (FM), age and gender. Then, gender does not come out as a significant contributor to the explained variation.
- Diet induced energy expenditure (DEE) is defined as the increase in energy expenditure above basal fasting level divided by the energy content of the food ingested and is commonly expressed as a percentage of energy intake. The postprandial rise in energy expenditure lasts several hours and is often regarded as completely terminated at approximately 10 h after the last meal. DEE, based on observations as mentioned above, is assumed to be 10% of ADMR in subjects consuming an average mixed diet and being in energy balance.
- Activity induced energy expenditure (AEE) is the most variable component of ADMR. The doubly labelled water method has provided truly quantitative estimates of AEE in daily life. Subsequently, however, there is no consensus on the way to normalize AEE for differences in body size. A frequently used method to quantify physical activity is by expressing ADMR as a multiple of BMR or SMR. An elaborate analysis of data on AEE was based on all doubly labelled water estimates of ADMR until the middle of 1994. It included 574 measurements accompanied by direct measurements of BMR, in subjects in the 'normal' free-living state, 319 women and 255 men. There was a constant gender effect on ADMR and the components BMR and AEE, women being 11% lower than men of the same age and body size. Differences between women and men were nearly removed by adjusting for body size by using ADMR/REE. The distribution of ADMR/REE had a median value of 1.6 for both women and men, i.e. REE, DEE and AEE were, respectively, 60%, 10% and 30% of ADMR.

Disease related alterations in energy expenditure

Severe acute diseases and nearly all chronic wasting disorders such as chronic obstructive pulmonary disease (COPD), cancer, AIDS, hepatic disease, chronic heart and chronic renal failure are characterized by hypermetabolism (i.e. elevated REE). Prevalence rates and severity of hypermetabolism vary substantially depending on the definition of hypermetabolism and the reference values used. A generally used definition is a REE $>$ 10% of predicted.

The most common approach to predict REE for an individual in clinical practice is to apply the Harris–Benedict equations.

- Male: $\text{REE} = 66.5 + (13.8 \times \text{weight}) + (5.0 \times \text{height}) - (6.8 \times \text{age})$
- Female: $\text{REE} = 655.1 + (9.6 \times \text{weight}) + (1.8 \times \text{height}) - (4.7 \times \text{age})$

These equations are based on sex, age, height and body mass, but do not take body composition into account. This may lead to an overestimation of hypermetabolism in underweight patients since the relationship between energy expenditure and body weight has a *y* and *x* intercepts significantly different from zero. Furthermore weight loss due to decreased dietary intake is accompanied by metabolic adaptations resulting in a relative preservation of fat-free mass. On the other hand in several chronic wasting diseases selective loss of FFM with relative preservation of FM and even body weight have been described. Under these circumstances hypermetabolism will be underestimated.

To assess the presence of hypermetabolism in individuals or in selected patient groups it is therefore very important to measure body composition simultaneously and to compare measured values with reference values including body composition of an appropriately matched control group. Hypermetabolism in both acute disease and chronic wasting conditions appears to be a marker of a systemic inflammatory response. This is not remarkable since systemic inflammation is associated with energy inefficient alterations in substrate metabolism including elevated protein turnover for acute phase protein synthesis. In most hypermetabolic patients ADMR is normal, however, due to an adaptive decrease in AEE. Measurement of REE per se without an indication of AEE is therefore not useful to assess energy balance in patients. In clinical practice, in order to adjust nutritional therapy regular standardized weight measurements if possible combined with accurate dietary records will therefore provide a better insight in ADMR.

Summary

Energy expenditure is mostly measured by indirect calorimetry, based on the measurement of oxygen consumption and carbon dioxide production with a ventilated hood, in a respiration chamber or with doubly labelled water in the clinic or in the daily living environment. Daily energy expenditure consists of four components, i.e. the sleeping metabolic rate (SMR), the energy cost of arousal, the thermic effect of food or diet induced energy expenditure (DEE), and the energy cost of physical activity or activity induced energy expenditure (AEE). Sometimes daily energy expenditure is divided into three components, taking sleeping metabolic rate and the energy cost of arousal together as energy expenditure for maintenance or basal metabolic rate (BMR). BMR is usually the main component of average daily metabolic rate (ADMR). BMR is mainly determined by body size or fat-free mass. DEE is a function of dietary intake and amounts 10% of ADMR for subjects fed in energy balance. AEE is the most variable component of ADMR. During severe acute disease and in many chronic wasting diseases BMR is elevated. ADMR under these circumstances is, however, often normal due to adaptive decreases in AEE.

Conflict of interest

There is no conflict of interest.

Further reading

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