Increased Energy Expenditure in Hemodialysis Patients[1]

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ABSTRACT

Malnutrition is prevalent in chronic hemodialysis patients and is related to multiple factors; the hemodialysis procedure itself has been suggested as a catabolic factor. To examine the possible role of hemodialysis on energy metabolism, resting energy expenditure and respiratory quotient in ten chronic hemodialysis patients was measured in this study, using a whole-room indirect calorimeter. Measurements were done continuously: for 2 h before hemodialysis, during 4 h of hemodialysis, for 2 h after hemodialysis, and separately on a nondialysis day after 12 h of fasting. Age-, sex-, and body mass index-matched healthy volunteers were used as control subjects. Chronic hemodialysis patients have a significantly higher resting energy expenditure on a nondialysis day (1.18 ± 0.15 kcal/min; $P < 0.01$) as compared with control subjects (1.10 ± 0.16 kcal/min). Resting energy expenditure further increased significantly during the hemodialysis procedure (1.32 ± 0.18 kcal/min, averaged over the 4 h of hemodialysis; $P < 0.01$ *versus* predialysis) and was also significantly higher compared with the postdialysis period and nondialysis day resting energy expenditure ($P < 0.001$ for both). This effect was most pronounced during the first (1.37 ± 0.19 kcal/min) and second (1.33 ± 0.18 kcal/min) hours of hemodialysis ($P < 0.001$ for both). Respiratory quotient was not significantly affected by hemodialysis. It was concluded that chronic hemodialysis patients have higher than normal resting energy expenditure levels, which is further increased during hemodialysis. This process may significantly potentiate the protein-calorie malnutrition seen in this patient population.

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Malnutrition is common in chronic hemodialysis (CHD) patients. Multiple factors affect the nutritional status of these patients, including decreased dietary protein and energy intake, hormonal derangements, and dialysis-related factors such as inadequate dose of dialysis, dialysis membrane bioincompatibility, and dialytic losses of amino acids and albumin (1–5).

Increased resting energy expenditure (REE) in CHD patients is another potential factor that may worsen malnutrition. Earlier studies suggested that REE was not different between normal healthy control subjects and chronic renal failure patients both before and after initiation of dialysis (6–8). However, these studies were subject to several limitations, particularly in the methodology used for measuring energy expenditure, namely the metabolic cart. This method can only be performed for limited time periods (30 to 40 min) and must be repeated several times to obtain values during lengthy procedures, causing errors estimated to contribute as much as 6 to 10% of REE measurements within subjects (9). A more precise and complex procedure, whole-room indirect calorimetry (also known as the metabolic chamber [MC]), is considered the "gold standard" for measuring REE (9,10). The REE measurements can be done accurately, continuously, and comfortably for periods of up to 24 to 48 h with precise control of the environment, which is not possible with alternative methods of indirect calorimetry (11).

In this study, we measured REE and respiratory quotients (RQ) in ten stable chronic hemodialysis patients. Measurements of these parameters were performed continuously both on a dialysis day (before, during, and after a hemodialysis procedure), on two separate occasions with two dialysis membranes with different complement activation properties, and on a nonhemodialysis day. We compared our results with REE and RQ of age-, sex-, and body mass index (BMI)–matched control subjects to define differences between dialysis patients and healthy control subjects.

METHODS

Patient Characteristics

Studies were performed on five male and five female patients who were clinically stable and were on chronic hemodialysis treatment for a minimum of 6 months. Patient characteristics are shown in Table 1. Two insulin-dependent diabetic patients who were under good blood glucose control and two patients with systemic lupus erythematosus whose disease was in remission and who were not on corticosteroids

TABLE 1. Characteristics of the study patients (CHD) and matched control subjects[a]

	CHD	Controls
Age	38.3 ± 13.0	37.7 ± 10.8
Male/female	5/5	5/5
Etiology of Renal Disease		N/A
Hypertension	3	
Insulin Dependent Diabetes Mellitus	2	
Chronic Glomerulonephritis	2	
Systemic Lupus Erythematosus	2	
Adult Polycystic Kidney Disease	1	
Weight (kg)	75.0 ± 18.7	76.1 ± 20.1
Height (cm)	169 ± 9.4	168.8 ± 6.7
Body Mass Index	26.3 ± 5.9	26.4 ± 5.6
Serum Albumin (g/dL)	4.08 ± 0.32	N/A
Time on Dialysis (months)	31.9 ± 30.1	N/A

[a] N/A, not applicable.

were included as part of the patient group. The patients were specifically chosen from self-care units so that the majority of the dialysis procedure could be performed by the patient, thus reducing any interruption during the measurements of REE. The study protocol was approved by the Institutional Review Board of Vanderbilt University and written informed consent was obtained from all patients. Ten age-, sex-, and BMI-matched healthy control subjects who were previously studied in the metabolic chamber were chosen for comparison.

Study Design

The study was designed as a prospective, randomized investigation. Patients were randomly assigned to one of the hemodialysis membranes on two consecutive treatment days (Figure 1). On Study Day 1, patients were admitted to the Clinical Research Center at approximately 7 a.m. They were fed a light meal with predetermined components approximately 1 h before initiation of study protocol. The dietary composition of these meals was on average 705 ± 223 kcal, 16% protein, 32% fat, and 52% carbohydrate. This was done to keep the patients fasting during the entire 8-h study period, including during the hemodialysis procedure. Subjects were then studied in the metabolic chamber for a 2-h predialysis period. At the end of this period, patients underwent hemodialysis with the assigned dialyzer (F-80, Fresenius, Walnut Creek, CA, made of non-complement-activating polysulfone; or T150, Terumo Corporation, Tokyo, Japan, made of complement-activating cellulose) for 4 h with a blood flow rate of 400 mL/min and a dialysate flow of 500 mL/min. Pre- and postdialysis blood samples were also obtained for commonly measured blood chemistries. Ultrafiltration rates were determined by the patients' needs and "estimated dry weight." The mean rate of fluid removal was 3.18 ± 0.93 L/dialysis session. The dialysate composition was: sodium, 139 mEq/L; potassium, 2 mEq/L; calcium, 2.5 mEq/L; glucose, 200 mg/dL; and bicarbonate, 39 mEq/L.

During each hemodialysis treatment, patients were supervised by a hemodialysis nurse outside the metabolic chamber who had immediate access into the chamber. For the majority of the treatments, this 4-h period was continuous, without any interruption of the measurement. The hemodialysis procedure was initiated and terminated by the nurse, and the time period for these procedures (approximately 10 to 15 min) were not included in the REE and RQ measurement. Patients were kept in the metabolic chamber for another 2 h for measurement of postdialysis REE and RQ. An identical protocol was repeated with the other dialyzer membrane at the next scheduled HD treatment. The patients were also admitted to the metabolic chamber for measurement of their REE and RQ on a nondialysis day while they fasted. This measurement was done for 1 h, usually on the day between the two HD measurements.

Whole-Room Indirect Calorimeter

Continuous measurements of REE and RQ were performed in the whole-room indirect calorimeter as described previously. The metabolic chamber is a small environmental room (8.5 × 11 × 7.8 ft; 19,500 liters in net volume) with a desk, a chair, a toilet/sink, a telephone, and a TV/VCR set. The room is air-tight, with an entrance door (3.3 × 6.5 ft) and an air lock (2 ft × 10 in) for the passing food and other items into and out of the room while the subject is inside the chamber. The chamber uses a fan which is controlled by a computer that purges a certain amount of air out of the chamber according to the rate of CO_2 a subject produces. Oxygen

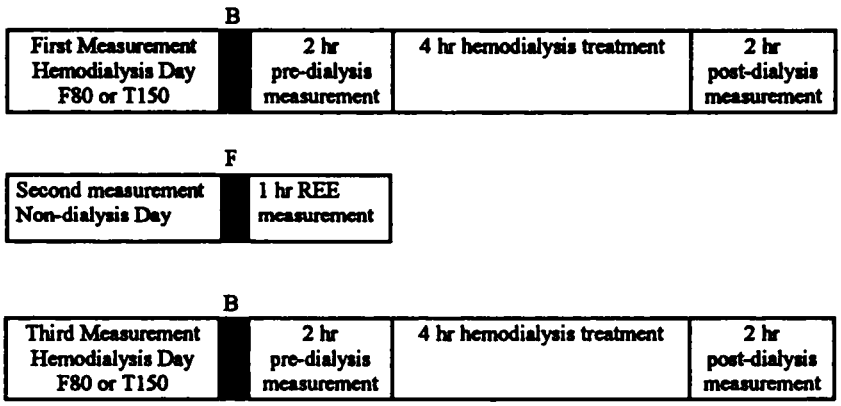

Figure 1. Schematic presentation of study design. Data was collected every minute during measurements. Breakfast was given 1 h before initiation of study. B, light breakfast; F, fasting for 12 h; REE, resting energy expenditure.

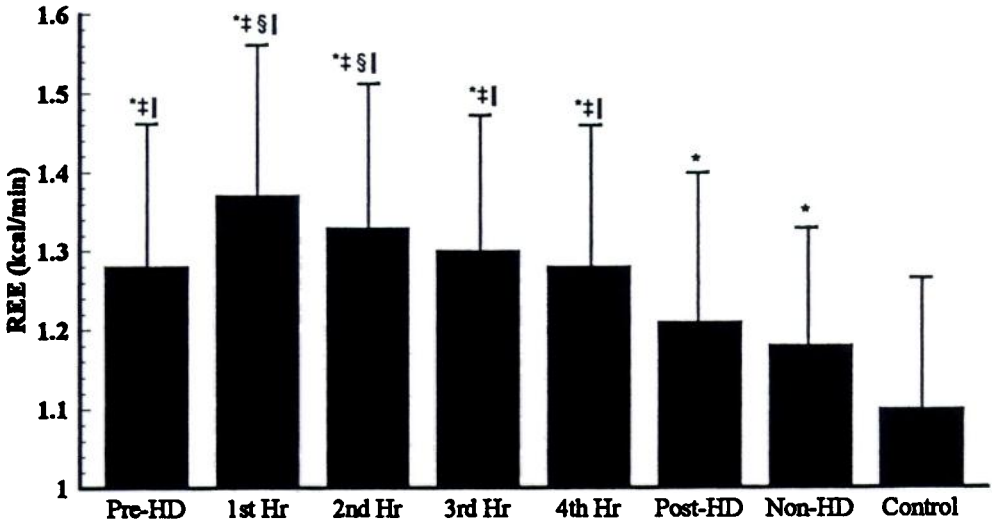

Fig. 2. Resting energy expenditure (REE) measurements during different hours of hemodialysis and different periods of the study. REE measurements were averaged for 2-h predialysis (Pre-HD) and postdialysis (Post-HD) periods, as well as for each hour of hemodialysis. Values are compared with nondialysis (Non-HD) day measurements and measurements from control subjects. All data are mean ± SD. * $P < 0.01$ *versus* CTL; ‡ $P < 0.01$ *versus* Non-HD; § $P < 0.05$ *versus* Pre-HD; ‖ $P < 0.001$ *versus* Post-HD.

consumption (V_{O2}) and carbon dioxide production (V_{CO2}) of each subject was calculated by measuring the changes of oxygen and carbon dioxide content of the air trapped inside the chamber and by the flow rate of the purged air times its concentration of gases. A special multichannel air-sampling system ensures an even sampling of the expired gas by the subject. Temperature, barometric pressure, and humidity of the room are precisely controlled and monitored (22.5 ± 0.15°C, 700.0 to 765.0 ± 0.15 mm Hg, and 11 ± 0.2 mm Hg on a 24-h basis year-round, respectively).

The resting energy expenditure and respiratory quotient of each subject over a given period of time were calculated from these variables using the following equations (1,2):

$$EE = \alpha V_{O2} + \beta V_{CO_2} + \gamma N + \delta V_{CH_4}$$

$$RQ = \frac{V_{CO_2}}{V_{O_2}}$$

where V_{O2} is oxygen consumption, V_{CO2} is carbon dioxide production, N is urinary nitrogen, and V_{CH4} methane production. V_{CH4} can be neglected in human studies. Urinary nitrogen is not included in the measurements because patients were anuric. The four parameters α, β, γ, and δ are coefficients associating these variables with metabolic rate and are considered to be similar in uremic patients and healthy subjects. Although these values may vary slightly because of nutrition, activity, and body habitus of the subjects, for the practical purpose of metabolic rate calculation these variations are very small (9,12,13). They also vary slightly with different diets but can be considered as constants under relatively constant diets (14–16). The dietary habits of dialysis patients and healthy control subjects were not different, as both groups had similar percentages of protein, carbohydrate, and fat in their diets.

The most common interference in REE measurement is spontaneous physical activity such as posture changes and/or slight body movements, which can contribute to an increase in REE because of the energy demand from muscles. To eliminate this problem, the metabolic chamber was equipped with a large force platform system, supported by multiple force transducers. Forces, movements, accelerations, the amount of mechanical work, and work efficiency of physical activity are sensed by the transducers and computed by an on-line computer (11). In addition, because REE decreases during sleep, we designed a touch button that activates a buzzer if the button is not touched by the awake patient every 10 min.

During hemodialysis, bicarbonate ions will diffuse into the blood because of concentration differences across the dialyzer (17). To account for the possible effect of increased blood carbon dioxide levels during HD on REE and RQ calculations, we measured arterial and venous carbon dioxide levels at multiple time points (predialysis; 5, 10, 15, 30, 60, and 120 minutes after initiation of dialysis; and postdialysis) for all study patients on a separate hemodialysis session so as not to interrupt REE and RQ measurements. We also measured the effect of possible heat production by the hemodialysis machine on our measurements. Several experiments showed that measurements were identical when the dialysis machine was in or out of the room, or whether it was operating or not while in the room (data not included in the text).

Statistical Analysis

Paired *t* tests were used to determine if individual periods differed between two dialysis sessions, between two membranes, or between dialysis and nondialysis days. Repeated measures analysis of variance was done for comparison of overall patterns of differences for either order or membrane, taking into account multiple measurements within a subject/membrane combination. For comparisons between the dialysis and control group, a paired *t* test was used to determine whether the difference was statistically significant between two groups, because control subjects were individually matched to study subjects. Data are presented as mean ± SD. All data analyses was done using SAS statistical software packages (SAS Institute, Cary, NC).

RESULTS

Resting Energy Expenditure

There was no statistically significant difference in REE measurements between the two dialysis sessions or at any time point during dialysis for each patient. Predialysis and postdialysis REE measurements were also not statistically different during the two different dialysis sessions within patients. Therefore, the average of the two HD measurements was used for further analysis of REE, yielding one data per patient.

The mean ± SD of the hourly measurement of REE during hemodialysis is depicted in Figure 2. On average, there was a mean 0.099 ± 0.05 kcal/min (7.7%) increase in REE measurement during the hemodialysis procedure. This increase was significantly higher than predialysis measurements at Hours 1 and 2 (1.37 ± 0.19 kcal/min during the first hour and 1.33 ± 0.18 kcal/min during the second hour *versus* 1.28 ± 0.18 kcal/min predialysis; $P < 0.01$ for both), consistent with an increase in REE related to the HD procedure. Resting energy expenditure at Hours 3 and 4 were also higher than the predialysis value, but these differences were not statistically significant. However, compared with postdialysis measurements, the hourly REE measurements for all time points during HD were significantly higher ($P < 0.005$ for all time points), as well as the nondialysis day measurements ($P < 0.001$ for all tests).

Study subjects' resting energy expenditure measurements averaged for extended time periods during the dialysis days (predialysis period, dialysis period, and postdialysis period) and separately for the nondialysis day REE are shown in Table 2, along those of matched healthy control subjects. As shown in the table, REE averaged over 4 h of hemodialysis treatment (1.32 ± 0.18 kcal/min) was significantly higher than predialysis (1.28 ± 0.18 kcal/min, $P < 0.05$), postdialysis (1.21 ± 0.19 kcal/min, $P < 0.001$) and nondialysis days' (1.18 ± 0.15 kcal/min, $P < 0.001$) REE measurements. Predialysis REE was also significantly higher than postdialysis and nondialysis days' measurements ($P < 0.05$ for both).

When the measurements of REE in HD patients were compared with those of matched healthy control subjects (1.10 ± 0.16 kcal/min), average hemodialysis and postdialysis REE measurements were significantly higher than those of healthy control subjects (all $P < 0.01$; Table 2). Specifically, nondialysis day REE measurements in these patients, done after overnight fasting, were significantly higher than those of healthy matched control subjects (1.18 ± 0.15 kcal/min *versus* 1.10 ± 0.16 kcal/min, $P < 0.01$), consistent with a higher than normal REE in hemodialysis patients.

The fat-free mass (FFM), adjusted to BMI, was also measured in our study patients and control subjects, using bioelectrical impedance analysis. Resting energy expenditure adjusted for FFM using BMI was higher for the CHD patients compared with control subjects (87.5 ± 5.5 kcal/unit of BMI in CHD patients *versus* 83.4 ± 3.9 kcal/unit of BMI in healthy control subjects); this difference was also statistically significant ($P < 0.05$; paired t test). Also of note, when analyzed separately, the results of the REE measurements of the two insulin-dependent diabetic patients were similar to those of the rest of the study subjects.

Respiratory Quotient

A similar pattern, although not as pronounced, was observed in RQ measurements. Because there were no membrane differences at any time point or overall, the average value of the two HD sessions was again used for further analysis.

Figure 3 and Table 2 depict the hourly and average measurements of RQ for dialysis patients during study periods, as well as for control subjects. There were no significant differences between predialysis measurements and either hourly or average dialysis session measurements. However, RQ during HD was significantly higher at each hour compared with postdialysis ($P < 0.001$ for all tests) and healthy control subjects ($P < 0.001$ for all tests). Postdialysis RQ was significantly lower than the average predialysis period and nondialysis day RQ measurements (Table 2; all $P < 0.001$).

Effect of Dialysate CO_2 on REE and RQ Measurements

Figure 4 shows arterial and venous P_{CO_2} measurements at the inlet and outlet of the dialyzer, as measured on the same study patients with similar study conditions during a separate hemodialysis session. When averaged over the whole dialysis session, there was an increase of 9.87 ± 2.97 mm Hg in partial

TABLE 2. Resting energy expenditure (REE; kcal/min) and respiratory quotient (RQ) measurements of study patients during different periods of measurements *versus* control subjects[a]

Value	Pre-HD	Tx-HD	Post-HD	NDD	CTL
REE	1.28 ± 0.18[b,c,d]	1.32 ± 0.18[b,c,d,•]	1.21 ± 0.19[b]	1.18 ± 0.15[b]	1.10 ± 0.16
RQ	0.90 ± 0.03[b,c,d]	0.90 ± 0.04[b,c,d]	0.82 ± 0.03[c]	0.86 ± 0.03[b]	0.84 ± 0.03

[a] Pre-HD, prehemodialysis; Tx-HD, average hemodialysis; Post-HD, posthemodialysis; NDD, nondialysis day; CTL, normal controls.
[b] $P < 0.01$ *versus* CTL.
[c] $P < 0.01$ *versus* NDD.
[d] $P < 0.001$ *versus* Post-HD.
[•] $P < 0.05$ *versus* Pre-HD.

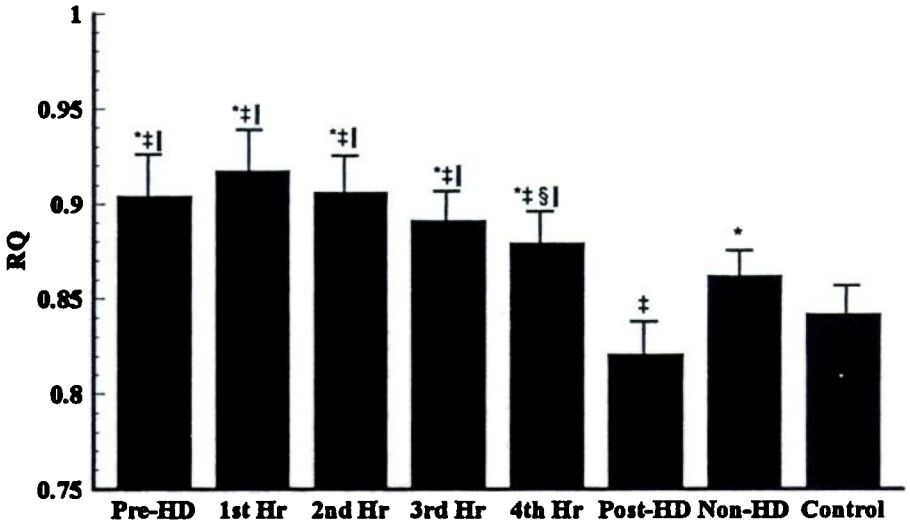

Figure 3. Respiratory quotient (RQ) measurements during different hours of HD and different periods of the study. RQ measurements were averaged for 2-h predialysis (Pre-HD) and postdialysis (Post-HD) periods, as well as for each hour of HD. Values are compared with nondialysis (Non-HD) day measurements and control subjects. All data are mean ± SD. * $P < 0.01$ *versus* CTL; ‡ $P < 0.01$ *versus* Non-HD; § $P < 0.05$ *versus* Pre-HD; ‖ $P < 0.001$ *versus* Post-HD.

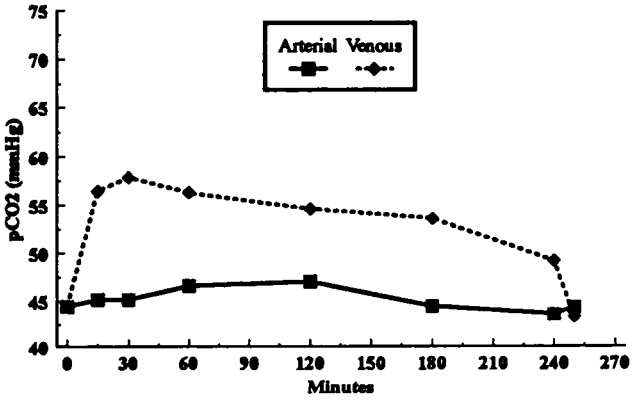

Figure 4. Measurement of P_{CO2} at different intervals during hemodialysis. Afferent arterial and efferent venous blood samples were obtained across the dialyzer from the blood lines simultaneously.

pressure of CO_2 across the dialyzer with a total of 0.594 L of CO_2 being retained over 4 h of dialysis (0.0025 L/min); this is less than 1% of total CO_2 generated by the body.

Blood Chemistries

Measurement of pre- and posthemodialysis blood chemistries showed expected changes after hemodialysis treatment. There was no difference in these measurements between the two different hemodialysis sessions within patients.

DISCUSSION

The results of this study demonstrate that chronic hemodialysis patients have a significantly higher REE compared with that of a matched control population; this is particularly evident during the hemodialysis procedure. The difference in REE between hemodialysis patients and healthy control subjects is further highlighted if one considers that in healthy individuals, kidneys account for 8% of REE. Because none of our patients had residual renal function, the high REE in CHD patients is even more pronounced if adjusted for lack of renal tissue. Finally, when adjusted for FFM, the increased REE in CHD patients is even more notable, suggesting that even in these relatively well-nourished patients, the lean body mass is reduced. These observations have important clinical implications for patients with chronic renal failure and ESRD who may already have insufficient dietary protein and energy intake.

Earlier studies reported no significant difference in REE between healthy and chronic renal failure patients, both before and after initiation of renal replacement therapy. In a study by Monteon *et al.*, chronically uremic patients (before initiation of dialytic therapy), as well as patients on hemodialysis, were found to have REE not statistically different from those of healthy control subjects (6). Similar results were reported by Schneeweiss and colleagues (7). Notably, both of these studies were performed on nondialysis days. More recently, Olevitch and coworkers reported REE measurements in dialysis patients during the hemodialysis procedure. They also found no significant differences in REE during the hemodialysis procedure (8). However, the metabolic carts used in those studies have several shortfalls. The variability of measurements, which can be up to 6 to 10% of the absolute value, are well within the range of our results. Indeed, our results consistently showed

an average of 15 to 20% higher REE in patients during hemodialysis, as well as a 7.5% higher REE during nondialysis days, compared with control subjects. We were also able to measure REE and RQ throughout the entire 4-h HD procedure without any interruption and obtained a continuous and more accurate overall assessment of the impact of the dialysis procedure on REE (9,18). Factors that may affect REE (such as temperature) were held constant and the minimal physical activity was accounted for appropriately (19).

It is possible that the increase in REE observed during the early part of hemodialysis in nonfasting days may be a result of the thermic effect of the light breakfast consumed approximately 1 h before the initiation of the study on a dialysis day. The thermic effect of food, which is approximately 40 kcal in our study patients, is closely related to the amount and content of the food and is most pronounced at 30 to 45 min after meals and decreases subsequently (18). Because we have observed an additional and statistically significant increase in REE simultaneous with initiation of hemodialysis, approximately 3 to 4 h after the consumption of the meal, this increment in REE is probably related to the hemodialysis procedure. Nevertheless, the thermic effect of food can not be entirely excluded. Similarly, we examined whether the increased REE during hemodialysis is related to the absorption of glucose from dialysis solutions. The total amount of thermogenesis induced by the absorption of 20 to 25 g of glucose (20) during hemodialysis is less than 0.015 kcal/min and represents less than 10% of the observed increase in REE during hemodialysis.

We also have not found any significant differences between the two different study dialyzers with different biocompatibility properties. This suggests that the increase in REE in our study population is not significantly affected by the biocompatibility of the hemodialysis membranes. It is also possible that our study population was too small to detect differences between these two dialyzers.

There are several clinically significant elements of our results. Healthy individuals respond to increased energy expenditure by increasing their dietary nutrient intake. However, several studies have documented the observation that dialysis patients' nutrient intake is lower than recommended (1), possibly because of the anorectic effects of uremia (21,22). Furthermore, CHD patients may require even higher than normal dietary protein and energy intake to maintain a neutral nitrogen balance (23) because of the catabolic effects of the hemodialysis procedure, as well as loss of nutrients during dialysis (5,24). Thus, in this setting, the increased REE may contribute to the high prevalence of malnutrition in this patient population.

What is perhaps more important is the maladaptive response of REE to this decreased intake. Recent studies showed that healthy individuals adapt to decreased nutrient intake by decreasing their REE (25). In contrast, our patient population have an inappropriately higher than normal REE that increases further at the time of dialytic amino acid and nutrient loss. Indeed, in the absence of compensatory intake, for each 0.1-kcal/min increase in REE, chronic hemodialysis patients would be expected to lose, over 1 yr, an additional 4 to 5 kilograms of fat tissue ([144 kcal/day × 365 days]/9.5 kcal [energy equivalent of 1 g of fat]) from their body reserves (18).

This negative energy balance is further exacerbated during the HD procedure. The increase in REE is most intense during the first and second hours of dialysis and decreases during the third and last hours of HD. Nevertheless, the average increase in REE of 0.14 kcal/min over 4 h of dialysis is equivalent to 100 kcal/wk and would result in an additional loss of 0.5 kg of fat tissue or approximately 1.2 kg of lean body mass over 1 yr ([100 kcal/wk × 52 wk]/4.4 kcal [energy equivalent of 1 g of protein]) (18).

By adjusting for light physical activity (26) and per kg body weight ([1.18 kcal/min × 1440 min × [1.6 to 1.7]]/75 kg), the energy requirements for our patient population on a nondialysis day is approximately 36 to 39 kcal/kg per day. This range is slightly higher than the previously recommended energy intake to provide neutral nitrogen balance (27), but clearly much higher than the reported average daily energy intake of CHD patients (28,29). However, it is clear that not all hemodialysis patients are malnourished. It is possible therefore that in the face of increased REE, many CHD patients consume a sufficient amount of dietary energy intake and decrease their overall activity level and total energy expenditure to compensate for it. However, although small in magnitude, this increase in REE may contribute to malnutrition in patients who may not be able to have a compensatory increase in their intake.

The exact etiology of the increased REE in CHD patients is not well established. However, several different mechanisms can be postulated. One explanation is the increased workload of the myocardium, which is commonly seen in CHD patients because of interdialytic volume expansion, chronic anemia, coronary artery disease, and underlying cardiomyopathy. Indeed, a recent study suggested that increased cardiac metabolic rate is an important contributor to malnutrition (30). Another explanation is the effect of increased sympathetic nervous system. It has been shown that REE increases with elevated levels of epinephrine and norepinephrine (30). The uremic state is characterized by elevated sympathetic nervous system activity and increased levels of cortisol, glucagon, and insulin (31). This hypothesis may also explain the increase in REE in CHD patients, particularly during the hemodialysis procedure, because the initiation of HD induces a response that involves activation of the sympathetic nervous system and related hormones, including epinephrine and cortisol (32). Finally, increased total body potassium has been shown to be associated with an increase in energy expenditure, and this may be an additional explana-

tion for the results of our study (33). Nevertheless, the exact mechanism involved in increased REE in CHD patients remains speculative.

In contrast to changes in REE, the changes in respiratory quotient, a measure of metabolism of nutrients, were not as remarkable in our study. The higher than healthy RQ measurements during predialysis and the 4-h hemodialysis procedure probably reflect the preferential metabolism of carbohydrates during those periods because of the prestudy breakfast and absorption of glucose during hemodialysis. In contrast, the sharp decrease in RQ after termination of hemodialysis is more consistent with the utilization of protein and fat stores for fuel metabolism (34). This is important to note because the immediate postdialysis period is probably the most protein-catabolic phase of hemodialysis therapy (5,35).

In summary, our results show that REE of CHD patients is significantly higher than that of matched healthy control subjects. This higher level is further increased during the hemodialysis procedure. The increases in REE during nondialysis periods and hemodialysis comprise an additional increase of 5 to 15% of REE, respectively, compared with healthy individuals and may be a contributing factor in the increased prevalence of protein-calorie malnutrition in the CHD patient population.

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Since the cells of these plaques are in no way related to the capillaries, their function is different from the other elements of the nephron. Taking into account our interpretation of the function of the tissue complex at the vascular pole in the kidney, this structure . . . might communicate the events in the corresponding tubular segment to the intraglomerular circulation. In this context, this group of epithelial cells may be regarded as a sensory plaque, placed downstream from the most important functional segment of the nephron, thus resulting in the possibility of an automatic regulation of the glomerular circulation, controlled either by the "emptiness" or "fullness" of the intercalated segment or by the physicochemical composition of the passing urine.

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