Determinants of 24-hour Energy Expenditure in Man

Methods and Results Using a Respiratory Chamber

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Abstract

Daily human energy requirements calculated from separate components of energy expenditure are inaccurate and usually in poor agreement with measured energy intakes. Measurement of energy expenditure over periods of 24 h or longer is needed to determine more accurately rates of daily energy expenditure in humans. We provide a detailed description of a human respiratory chamber and methods used to determine rates of energy expenditure over 24-h periods in 177 subjects. The results show that: (*a*) fat-free mass (FFM) as estimated by densitometry is the best available determinant of 24-h energy expenditures (24EE) and explains 81% of the variance observed between individuals (24EE [kcal/d] = 597 + 26.5 FFM); (*b*) 24EE in an individual is very reproducible (coefficient of variation = 2.4%); and (*c*) even when adjusted for differences in FFM, there is still considerable interperson variability of the daily energy expenditure. A large portion of the variability of 24EE among individuals, independent of differences in body size, was due to variability in the degree of spontaneous physical activity, i.e., "fidgeting," which accounted for 100–800 kcal/d in these subjects.

Introduction

Despite several studies on energy expenditure in humans, it is not yet clearly established how much food humans require for weight maintenance (1–6). The reason for this lack of information is that most studies on energy expenditure have been performed over short periods of time (minutes or hours) and extrapolation of these results to 24 h gives an inaccurate estimate of 24-h energy requirements. As suggested by Durnin et al. (7), to determine energy requirements more accurately in humans, energy expenditure should be measured over periods of days or at least over 24 h. For these reasons, two human respiratory chambers (indirect calorimeters) have been built during the last 10 yr (8, 9) to perform further studies of the causes of energy imbalance in subjects with disorders such as massive obesity, hyper- or hypothyroidism, anorexia nervosa, and cancer.

In this article we provide a description of the respiratory chamber built by the National Institutes of Health, in Phoenix, Arizona, and describe the determinants of 24-h energy expenditure in humans as measured with this chamber. Results on 177 subjects with a wide range of body weight and body composition are presented, and the possible determinants of energy expenditure are discussed. 81% of the variance in 24-h energy expenditure between individuals is explained by differences in fat-free mass (FFM)[1]. Differences in the thermic effect of food and, more importantly, in spontaneous physical activity, also contribute significantly to differences in 24-h energy expenditure (24EE) in humans.

It is concluded that, even when corrected for differences in FFM, or expressed as a ratio of sleeping metabolic rate, individuals vary considerably in their energy expenditure rates, and therefore, in their energy requirements. These results, like some previously reported (6), do not support a universal recommendation of fixed energy requirements for all individuals.

Methods

Description of the Phoenix respiratory chamber. The recently constructed respiratory chamber at the Clinical Diabetes and Nutrition Section of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, in Phoenix, Arizona, was modeled after the chamber built in the late 1970s by Professor Jéquier and colleagues, in Lausanne, Switzerland (9, 10). The chamber itself is an "environmental walk-in room" (Forma Scientific, Marietta, OH). Its dimensions are 3.33 m long, 2.45 m wide, and 2.39 m high, representing a total volume of 19,500 liters, with a 19,000-liter net volume when the furniture is in the room. The walls of the chamber consist of two layers of 1-mm-thick aluminum with a 10-cm layer of urethane between them. Louvered polystyrene ceiling tiles are suspended 23 cm below the ceiling, leaving space for a wide blower wheel which circulates the air throughout the chamber. This air circulation system, in conjunction with a heating and cooling coil connected to an external compressor, keeps the chamber at a constant uniform preset temperature of 24.0±0.5°C. Because of the air homogenization, oxygen and carbon dioxide concentrations should be constant throughout the chamber at any given time. The chamber has a door, two windows, one with a view into the ward and the other out of the hospital, and a two-door airlock through which meals can be passed (Figs. 1 and 2). The chamber is furnished with a toilet, sink, fold-out sofa bed, desk, chair, table, television set, radio, and two intercoms, one connected to the nurses' work station on the Metabolic Ward and the other to the exterior of the door, enabling visual and audio contact with the subject.

Principle and equipment involved in a respiratory chamber. The respiratory chamber forms an open-circuit, indirect calorimeter in which both the oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) of a subject can be continuously measured (Fig. 2). Fresh atmospheric air is continuously drawn through the chamber, and the mixed air leaves the chamber at three different levels through perforations in three 5-cm diam ducts covering the length of two perpendicular walls (Figs. 1 and 2). The flow rate at the outlet is measured using a ventilation measurement module (model VMM 1, Alpha Technologies, Laguna Hills, CA), which consists of a high-precision, ultralightweight turbine volume transducer. Air temperature and barometric pressure are also measured

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1. *Abbreviations used in this paper:* EĖ, energy expenditure rate; EĖrest, resting energy expenditure; FFM, fat-free mass; RQ, respiratory quotient; 24EE, 24-h energy expenditure; $\dot{V}CO_2$, carbon dioxide production rate; $\dot{V}O_2$, oxygen consumption rate.

Figure 1. The Phoenix respiratory chamber (19,000 liter) based on the principle of open-circuit indirect calorimetry. Note in the upper photograph the radar system located above the mirror and in the lower photograph the air sampling lines disposed on two walls at three different levels.
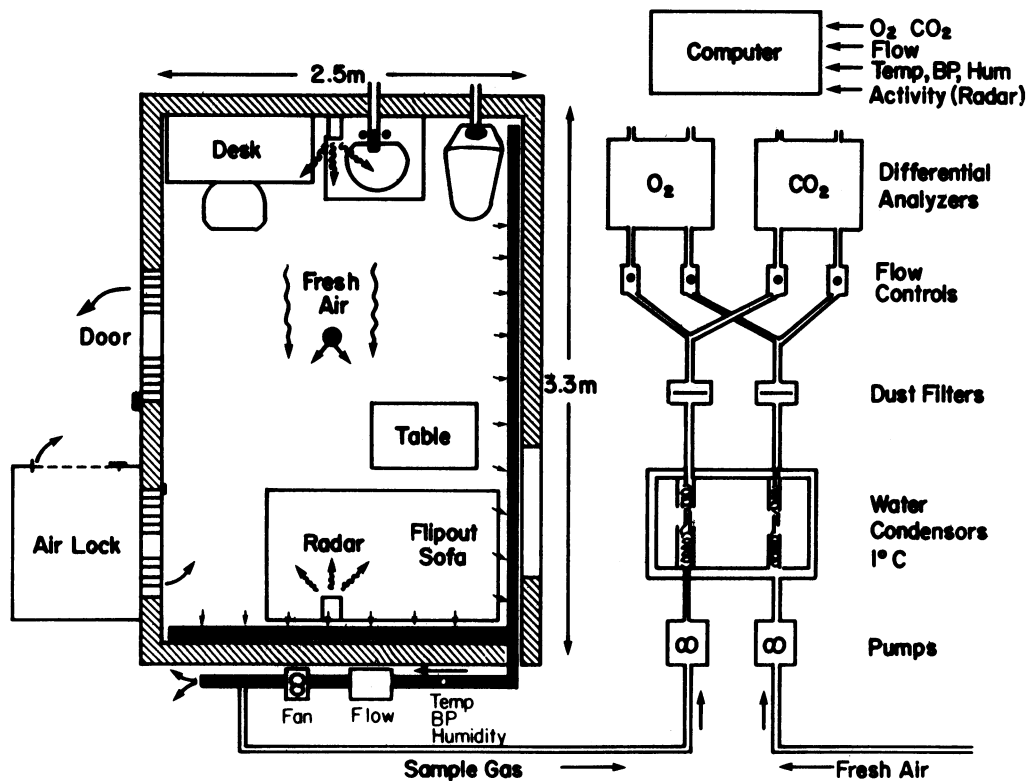
Figure 2. Schematic representation of the Phoenix respiratory chamber system. This chamber is an open-system indirect calorimeter through which air is drawn by a fan. Flow, temperature, barometric pressure, and humidity of this air, which is similar in physical characteristics to that of the chamber, are measured. A sample is then dried and measured for O_2 and CO_2 concentrations by differential analyzers.

by the same ventilation measurement module. Water vapor pressure is determined in the outflowing air by a dew point hygrometer (YSI 91, Yellow Springs Instruments Co., Yellow Springs, OH). After the determinations of flow, temperature, barometric pressure, and humidity, a fraction of the outflowing air is continuously withdrawn by a pump, dried by condensers located in a stable 1.0°C refrigerator, filtered for dust, and then analyzed for oxygen (O_2) (Magnos 4G, Hartmann and Braun, Frankfurt, Federal Republic of Germany) and carbon dioxide (CO_2) (Uras 3G, Hartmann and Braun). These two differential analyzers compare the O_2 and CO_2 concentrations of outgoing air with that of fresh ingoing air, and therefore measure the differences in O_2 (ΔO_2) and CO_2 (ΔCO_2) concentrations between fresh air and room air. Any physical perturbation, e.g., changes in barometric pressure or temperature, is likely to have similar effects on each channel (sample and reference) and no effect on the delta concentration. The analyzers' full scale readings were set for 0–2% and 0–1% for ΔO_2 and ΔCO_2 determinations, respectively. These two analyzers are very sensitive, 1% of full scale, i.e., 0.002% and 0.001% for O_2 and CO_2, respectively. These analyzers are also very stable; on 100 24-h recording tests, the mean±standard deviation drifts of the zero values were 0.000±0.004% and 0.000±0.001% for O_2 and CO_2, respectively, and the mean drifts of the gain values were −0.001±0.010% and −0.001±0.007% for O_2 and CO_2, respectively.

Our calibration procedure does not rely on the use of purchased standard gas mixtures. The zero values of both analyzers are calibrated by flowing fresh air through the sample and reference lines simultaneously, whereas the gain values are calibrated using mixtures of fresh air and pure N_2 or CO_2 obtained by a precision gas mixing pump (Digamix SA 18, Wosthoff OHG, Bochum, Federal Republic of Germany). Fresh air concentration is decreased by 1.676% for O_2 (92 parts fresh air + 8 parts 100% N_2) or increased by 1.000% for CO_2 (99 parts fresh air + 1 part 100% CO_2). This calibration procedure has the advantage of closely corresponding to the situation of a subject in the respiratory chamber, with extraction of oxygen from and addition of carbon dioxide to fresh air.

For data acquisition, the analogue voltage output of the different devices, O_2 and CO_2 analyzers, flowmeter, temperature, humidity and barometric pressure probes, and the two radar systems used to measure physical activity (see below), are processed by an IBM personal computer

(IBM Corp., Boca Raton, FL) via an analogue–digital converter (Data Translation, Marlboro, MA) and read ~50 times/s. Calculated values are displayed every minute and means are printed every 15 min on an IBM PC graphics printer (IBM Corp.). For quick visualization of changes in the gas concentrations over time, the analogue voltage outputs from the two gas analyzers are also recorded on a chart recorder (SR 6342L, Graphtec, Irvine, CA).

The total cost of materials for this respiratory chamber was ~$90,000 in 1984.

Principle of oxygen consumption and carbon dioxide production calculations using a respiratory chamber. If the respiratory chamber was a completely closed system, the oxygen consumption ($\dot{V}O_2$) and the carbon dioxide production ($\dot{V}CO_2$) of a subject would result in a drop in oxygen concentration and an increase in carbon dioxide concentration within the chamber at a rate inversely proportional to the net volume of the chamber. When fresh air is drawn through the chamber, part of the subject's $\dot{V}O_2$ is replaced by a net influx of oxygen and part of his/ her $\dot{V}CO_2$ is accounted for by a net efflux of CO_2. Therefore, over a given period of time, $\dot{V}O_2$ is the sum of the decrease in O_2 in the chamber and the net amount of O_2 added to the chamber. Similarly, $\dot{V}CO_2$ is the sum of the CO_2 buildup in the chamber and the net amount of CO_2 extracted from the chamber. Therefore, both $\dot{V}O_2$ and $\dot{V}CO_2$ are the sums of a closed-system term (i.e., changes in gas volume within the chamber) and an open system term (i.e., influx or efflux of a volume).

The equation for the $\dot{V}CO_2$ rate over a period of time is:

$$\dot{V}CO_2 = \dot{V}CO_{2c} + \dot{V}CO_{2o}, \tag{1}$$

where $\dot{V}CO_{2c}$ and $\dot{V}CO_{2o}$ are the closed- and open-system terms, respectively.

Eq. 1 becomes:

$$\dot{V}CO_2 = [(FCO_{2e} - FCO_{2b}) \cdot Vol/(e - b)] + [\bar{V} \cdot \overline{FCO_2}], \tag{2}$$

where e is the end of the time period (15 min), b is the beginning of the time period (0 min), $(e - b)$ is the duration of the period in minutes, 15 min in our experiments, FCO_{2e} is the CO_2 fraction enrichment at the end of the period, FCO_{2b} is the CO_2 fraction enrichment at the beginning

of the period, Vol is the net volume of the chamber (19,000 liters), $\bar{V}$ is the mean extraction flow rate during the period ($e - b$), and $\overline{FCO_2}$ is the mean CO_2 fraction enrichment during the ($e - b$) period between the ingoing air (fresh air) and the air leaving the chamber.

In Eq. 2, both Vol and $\bar{V}$ are corrected for standard temperature and pressure conditions. Because the open-system term is measured many times per second, Eq. 2 becomes:

$$\dot{V}CO_2 = [(FCO_{2e} - FCO_{2b}) \cdot 19,000/15] + \sum_{i=1}^{n} (\dot{V}i \cdot FiCO_2)/n, \qquad (3)$$

where n is the number of readings during the 15-min period ($e - b$).

FCO_{2e} and FCO_{2b} are calculated as average values of 2-min readings around the b and e times to minimize the error of a single reading.

When the respiratory quotient (RQ) is different from 1.0, the inspired volume is not equal to the expired volume and therefore the inflow is different from the measured outflow. To adjust for this, the Haldane correction (11) is applied on both the open-system and closed-system terms to calculate the oxygen consumption ($\dot{V}O_2$ l/min).

$$RQ_c = 0.7905/\{[(FO_{2b} - FO_{2e})/(FCO_{2e} - FCO_{2b})] - 0.2095\}; \qquad (4)$$

$$RQ_o = 0.7905/[(\overline{FO_2/FCO_2}) - 0.2095], \qquad (5)$$

where 0.7905 is the non-O_2 fraction in atmospheric air, 0.2095 is the O_2 fraction in atmospheric air, RQ_c and RQ_o are the respiratory quotients for the closed- and open-system, respectively, FO_{2b} and FO_{2e} are the ΔO_2 concentrations at the beginning and the end of the period, and $\overline{FO_2}$ and $\overline{FCO_2}$ are the average O_2 and CO_2 delta concentrations during the period ($e - b$).

$$\dot{V}O_2 = (\dot{V}CO_{2c}/RQ_c) + (\dot{V}CO_{2o}/RQ_o); \qquad (6)$$

$$RQ = \dot{V}CO_2/\dot{V}O_2. \qquad (7)$$

It is then possible to calculate the energy production rate in a steady-state condition (10), which is equal to the energy expenditure rate (EĖ):

$$E\dot{E} = \dot{V}O_2 \times [4.686 + (RQ - 0.707) \times 0.361/0.293], \qquad (8)$$

where 4.686 is the caloric equivalent of the liter of O_2 when the RQ is 0.707, 0.707 is the RQ when fat is oxidized, 0.293 is the difference between the RQ for carbohydrate and fat oxidation, 0.361 is the difference in the caloric equivalent of the liter O_2 between an RQ = 1.000 and an RQ = 0.707 (5.047 − 4.686 kcal/liter O_2).

Every 15 min, meaned $\dot{V}CO_2$, $\dot{V}O_2$, RQ, EĖ, and activity are stored on a magnetic disk and used later to calculate the 24-h results. When 24-h urinary urea nitrogen production is available, carbohydrate, lipid, and protein oxidations are calculated (12). Similar indirect calorimetry calculations, presented differently, have been proposed by McLean and Watts (13).

Testing the respiratory chamber. To test for possible gas leaks, air was blown into the chamber and the maintenance of the differential pressure between the interior and exterior of the chamber was recorded. A rapid drop of this pressure (10 s for 10 cmH$_2$O) indicated the presence of significant gas leaks. Every possible leak was carefully plugged.

The net volume of the chamber was determined eight times by CO_2 dilution calculation. The measurement was performed as follows: 90–100 liters of CO_2 was introduced rapidly into the chamber (15–20 s) from a 120-liter Tissot gasometer (W. E. Collins, Braintree, MA). CO_2 concentration was measured continuously and the steady-state value obtained after 5 min was used to calculate the net volume of the chamber. The latter was found to be 18,990±520 liters (mean±SD).

In Eq. 1, when $\dot{V}CO_2$ is equal to zero, $\dot{V}CO_{2o}$ should be equal to $-\dot{V}CO_{2c}$. Therefore, it is possible to check the accuracy of using a 19,000-liter volume by comparing $\dot{V}CO_{2o}$ with $\dot{V}CO_{2c}$ during "wash-out studies." After an enrichment in CO_2 (by injection of CO_2 or by propane or acetone combustion), the extraction rate of CO_2 ($\dot{V}CO_{2o}$) was compared with the decrease in CO_2 in the chamber ($\dot{V}CO_{2c}$) on eight different occasions. The net $\dot{V}CO_2$, which equals $\dot{V}CO_{2o} + \dot{V}CO_{2c}$ and should equal 0.0 ml/

min, was found to be 0.9±2.7 ml/min (range −3.6 to +4.4 ml/min) over 13–16 h, i.e., <0.5% of a subject's $\dot{V}CO_2$ (~250 ml/min).

Response time and variability of the respiratory chamber. The 99% response time for the respiratory chamber measured during CO_2 dilution was 4 min; 93% of the total response was observed after 3 min and 97% was observed after 3.5 min. We allowed a 3-min delay for the respiratory exchange measurements compared with the instantaneous measurement of spontaneous physical activity.

The variability of the energy expenditure measurement in the chamber was assessed by 18 propane combustion tests over periods of 3–6 h.

Measurement of spontaneous physical activity. Spontaneous physical activity was assessed by two different methods in the respiratory chamber.

First, the subjects wore a wrist motion sensor on the nondominant wrist. The sensor consisted of a mercury tilt switch oriented so that the transducer was equally sensitive to all directions. This sensor was interfaced with a portable eight-channel microcomputer for continuous analysis of information (Vitalog PMS-8, Vitalog Corp., Redwood City, CA). At the end of the 24-h measurement, the information was read out on an Apple II computer (Apple Computer, Inc. Cupertino, CA) and averaged over 15-min periods. One activity unit was equivalent to 15 tilts of the wrist and was only the reflection of forearm movements.

Secondly, in June 1985, two microwave motion sensors (MICD 930, Honeywell Inc., Minneapolis, MN) were mounted in the chamber to monitor the spontaneous physical activity of the subject (14). Both units, placed at the two ends of the respiratory chamber, continuously emit a signal (two separate wave lengths) which is reflected by the walls. When hitting a moving object or body the frequency of the signal is changed (Doppler effect) and measured by a transceiver. The sensitivity of the system was set to detect any movement greater than chest movement in breathing. The output of both radars was analyzed by our data acquisition system and averaged over a 15-min period; one activity unit expressed in percent represents the proportion of time during which the subject is moving. For example, a 5% average activity over 24 h would correspond to 72 min of continuous motion. The measured spontaneous physical activity is irrespective of work intensity. The radar method, furthermore, does not interfere with the volunteer's behavior. It was also found to be more reliable and also better correlated to energy expenditure than the wrist motion sensor.

Subjects. During the last 10 mo of 1985, 177 volunteers (103 males, 74 females) (131 Southwestern American Indians—68 males, 63 females; and 46 Caucasians—35 males, 11 females) were studied in the respiratory chamber. Their physical characteristics are presented in Table I.

On admission, all subjects, apart from having diabetes and obesity, were determined to be in good health by medical history and physical examination, and none were taking medication. Subjects had no clinical evidence of hypo- or hyperthyroidism by medical history and physical examination. After written informed consent was obtained, an electrocardiogram was recorded and blood was drawn after an overnight fast for complete blood count, blood urea nitrogen, creatinine, serum calcium, phosphorus, total protein, albumin, electrolytes, and glutamine oxaloacetic transaminase. After 2 d of eating at least 250 g of carbohydrates per day, each subject was given a 75-g oral glucose tolerance test. 27 volunteers were found to have noninsulin-dependent diabetes mellitus (15 females, 12 males—26 Indians and one Caucasian) according to the

Table I. Physical Characteristics of 177 Volunteers and Energy Intake in the Respiratory Chamber

Characteristic	Mean	Range
Age (yr)	27	18–65
Weight (kg)	96.9	41.3–178.1
Body fat (%)	32	3–50
FFM (kg)	64.2	34.0–105.9
Energy intake (kcal/d)	2,360	1,610–3,615

National Diabetes Data Group criteria (15). Eight of the diabetic volunteers had a fasting plasma glucose concentration >200 mg/dl, and the mean value for the 27 patients was 170±76 mg/dl.

After admission, the volunteers were placed on a "weight maintenance" diet calculated on the basis of their body weight. The diet, made of standard foodstuffs, was composed of 20% protein, 50% carbohydrate, and 30% fat.

Body composition. Body composition was estimated by underwater weighing (16). Briefly, after an overnight fast, each subject was weighed on a metabolic balance while dressed in a previously weighed robe and after emptying his/her bladder. The subject was then weighed eight times after a forced expiration and while completely submerged in a tank of thermoneutral water (~35°C). Each subject's body density was calculated from his/her weights in air and water after correcting for the simultaneously measured residual lung volume using the helium dilution technique. Percent body fat was estimated according to the equation of Keys and Brozek (17), and FFM was calculated as FFM = body weight − (body weight × percent body fat). The coefficient of variation of our underwater weighing method to determine percent body fat is 7%, as previously published (18).

Energy expenditure measurements. Between the third and the tenth day of admission, each volunteer spent a day in the respiratory chamber. After an overnight fast, three electrocardiogram leads and one wrist motion sensor were placed on the volunteer and hooked up to the Vitalog PMS-8 portable microcomputer. Measurements in the respiratory chamber were performed continuously for 23 h from 0800 to 0700 h the following day and then extrapolated to 24 h. No vigorous exercise was allowed in the chamber and spontaneous activity was estimated by the wrist motion sensor in all 177 subjects and by the radar system in 118 of these subjects. Because of the confinement within the chamber, only 80% of the "weight maintenance" calories given on the Metabolic Ward were given in the chamber. Meal times were 0800, 1130, 1630, and 1930 h.

To increase the CO_2 concentrations and decrease the O_2 in the chamber, the air extraction flow rate was kept at a low level (~10–12 liters/min) during the first 4–7 h of the test. When the CO_2 concentration reached ~0.7%, the flow rate was increased (35–60 liters/min) to keep the CO_2 concentration below 0.8%.

Sleeping metabolic rate was defined as the average energy expenditure of all 15-min periods between 2330 and 0500 h, during which the sum of both activity indices was ≤2 when activity was measured by both systems or during which wrist activity was ≤1 when measured by the wrist sensor alone. At 0700 h the following morning, 11 h after the evening snack, the chamber was opened and while the volunteer was still lying on the bed, a plastic transparent ventilated hood was placed over his/her head for ~40 min. After 20–25 min of adaptation to the hood, time during which the analyzers were calibrated, the basal metabolic rate (BMR) was measured for another 9–15 min by connecting the hood system to the analyzing equipment of the chamber.

Individual variation of 24-h energy expenditure. To measure the reproducibility of the 24-h energy expenditure measurement, 12 of the 177 subjects, whose characteristics are given in Table II, were studied a second time in the respiratory chamber at least 1 wk apart. The subjects were fed the same number of calories on both occasions in the chamber.

Thermic effect of food. The thermic effect of the four meals was calculated as previously described (19) and as described in Fig. 3. In brief, the mean resting energy expenditure (EErest) from 0800 to 2300 h (15 h), which includes the thermic effect of the meals, was obtained by the intercept of the linear regression line for energy expenditure versus activity measured by radar:

$$EĖ = EĖrest + k × (\% \text{ activity}).\qquad(9)$$

The difference between EErest (in kilocalories per minute) and the BMR represents an estimate of the thermic effect of the meals when computed over 15 h. 15 h is an estimate of the duration of the thermic effect of the four meals. The thermic effect of food was also expressed as a percentage of the energy intake.

Cost of physical activity. The combined output from our radar devices gives the proportion of time during which the subject is active (percent activity), independent of the type of movement and the workload. In
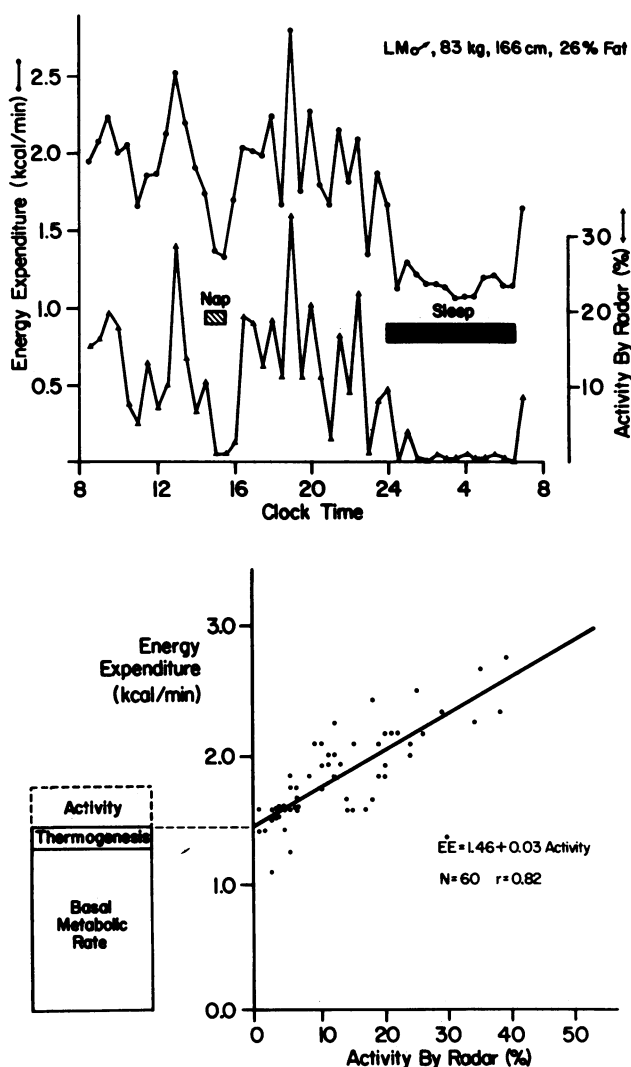

Figure 3. (*Upper panel*) Energy expenditure and activity (averaged over 30-min periods) during the time course of the day in one subject (L.M.). (*Lower panel*) Relationship between energy expenditure and activity in the same subject, each point representing a 15-min period from 0800 to 2300 h. By simple regression analysis, the resting energy expenditure (EErest) can be calculated as the y intercept and the thermic effect of the four meals is calculated as the difference between EErest and the BMR expressed over 15 h. The energy cost of spontaneous physical activity is the slope of the linear regression line.

Table II. Characteristics of 12 Subjects (10 Males, 2 Females) Whose 24EE Was Measured Twice in the Respiratory Chamber

Characteristic	Mean	Range
Age (*yr*)	37	21–64
Weight (*kg*)	99.5	69.4–145.3
Body fat (%)	30	13–45
FFM (*kg*)	67.9	51.2–92.9
Energy intake (*kcal/d*)	2,430	2,130–2,870

each subject there was a significant correlation between the mean activity measured by radar over 15-min intervals from 0800 to 2300 h and the corresponding energy expenditure during the same time periods (Fig. 3). This relationship was linear and its slope (k in Eq. 9 = Δ energy expenditure/Δ activity) represents the cost of physical activity per unit of activity. The product of the mean 24-h activity measured by radar times the cost of physical activity was used as an index of the 24-h energy cost of spontaneous physical activity.

Statistical methods. Throughout the text, data are presented as mean±standard deviations. Analysis of covariance and single and multiple linear regression analysis were performed using the general linear models of the SAS Institute (Statistical Analysis System, Cary, NC). The slopes of the simple regression lines were compared by a test of homogeneity of slopes by analysis of covariance. The within-subject variability of 24-h energy expenditure was calculated for the 12 subjects studied twice by fitting a one-way analysis of variance model with 12 factor levels (one for each subject) and sample size two at each level. The within-individual variability in the 12 subjects was compared with the among-individual variability in the 177 subjects using a one-tailed F statistic. The variability of the indirect calorimetric method (propane combustion) was similarly compared with the within- and among-individual variabilities.

Results

Variability of the method. If one takes 2,400 kcal/d as a typical energy expenditure in humans, this would correspond to a 207-g/d propane combustion using 527 liters O_2 and producing 314 liters CO_2 in a day with a 0.60 RQ. We have performed 18 3-6-h propane combustion tests and extrapolated the results to a 207 g/d combustion rate. The measured $\dot{V}CO_2$ and $\dot{V}O_2$ were 305±9 liters/d and 515±15 liters/d, respectively, with a 0.59 RQ: if Eq. 8 is used to calculate energy expenditure this would result in a 2,345±67 kcal/d with a coefficient of variation of 2.9%. The 2–3% underestimation of $\dot{V}CO_2$ and $\dot{V}O_2$ is probably due to incomplete combustion of the propane. Nevertheless, these results indicate that the measurements in this chamber are very reproducible. The variance of these measurements expressed in energy terms was 4,766 (kcal/d)^2.

Variability within individual. When duplicate measurements were made in 12 subjects, the mean 24EE was 2,433±113 and 2,438±110 kcal/d on the first and second measurements respectively (Fig. 4). With a range from 0.2 to 9.0%, the coefficient of variation (CV) of the 12 repeat measurements was 2.4%. The within-individual variance was 7,660 (kcal/d)^2. The variance of the method and the within-subject variance were not statistically
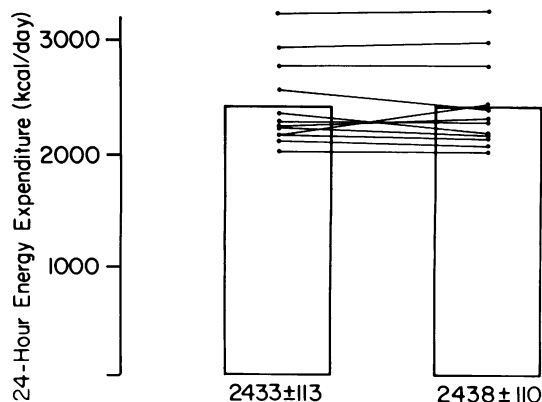
different (Fig. 5). In the 12 subjects, the coefficients of variation for the BMR and the sleeping metabolic rate measurements were 3.7% (range 0.1–7.8%) and 4.7% (range 3.7–6.1%), respectively. However, determination of the thermic effect of food was not very reproducible (mean CV = 43%, range 1–68%).

24-h energy expenditure. 24EE varied considerably from subject to subject, ranging from 1,371 to 3,615 kcal/d, and averaging 2,292±420 kcal/d for the entire group. Physical characteristics, such as body weight, height, or surface area, were found to be closely related to 24EE and are given in Table III. 73–82% of the variance in 24EE was explained by differences in height and weight. 24EE was also found to be significantly related to FFM (Fig. 6), the assumed metabolically active tissue (24EE [kcal/d] = 597 + 26.5 FFM, r^2 = 0.81, P < 0.0001) without any additional statistically significant effect of sex, age, or diabetes status, as tested by analysis of covariance and multiple linear regression analysis. The variance around the regression line of 24EE on FFM (33,439 [kcal/d]^2) was significantly higher than the variance of the repeated measurements on 12 subjects (7,660 [kcal/d]^2; F = 4.37, P < 0.0001) (Fig. 5). Percent fat, an index of obesity, estimated by underwater weighing, was a significant determinant of 24EE and accounted for 4.8 kcal/d per unit of percent fat (24EE = 488 + 25.8 FFM + 4.8% fat, r^2 = 0.82, P < 0.0001).

Energy expenditure for individuals varied in a range of approximately ±15% of that predicted by their FFM, with extreme values of 432 kcal/d above and 426 kcal/d below the regression line. In the 118 subjects whose spontaneous physical activity was measured by radar, subjects with a higher 24EE than that predicted by their FFM were slightly more obese (34±9 vs. 30±11% fat, P < 0.05) but frankly more active (9.6±2.3 vs. 7.7±2.0% activity, P < 0.0001) than those with a lower 24EE than that predicted. However, when adjusted for differences in FFM and activity level, 24EE was not influenced by body composition (percent fat).

During the course of the 23-h measurement, energy expenditure varied significantly in each individual, with lower values observed during sleep. The energy expenditure varied linearly with the activity, resulting in a significant correlation between these two variables in all of the subjects, with a mean correlation coefficient of 0.79. As an illustration of the changes in energy expenditure and activity during the course of the 23 h, Fig. 7 shows the mean energy expenditure and activity in two groups of males whose physical activity was measured by radar selected
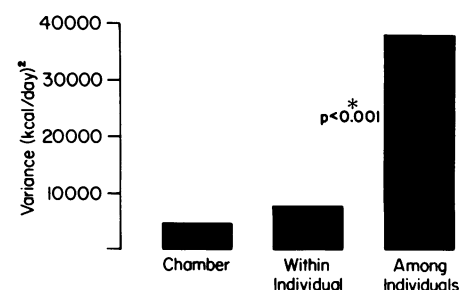

Figure 4. Results of 24EE measured twice in 12 subjects. The mean coefficient of variation of 24EE equals 2.4% (range 0.2–9.0%).

Figure 5. Variances in 24EE within individual (repeated measurements in 12 subjects) and among individuals after adjusting for FFM (n = 177). The first bar represents the variance of the respiratory chamber determined by propane combustion (n = 18). Both the methodologic and within-individual variances were significantly lower than the among individual variances.

Table III. Simple or Multiple Linear Regression
Analyses between 24EE and Body Weight,
Height, Surface Area, FFM and Percent Fat

Equation	r^2
Weight and height	
24EE = 1,043 + 13.0 body wt	0.73
24EE = −1,255 + 11.3 body wt + 14.7 height	0.82
24EE = −392 + 1,323 surface area	0.81
Body composition	
24EE = 597 + 26.5 FFM	0.81
24EE = 488 + 25.8 FFM + 4.8% fat	0.82

Body wt is measured in kilograms, height in centimeters, surface area in square meters, and FFM in kilograms. 24EE is given in kilocalories per day. (n = 177.)

on the basis of their body composition: a group of extremely obese subjects (percent fat > 35, n = 16) and a group of thinner subjects (percent fat < 20, n = 16). It can be seen that the more obese subjects had a greater energy expenditure over the course of the day. In the two groups, energy expenditure had a pattern which paralleled that observed for activity, with peak values corresponding to the subjects' mealtimes.

Basal metabolic rate. BMR also varied considerably between subjects, ranging from 1,102 to 2,935 kcal/d when expressed on a 24-h basis with an average value of 1,813±363 kcal/d (Table IV). 24EE was therefore 27±12% higher than BMR expressed on a 24-h basis, but varied among subjects from −10% to +55% of the BMR. The only two subjects who had a 24EE/BMR ratio below 1.0 (0.93±0.01) were characterized by an unusually high BMR when compared with the other 170 subjects (39.1 vs. 28.6 kcal/kg FFM · d, P < 0.01). BMR, like 24EE, was correlated to FFM (Fig. 8): BMR (kcal/d) = 478 + 20.9 FFM (r^2 = 0.67, P < 0.0001). Unlike 24EE, BMR was not related to the percentage of fat. Although there are greater variations between people in the basal state when compared with 24 h, these variations might be partially compensated for during the rest of the day by differences in physical activity and/or differences in the thermic effect of food, as well as differences in the duration of sleep.

Sleeping metabolic rate. Sleeping metabolic rate also varied widely between people, from 850 to 2,699 kcal/d when expressed on a 24-h basis (1,618±303 kcal/d) (Table IV). In the 177 subjects
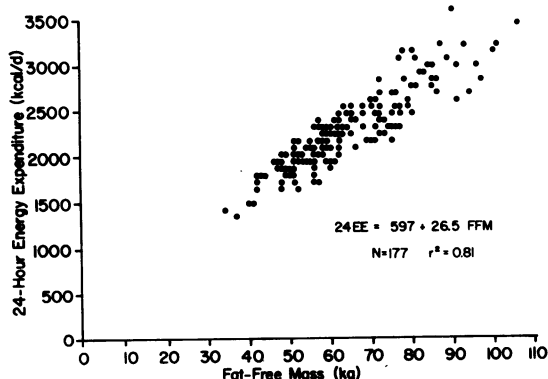

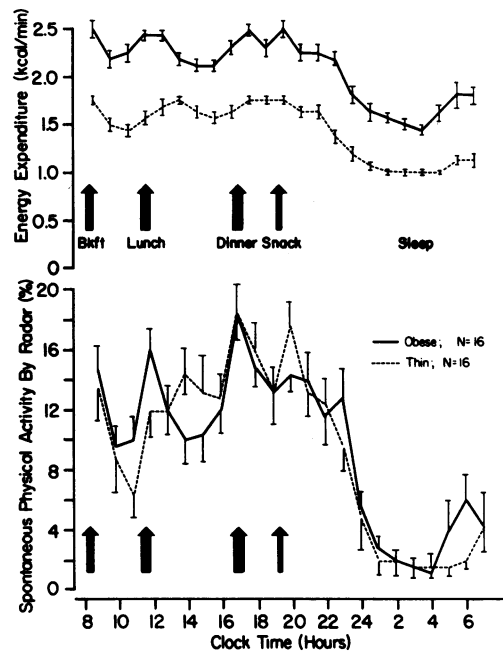*Figure 6.* Relationship between 24EE and FFM in 177 subjects. 28 observations are hidden.

Figure 7. Energy expenditure (*upper panel*) and spontaneous physical activity (*lower panel*) during the time course of 24 h in the males with a percent fat > 35% (n = 16) and the males with a percent fat < 20% (n = 16).

studied, the sleeping metabolic rate represented an average energy expenditure for periods varying from 30 to 530 min. As with 24EE and BMR, sleeping metabolic rate was significantly correlated to FFM (Sleep [kcal/d] = 495 + 17.5 FFM, r^2 = 0.69, P < 0.0001) (Fig. 8).

Thermic effect of food. Among the 118 subjects in whom physical activity determinations by the radar system were available, the thermic effect of food averaged 165 + 155 kcal/d, i.e., 7.0±6.6% of the 2,330±345 ingested calories (Table IV). Expressed as a percentage of energy intake, the thermic effect of food was not correlated to any physical characteristics of the subjects.

Spontaneous physical activity. Radar was used to determine the percentage of time during which the subject was moving in 118 subjects (Table IV). The mean was 8.7% of the 24-h period, varying considerably from 3.9–16.6%. Activity in each volunteer during each 15-min period between 0800 and 2300 h correlated significantly with energy expenditure measured during the same interval. The slopes of the latter relationships (k = Δ energy expenditure/Δ activity in Eq. 9), which represent the energy cost of spontaneous physical activity, were significantly related to both body weight (r = 0.68) and FFM (r = 0.71). These slopes varied from 0.0109 to 0.0541 kcal/min per percent activity (mean 0.0281±0.0084). When expressed on a 24-h basis, each percentage point of spontaneous activity (continuous activity for 1% of 24 h, i.e., 14.4 min) represented an average extra energy expenditure of 40.5±12.1 kcal (range 15.7–77.9 kcal). The mean energy expenditure attributable to spontaneous physical activity (cost of activity × percent activity) was 348 kcal/d, varying from 138 to 685 kcal/d.

In that the cost of physical activity is proportional to body weight, another way of looking at the contribution of activity to the 24EE (dependent variable) was to include the product of (percent activity × body weight) as an independent variable in

Table IV. Energy Expenditure Rates, Activity, Thermic
Effect of Food, and Cost of Spontaneous Physical Activity
in 118 Subjects Whose Activity Was Measured by Radar

	Mean	Range
Energy intake (kcal/d)	2,330	1,610–3,515
24EE (kcal/d)	2,275	1,371–3,485
Daytime energy expenditure* (kcal/min)	1.78	1.06–2.69
Sleeping metabolic rate‡ (kcal/min)	1.12	0.70–1.87
BMR (kcal/min)	1.25	0.77–2.03
Energy expenditure without activity§ (kcal/min)	1.44	0.87–2.07
Thermic effect of food‖ (kcal/d)	165	−258–476
Thermic effect of food/energy intake (%)	7.0	−14–20
Spontaneous physical activity (%)	8.7	3.9–16.6
Cost of spontaneous physical activity¶ (kcal/d per %)	41	16–78
Absolute energy cost of physical activity** (kcal/d)	348	138–685

* Mean energy expenditure from 0800 to 2300 h.
‡ Mean energy expenditure from 2330 to 0500 h when very little or no motion was detected (see text).
§ Intercept of the relationship between energy expenditure and activity from 0800 to 2300 (EĖrest).
‖ (EĖrest − BMR) × 15 × 60 (measured over 15 h).
¶ Slope of the relationship between energy expenditure and activity.
** Spontaneous activity × cost of activity.

Comparison of 24-h energy expenditure, basal, and sleeping metabolic rate. When the slopes of the three relationships between FFM and 24EE, BMR, and sleeping metabolic rate (Fig. 8) were compared, each slope differed significantly from the others ($P < 0.0001$) for the three comparisons. For each kilogram of FFM, an average 17.5 and 20.9 kcal/d was expended in the sleeping and basal states, respectively, whereas 26.5 kcal/d was expended when the subjects were fed and able to move (24EE). After correcting for the effect of activity, an estimated 20.5 kcal/d were accounted for by each kilogram of FFM, which did not differ from that measured for BMR (20.9 kcal/kg FFM · d).

Fig. 9 shows that 24EE varies considerably between individuals, from 28.5 to 43.0 kcal/kg FFM · d. The frequency distribution is normal, with a mean value of 36.3 kcal/kg FFM × d. Similarly, when 24EE was expressed as a ratio of the sleeping metabolic rate (24EE/sleep), the range varied considerably, from 1.15 to 1.70, with a mean of 1.41. Thus, differences in spontaneous physical activity can account for large differences in 24EE.

Discussion

In the last decade, there has been an intensive search for defects in energy expenditure that might be specific causes of human obesity. The defects sought have been: (a) reduction in the thermic effect of food (20–24); and (b) a decreased cost of physical exercise in the postprandial or fasting state (25, 26). The results have often been contradictory, perhaps because of attempts to extrapolate studies of only a few hours' duration to the energy expenditure of days or even years. In a similar manner, recommendations for energy intake have been made from com-

addition to FFM in a multiple regression analysis. This product was highly significant ($P < 0.0001$) in predicting 24EE, resulting in the following equation: 24EE (kcal/d) = 667 + 20.5 FFM + 0.38 (percent activity × body weight) (Fig. 8). The contribution of the activity term in this equation averaged 314 kcal/d and varied from 95 to 903 kcal/d. These results are very similar to the first independent approach described above.
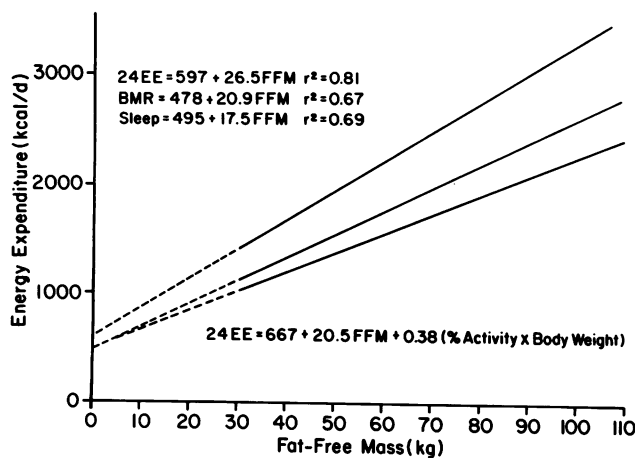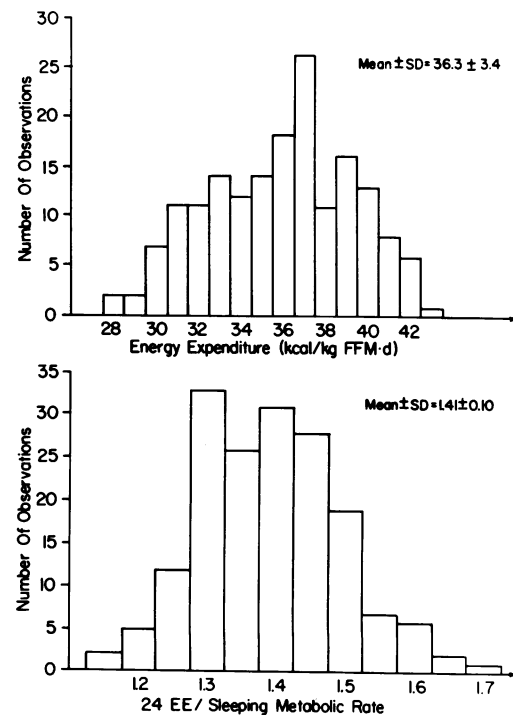

Figure 8. Relationships, by simple regression analysis, between 24EE, BMR, sleeping metabolic rate, and FFM in 177 subjects. The slopes are statistically significantly different from each other whereas the intercepts are not different. By multiple regression analysis, the effect of percent activity × weight on 24EE is given for 118 subjects.

Figure 9. Distribution of measured 24EE ($n = 177$) expressed per kilogram of FFM (upper panel). Part of the individual variability of 24EE expressed per kilogram of FFM could be due to inaccuracy in estimating the FFM. An alternative way of expressing individual variability in 24EE that is independent of FFM is the ratio 24EE/sleep (lower panel).

putations of energy expenditure or from direct observation of dietary intakes (1-3). The conclusions have rarely agreed. For these reasons, there is a need for better methods to assess the daily energy requirements in humans (7).

There is no doubt that the study of energy balance in humans requires measurement of energy expenditure over periods of at least 24 h. New methods such as the use of doubly labeled water (6, 27, 28) for measurement of energy expenditure in free, living subjects may prove very useful in understanding the possible causes of human obesity and in the assessment of energy requirements in humans. As a result of improvements in the quality (sensitivity and stability) of oxygen and carbon dioxide analyzers, the classical principle of indirect calorimetry, however, can now be used to determine energy expenditure in comfortable respiratory chambers over a period of 1-7 d (8, 9). The first such chamber built in North America is described; this is a modification of the Lausanne respiratory chamber built in the late 1970s (9, 10). The size of these chambers is sufficient to allow the subject spontaneous activity. By measuring energy expenditure and spontaneous physical activity over the time course of the day, the overall 24EE can be divided into its components—sleeping metabolic rate, energy cost of arousal, thermic effect of food, and energy cost of physical activity. Our results indicate that measurements of energy expenditure in respiratory chambers are very reproducible (CV = 2.4%), confirming two recent studies (29, 30), and more so than other methods. Therefore, these chambers currently represent the most precise way of measuring medium-term energy expenditure in humans.

Energy expenditure variability. We have standardized our results of energy expenditure on the basis of FFM, an estimate of the metabolically active tissue. This choice is validated by the fact that in the basal state FFM, but not fat mass or percentage of fat, is related to BMR. Thus, as previously reported (10), FFM represents the best predictor of energy expenditure. Results obtained on 177 subjects show that 24EE varies considerably between people according to their body size. When 24EE was plotted vs. FFM (Fig. 6), however, 19% of the variance between people was unaccounted for by differences in FFM. From this, one can therefore conclude that, at any given range of FFM, it is possible to find subjects who deviate above or below the regression line by at least 15% of the predicted value (extreme values from −426 to +432 kcal/d). Because of the good reproducibility of the measurements (repeated measurements in individuals or propane combustion), errors in the method cannot be blamed for the observed variability in energy expenditure. Some of the remaining variance could be related to the error made on the estimate of the FFM as measured by underwater weighing (31). However, more importantly, body density as an index of body composition with all the assumptions made in the calculation, does not provide an exact value for the metabolically active tissue but represents only an approximation of the latter. It is therefore conceivable that part or all of the unexplained variance in 24EE can be related to the inaccuracy to estimate the metabolically active tissue mass. An alternative way of expressing the variability among individuals is the quotient of 24EE divided by the sleeping metabolic rate expressed on a 24-h basis: (24EE/sleep) (Fig. 9). Sleeping metabolic rate when used as a denominator corrects for differences in FFM between individuals and therefore deletes the confounding factors of differences in body weight and estimated composition. In addition, in terms of basal energy cost per kilogram of FFM, the ratio of 24EE/sleeping metabolic rate is likely to minimize any potential

effect of differences in age, sex, and "family membership" (32) when people are compared. This ratio represents therefore the fractional proportion of 24EE in excess of the minimum energy requirement observed during sleep: i.e., the cost of the arousal state, the cost of thermogenesis, and the cost of spontaneous physical activity. Fig. 9 shows that, on the average, subjects in a respiratory chamber expend ~41% more calories than their minimum requirements, i.e., sleeping metabolic rate. It also shows that this factor varies widely between individuals, confirming an older study performed by Booyens et al. (33). In studying 130 siblings from 54 families, we have recently shown that >50% of the variability in resting metabolic rate unexplained by differences in FFM, age, and sex was due to familial differences (32). It is therefore very likely that part of the overall variability observed in 24EE, independent of FFM, could be related to a familial aggregation of not only resting metabolic rate but also of spontaneous physical activity or thermic effect of food.

This large variability in energy expenditure between people would presumably be even larger in free living conditions in which larger differences in the level of physical activity are likely to be observed. If so, universal recommendations in energy requirement cannot be made at the individual level, owing to the important individual variability of energy expenditure.

Effect of obesity on 24EE. In contrast to what is observed in the basal state, the percentage of body fat independent of FFM also contributes to the prediction of 24EE (34) (Table IV). For a given FFM, the more obese subjects have a higher 24EE. Those subjects with an observed 24EE above that predicted (24EE above the prediction line based on FFM only) were, on the average, slightly more obese (34 ± 9 vs. $30\pm11\%$ fat, $P < 0.05$) and frankly more active (9.6 ± 2.3 vs. $7.7\pm2.0\%$, percent activity $P < 0.0001$) than those below the prediction line. However, when energy expenditure was predicted by including activity in the equation, subjects who fell above and below the predicted values had similar body compositions. This implies that more active subjects are likely to present with a relatively higher 24EE; furthermore, when the subjects are heavier, there is an even greater effect of increased spontaneous physical activity on energy expenditure. As shown in Fig. 7, the energy expenditure in obese subjects was higher at all times compared with that of a group of thinner subjects. This is mainly due both to the larger mass of metabolically active tissue and the higher energy cost of spontaneous physical activity in the obese when compared with thinner subjects. These, like previously reported results (10, 35), leave no doubt that under the conditions of the chamber, on average, the more obese expend more energy and therefore require more energy to maintain body weight. However, these results do not exclude the possibility that a reduced energy expenditure can lead to obesity.

Hypothesis. An important question to be answered is: who are the people most likely to gain weight? A cross-sectional study of people differing in their body weight and composition does not necessarily give insight into this question. It would be of great value to have the ability, by looking at cross-sectional results of energy expenditure, to predict a longitudinal outcome in terms of body weight. For example, it would be valuable to know if the subjects whose observed 24EE is lower than that predicted on the basis of FFM are predisposed to weight gain. The cross-sectional data, however, can only be used to form an hypothesis about prospective outcomes. We hypothesize that the subjects with a 24EE significantly below that predicted for their FFM (Fig. 6) are most likely to gain weight. In response to weight

gain, their 24EE will move toward the mean 24EE for the population at a similar FFM. This hypothesis is supported by two observations: (a) On the average, presumably as a consequence of weight gain, the subjects with a 24EE higher than that predicted on the basis of FFM are as obese as those with a lower than predicted 24EE. (b) After significant weight loss, post-obese subjects require less energy for weight maintenance as compared with subjects with normal body weight and composition (36). It is therefore possible that the pre-obese patient is a subject whose energy expenditure is low for his/her metabolic size and, consequently, weight gain may be a compensatory mechanism that ultimately results in increased energy expenditure by increased cost of spontaneous physical activity and possible increased rates of different processes of energy expenditure, for example, protein turnover, gluconeogenesis, substrate cycling, ion pumping, etc. This increase in energy expenditure will ultimately match energy intake, assuming that intake is not altered simultaneously. Similarly, we would predict that after weight loss, the energy expenditure of the post-obese will be abnormally low and he/she will again be predisposed to resume weight gain. Only future, prospective studies will confirm or deny this hypothesis.

Sleeping, basal, and 24EE comparisons. When expressed on a 24-h basis, each kilogram of FFM costs, on the average, ~18, 21, and 27 kcal/d in the sleeping, basal, and 24EE states, respectively. One of the most striking observations is the ~19% increase in energy cost per kilogram of FFM from the sleeping to the basal state; it implies that the state of arousal plays an important role in total 24EE. Important differences in energy expenditure can result from differences in the duration and possibly the quality of sleep. When the basal and averaged 24-h states were compared, there was a 6-kcal/d increase in energy cost per kilogram of FFM. This increase is most likely due to the cost of spontaneous physical activity because when corrected for the latter, the energy cost per kilogram of FFM decreased from 26.5 to 20.5 kcal/d. One can summarize that when comparing the sleeping metabolic rate, which represents the minimal tissue energy requirement, and 24EE, some extra energy is used when aroused, as well as extra energy used for physical activity and, to a lesser extent, for the thermic effect of food. The mechanisms involved in the changes in metabolic rate between the sleeping and the aroused basal state are unknown, but might include a stimulation of the sympathetic nervous system.

Effect of activity on 24EE. Even within the confines of the respiratory chamber, spontaneous physical activity measured by radar varied widely (from 3.9 to 16.6%) in the 118 subjects. Because the subjects were not allowed to carry out physical exercise such as isometric exercises or calisthenics, it is possible that such activity represents an unconscious need to be active. This activity was limited to (a) strolling around within the chamber and (b) movements of the limbs with little displacement of the body's center of gravity, e.g., fidgeting (37). Although these two types of activity do not have the same energy cost, they were not discriminated by the radar's measurements, which does not measure work intensity. However, among the subjects, a highly significant correlation was observed between activity and energy expenditure ($P < 0.0001$ in the 118 subjects). The slopes of the regression lines between energy expenditure and activity, which represent the energy cost of spontaneous physical activity, were correlated with body weight ($r = 0.68$). This implies that even in a respiratory chamber, the energy cost of activity is related to body size, with the heavier subjects requiring more

energy to move their bodies. Therefore, heavier subjects with high levels of spontaneous physical activity will expend a lot of calories related to activity.

By multiple linear regression analysis, the product of total spontaneous physical activity × body weight was found to be highly significant ($P < 0.0001$) in the prediction of 24EE. From the equation presented in Fig. 8, the importance of this activity term varied from 95 to 903 kcal/d, which is very similar to the range obtained by an independent method in which the energy expenditure attributable to activity was calculated as the amount of physical activity × the energy cost of activity (range 138–685 kcal/d). Thus, energy expenditure resulting from spontaneous physical activity is an important component in total 24EE, and therefore in energy balance. Whether spontaneous physical activity of the subjects inside the chamber is related to that of free living conditions remains to be established. If so, much larger differences in energy expenditure would likely be accounted for by differences in the general level of physical activity in free, living subjects.

Effect of the thermic effect of food on 24EE. The thermic effect of food accounted for ~7% of the ingested calories varying from −14 to 20% and representing an average of 165 kcal/d. Negative values indicate that the BMR was higher than the energy expenditure rate without activity (EErest), the latter being the intercept of the regression line between energy expenditure and activity. Both values can be subject to error owing to motion of the subject during the BMR measurement or to an intercept value over- or underestimated as a result of a few extreme points changing the slope of the relationship between energy expenditure and activity. For these reasons, the coefficient of variation of the calculated thermic effect of food was large (43%), varying from 1 to 68%. The thermic effect of food was not correlated with any physical characteristic of the subjects. Because of the inaccuracy of this method in measuring the thermic effect of food during a whole day, it is difficult to compare our results with those of Bessard et al. (38) and Segal et al. (39) who showed an inverse relationship between body fat and thermic effect of food when measured over shorter periods of time.

Summary. This study shows that a respiratory chamber can be used to measure, accurately and reproducibly, rates of daily energy expenditure in a large group of subjects. Among individuals, 24EE varies greatly, mostly as a result of individual differences in body size. The daily energy expenditure, however, also varies among individuals because of individual differences in spontaneous physical activity. As a result of the large variance in daily energy expenditure among individuals not explained by body size, universal recommendations for daily caloric needs based on body size alone will be inappropriate in large numbers of individuals. For these recommendations of daily caloric needs, more emphasis should be given, in future, to the level of general physical activity. The variability in 24EE among individuals of similar body size is a possible mechanism that may contribute to variability in the predisposition to obesity. An hypothesis proposing a defect in daily energy expenditure as a contributing factor to the pathogenesis of human obesity has been formulated and will only be tested and proven by prospective studies.

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