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Basal metabolic rate nitrogen turnover
burned children protein synthesis

Whole Body Protein Synthesis in Relation to Basal Energy Expenditure in Healthy Children and in Children Recovering from Burn Injury

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Summary

Dynamic aspects of whole body nitrogen metabolism in children recovering from burn injury have been examined in relation to basal metabolic rate (BMR). A continuous administration of [^{15}N]glycine was used to estimate the rates of whole body protein synthesis (S) and breakdown (C) in five acutely burned children (ages 5-16 years) and in nine healthy subjects (ages 9-18 years). S (grams of protein per kg body wt per day) and BMR were significantly correlated ($r = +0.73$; $P < 0.01$). There was no significant correlation of C with BMR. The ratio of S (grams of protein per day) to BMR (kilocalories per day) was the same in burned and healthy children; the mean value for all children was 0.10 ± 0.03 g protein synthesis/basal kcal. Calorie intake and S were significantly correlated ($r = +0.70$; $P < 0.01$). There were significant correlations between BMR and percentage of total body surface area burned ($r = +0.66$; $P < 0.01$), and BMR and age ($r = -0.57$; $P < 0.05$). Age did not correlate significantly with percent of total body surface burned.

Speculation

A significant proportion of basal energy expenditure is directly associated with energy needs for whole body protein synthesis and breakdown. The results of the present study demonstrated an increase in BMR in children recovering from burn injury, and the statistical correlations between the rate of S and BMR suggest that body protein synthesis accounts for approximately 50% of the variation in resting energy expenditure in the burned child. If more extensive data on the correlation between rates of S and energy expenditure can be obtained, it should be possible to exploit this relationship to estimate the energy intake required to support a rate of S that would equal or exceed the rate of C and result, therefore, in net tissue protein gain.

The nutritional and metabolic relationships between protein and energy have been discussed from several perspectives (1, 3-5, 8, 12, 18-22, 24, 26, 29, 30, 34, 35). The intakes of both nutrients have been shown to affect the efficiency of dietary protein utilization, which is altered at both deficient and excessive caloric levels.

Based on approximations of the energy requirement for protein synthesis, whole body protein synthesis has been estimated to account for about 25-50% of the resting metabolic rate (3, 22, 34). Our studies in healthy infants, young adults, and elderly people have shown a close relationship between whole body protein synthesis and daily energy expenditure (35). Recent investigations in our laboratory confirm these observations and extend them to school-age children and adolescents (21).

The energy costs of maintaining cell protein content and those required for a net gain in tissue protein are determined by the requirements for polypeptide chain synthesis and by the energy content of the new tissue formed (26). The precise energy content of the body weight gain is difficult to assess, but, in children and adults recovering from malnutrition, the energy stored as protein and fat approximates the total energy intake minus the energy expenditure (26, 29). In infants recovering from malnutrition, this energy cost is about 3.3 kcal/g body wt gain (29).

The stress response evoked by trauma or infection causes resting energy expenditure to rise (7, 14, 32); we have found marked increases in the rate of whole body protein synthesis in children with thermal injury complicated by infection (19, 20). In addition, increased rates of muscle protein breakdown have been observed in subjects experimentally infected with sandfly fever (31). An increase in whole body protein turnover, and consequently in energy expenditure, preserves protein balance in the vital organs and provides a mechanism for adapting to changing and unfavorable conditions (28).

Ashworth (1) and Brooke and Ashworth (4) have suggested that the marked postprandial increase in oxygen consumption in children recovering from malnutrition is related to the high energy requirements of protein synthesis. Furthermore, one may speculate that the elevated protein turnover associated with refeeding (1, 4, 23) accounts for the high energy costs of growth in previously malnourished children (25).

Clearly, energy requirements and utilization are intimately related to protein synthesis and requirements. In a previous study (19, 20), we hypothesized that the elevated rate of heat production in children recovering from burn injury probably was related to the increased rate of whole body protein synthesis. Therefore, this study was designed to examine further the relationship between energy expenditure and protein turnover in healthy children and in patients during varying states of recovery from burn injury. Our findings demonstrate a significant correlation between heat production and the rate of whole body protein synthesis.

MATERIALS AND METHODS

PATIENTS, ETHICAL CONSIDERATIONS, AND EXPERIMENTAL DESIGN

Children (ages 5-18 years) admitted to Shriners Burns Institute, Boston, Massachusetts, were the subjects for this study. Some of the patients were receiving treatment for acute burns, and others were admitted for reconstructive surgery.

Eight studies of whole body nitrogen turnover and oxygen

consumption were conducted in five acutely burned children at various times during recovery and at different protein and calorie intakes. Ten additional studies were conducted in nine children who had been burned more than 5 months prior to study and who had been admitted for reconstructive surgery. These children were healthy at the time of study except for patient *5*, who had a history of recurrent urinary tract infection. The clinical and metabolic characteristics of the children are presented in Tables 1 and 2.

Ten additional studies of oxygen consumption in five burn patients were utilized to examine the relationship between energy expenditure and degree of initial burn and open wound. Four of these patients were not studied for characteristics of nitrogen turnover, and their clinical information is not presented in Table 1. None of the studies were performed when the patients had clinical or laboratory evidence of septicemia.

The experimental protocol received the administrative approval of the Human Studies Subcommittee of the Massachusetts General Hospital and the Massachusetts Institute of Technology's Committee on the Use of Humans as Experimental Subjects. A pediatrician, not involved in the research, acted as a patient advocate and assisted us in obtaining informed and written consent.

The protocol was designed to obtain information on the relationships among the following variables: (*1*) extent of burn injury (*2*) protein and calorie intakes, (*3*) rates of whole body protein synthesis and breakdown, and (*4*) oxygen consumption (heat production).

All acutely burned patients admitted to the Shriners Burns Institute from December 1975 to July 1976 were considered for study. Patients were excluded from the ^{15}N turnover studies for various reasons, usually because of urinary incontinence or failure to obtain parental consent. Oxygen consumption could not be determined for patients with facial burns who could not accomodate the mouthpiece of the monitoring apparatus or who required ventilatory assistance. We attempted to study all patients within two weeks of burn injury and then at about 2- or 3-week intervals until their discharge from the hospital. The studies were carried out between surgical procedures.

Reconstructive surgery patients were selected for study from a large group of previously burned patients who participate in the reconstructive surgery program at the hospital. Selection of the elective surgery patients was based, in part, on the medical staff's judgment as to the likely cooperation of the subjects.

Calorie and protein intakes were provided intravenously and orally according to the patient's estimated needs. Most studies lasted four days. Stool collections were made on days 1–4. On the second and third days, [^{15}N]glycine was administered either orally or intravenously every 3 hr, and urine was collected every 4 hr during this 48-hr period. Dressings from the burn wounds were collected on days 1–3 for estimation of wound nitrogen loss. Total nitrogen intake for the 2 days of the [^{15}N]glycine study was determined. Measurements of resting oxygen consumption were made on day 2 or 3 of the study, and the mean of the determinations was used for analysis of the data.

EXPERIMENTAL MODEL

We used a modified version of the Picou and Taylor-Roberts model (Fig. 1) for estimating whole body rates of protein

Table 1. *Clinical information and characteristics of subjects studied for relationship between basal energy expenditure and rates of whole body protein synthesis*

Patient no.	Sex	Study[1] no.	Age, yr	Wt, kg	Ht, cm	Surface area, m^2	Initial total burn BSA, %	Initial 3rd-degree burn BSA, %	Open[2] wound BSA, %	Time post-burn, days	Time post-op., days
1	F	1	16	61.3	163	1.6	0	0			6
2	F	1	14	37.2	153	1.3	16	16	2	49	4
2	F	2	14	37.0	153	1.3	16	16	3	59	24
2	F	3	14	38.0	153	1.3	16	16	0	71	36
3	M	1	13	37.0	145	1.2	35	15	2	15	0
4	M	1	16	61.8	176	1.8	35	20	18	16	6
4	M	2	16	58.9	176	1.7	35	20	6	31	2
5	F	1	9	46.6	137	1.3	0	0			pre-op.
6	M	1	10	31.6	130	1.1	0	0			pre-op.
7	F	1	14	60.3	166	1.7	0	0			pre-op.
7	F	2	14	60.0	166	1.7	0	0			5
8	M	1	15	45.6	162	1.4	0	0			7
9	M	1	15	57.2	160	1.6	0	0			6
10	M	1	18	61.8	175	1.7	0	0			7
11	F	1	13	45.6	146	1.3	0	0			pre-op.
12	M	1	5	20.4	114	0.8	50	50	2	57	3
13	M	1	6	18.3	106	0.8	75	25	8	23	14
14	M	1	12	44.7	153	1.4	0	0			pre-op.

[1] Refers to consecutive studies on the same patient.

[2] Percentage of open wound is defined as the percentage of the surface area with excised burns plus half the sum of the percentage of BSA exhibiting eschar-covered burn wounds, second-degree burns, recently grafted wounds (less than 1 week), and new donor sites (less than 1 week).

Table 2. *Protein and calorie intakes, N balance, BMR, whole body protein synthesis and breakdown rates in burned and healthy children*

Patient no.	Study no.	Protein, g/kg/day	Cal, kcal/kg/day	N balance, mg N/kg/day	Whole body protein, g/kg/day			BMR, kcal/kg/hr
					Synthesis	Corrected synthesis	Breakdown	
1	1	2.4	72	+160	3.2	3.2	2.1	1.7
2	1	1.7	67	+16	3.2	3.0	2.9	1.3
2	2	1.2	58	+64	3.9	3.8	3.4	1.6
2	3	1.2	61	+48	4.1	4.1	3.8	1.2
3	1	1.6	63	−16	3.7	3.6	3.7	1.6
4	1	3.4	72	−272	3.0	2.6	4.3	1.7
4	2	1.9	62	−96	3.8	3.5	4.1	1.3
5	1	1.7	61	+16	3.1	2.9	2.8	1.1
6	1	2.8	65	+32	4.5	4.4	4.2	1.9
7	1	1.6	54	+64	3.4	3.3	2.9	1.0
7	2	1.4	56	0	3.1	3.0	3.0	1.1
8	1	2.1	68	+64	4.1	4.0	3.6	1.6
9	1	2.0	82	+48	3.4	3.2	2.9	1.1
10	1	1.9	73	+32	3.6	3.5	3.3	1.4
11	1	1.7	68	+64	4.1	3.8	3.4	1.3
12	1	3.6	116	+144	6.1	5.9	5.0	3.7
13	1	6.2	156	+272	4.5	4.1	2.4	3.3
14	1	2.6	107	+256	4.0	3.8	2.2	3.3

synthesis and catabolism (27). The model has been described in detail (27, 30), but several modifications were necessary for our patients.

As indicated in this figure, the rate of urinary total nitrogen excretion (E_t) was subtracted from the nitrogen flux (Q) to obtain the whole body protein synthesis rate (S). Because S might be overestimated due to additional losses of nitrogen in feces and open wounds, a "corrected S" was also calculated to account for these extraurinary losses as discussed below (Table 2).

The [^{15}N]glycine (83 atoms% excess; Stohler Isotope Chemical Corp., Waltham, MA) was administered at a rate of 0.5 mg ^{15}N/kg body wt/day, orally or intravenously, at 3-hr intervals. Sterile, pyrogen-free [^{15}N]glycine was prepared for intravenous use as an aqueous solution by the pharmacy of the Massachusetts General Hospital. Previous studies have indicated that the route of isotope administration does not affect estimates of whole body protein turnover (27, 30).

Total nitrogen intake (including blood products) was used to calculate nitrogen balance and to assess the associations between protein intake and protein turnover. When patients received intravenously administered nonprotein nitrogen, this intake was used in the calculation of food nitrogen (intake I in Fig. 1) and subsequent estimation of nitrogen flux within the metabolic pool.

Nitrogen intake in the acutely burned patient was generally provided by intravenous protein hydrolysates or defined-formula diets. The amount of solid food ingested was determined by an analysis of a duplicate preparation of all food offered. Nitrogen content of food refused was also determined.

Frequently, urine collections were made via existing catheters in the acutely burned children. Small urine losses occasionally occurred, but in none of the cases reported did this exceed an estimated 5% of the total. Measurements of urinary creatinine were used to monitor the completeness of the collections (36).

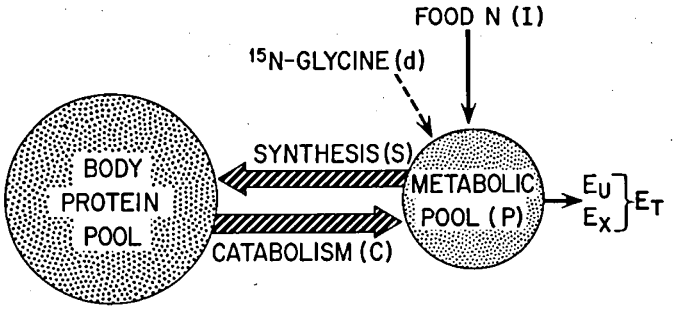
SAMPLES AND ANALYSES

Nitrogen concentrations in urine, stool, diet, and burn exudate, and urea nitrogen concentration in urine were determined by methods previously described (36). Aliquots from washings of burn dressings were pooled and concentrated by freeze-drying. Recovery experiments with whole blood added to clean dressings indicated that nitrogen losses from wounds may have been underestimated.

Urinary urea nitrogen was isolated as ammonia by the Conway diffusion method (15) after the urine had been pretreated with permutit (9). The ammonia was then reacted with hypobromite to produce N_2 gas (33), and the ^{15}N enrichment was determined with an isotope ratio mass spectrometer (model 3-60 RMS, Nuclide Corp., State College, PA). Replicate urine samples prepared for mass spectrometry were analyzed for [^{15}N]urea enrichment with a coefficient of variation of 1%.

The plateau values of ^{15}N enrichment used in the calculation of body nitrogen flux were determined from inspection of the [^{15}N]urea curves. Figure 2 shows an example of the change in ^{15}N enrichment of urinary urea nitrogen with time after administration of [^{15}N]glycine. For each separate study, the coefficient of variation in the "plateau values" was calculated, and, for the 18 studies, the mean coefficient value was 6.5%.

BMR was determined by measuring oxygen consumption in the early morning when the patients were awakened. The



d = Rate of Infusion of ^{15}N

e_u = Rate of Excretion of ^{15}N in Urea.

$$Q = \text{Flux of N Through Pool (P)} = \frac{d}{\text{Plateau Enrichment of Urinary Urea}}$$

$$F = \frac{e_u}{d} = \frac{E_u}{Q}$$

$$\therefore Q = \frac{E_u}{F} = I + C = S + E_T$$

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Fig. 1. The Picou and Taylor-Roberts model for studying dynamic aspects of whole body nitrogen metabolism by continuous infusion of [^{15}N]glycine. I, C and S are intake, protein breakdown, and protein synthesis, respectively (milligrams of N per kg per day); E_u, E_x, and E_t are urinary urea, urinary non-urea, and urinury total nitrogen excretions, respectively (milligrams of N per kg per day); and Q is the flux (milligrams of N per kg per day) of nitrogen for the metabolic pool, P. The rate of administration of ^{15}N is a d (milligrams of ^{15}N per kg per day). F is the fraction of the administered dose (d) that is excreted as [^{15}N]urea, or the fraction of total nitrogen entering the metabolic pool that is excreted as urea nitrogen. Q is equal to d divided by the average plateau enrichment (Sd), which is obtained from the isotope enrichment curve (see legend to Fig. 2) (Q = d/Sd).

measurements were made before the dressings were changed. Except for patient *4* (study 1) and patient *13*, the oxygen consumption studies were performed after the patients had fasted for eight hours or longer. Oxygen consumption was determined in patients *4* and *13* while they were receiving a continuous infusion of crystalline L-amino acids and glucose. In addition, subject *13* ate breakfast before the study. Although rates of oxygen consumption for patients *4* and *13* were not truly basal, the term basal metabolic rate is retained in this paper because it applies to the studies with all other patients. The above procedure was followed also in the oxygen consumption studies not shown in Table 2, except for two studies in one patient, which were carried out while he was fed parenterally.

Oxygen consumption was determined during a 6-min period by the closed-circuit method, with a Benedict-Roth apparatus (Clinical Spirometer, Warren E. Collins, Inc., Braintree, MA). Measurements were repeated 14 different times on six individuals to estimate the reproducibility of the determination. The mean coefficient of variation was 5.1% (SD = 4.8%). A respiratory quotient of 0.85 was assumed in converting oxygen consumption to estimated heat production.

Protein synthesis does not occur at a constant rate throughout the day, but changes during and between meals (1, 4, 10). Therefore, it was considered that the mean daily whole body synthetic rate might correlate better with a measurement of the mean resting metabolic rate throughout the day. During 14 of the ^{15}N turnover studies, oxygen consumption measurements were carried out repeatedly between 6 AM and 6 PM to cover the period of the day during which the major meals were given. The measurements were plotted on graph paper, and the total area under the curve was determined by planimetry. Our results, however, failed to reveal a significant relationship between the computed average resting metabolic rate and whole body protein synthetic rate. Therefore, these particular measurements will not be discussed further.

ANALYSIS OF RESULTS

Both linear and rank correlation methods were used for data analysis (6). In evaluating the protein turnover data, we utilized information from the attending surgeons regarding the initial burn size (percentage of total body surface area (BSA) burned and percent with third-degree burns). The percentage of BSA with open wounds at the time of study was also estimated from the descriptions given by the clinicians and from photographs. "Percentage open wound" is defined here as the percentage of BSA with full thickness open wounds (excised burns) plus half the sum of the percent of BSA exhibiting the following: eschar-covered burn wounds, second-degree burns, recently grafted wounds (less than 1 week), and new donor sites (less than 1 week).

RESULTS

The data on oxygen consumption, shown in Table 2, are expressed as a function of body weight rather than surface area. The correlation of whole body protein synthesis rate with basal metabolic rate was greater when the BMR was expressed per unit of body weight. This may be related to the difficulties inherent in accurately measuring body length in bed-ridden patients and body height in children crippled by injury. These problems would contribute to a greater experimental error in determinations of surface area than in measurements of weight. Furthermore, the DuBois formula used to calculate surface area has a coefficient of variation of 11% (11), which also contributes to the variability of the results. Another reason for not emphasizing energy expenditure in relation to surface area is that heat loss is not causally dependent upon surface area in warm-blooded animals (11, 13). For these reasons, we prefer to

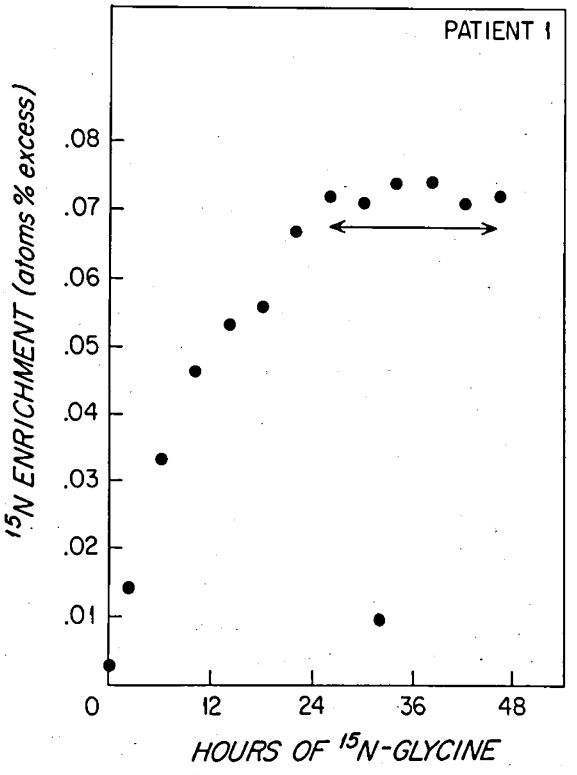

Fig. 2. Change in the ^{15}N enrichment of urinary urea with continuous administration of [^{25}N]glycine in a representative study. Data points used in the calculation of the plateau level of enrichment, Sd (see legend to Fig. 1), are indicated by the arrows.

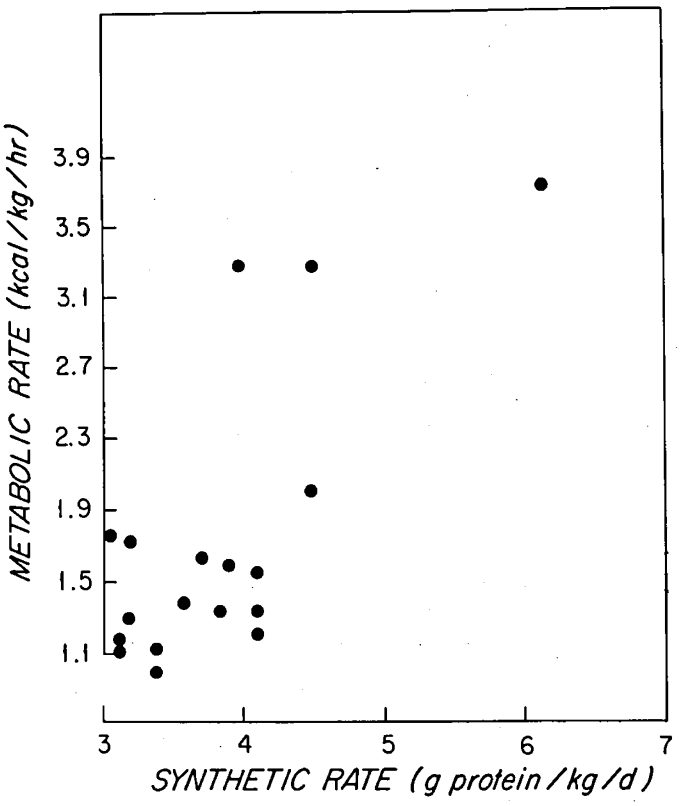

Fig. 3. Relationship between whole body protein synthesis rate and metabolic rate in healthy and burned children (linear correlation coefficient = +0.73; $P < 0.01$, rank correlation coefficient = +0.52, $P < 0.05$).

evaluate the energy studies in relation to body weight, although surface area provides the only convenient means of describing the extent of burn injury.

Figure 3 presents a scattergram of the data relating whole body protein synthesis rate (S) to BMR. Both variables were normally distributed and were linearly correlated ($r = +0.73$; $P < 0.01$). Because this result may depend upon the values for three of the subjects showing high rates of protein synthesis, a rank correlation coefficient was also calculated in order to remove this possible bias. The correlation remained significant ($r = +0.52$; $P < 0.05$). No significant correlation was found between whole body protein breakdown rate (C) and BMR. When estimates of S are corrected for extraurinary nitrogen losses (feces and open wounds), there was still a significant ($P < 0.01$) positive linear correlation with BMR ($r = +0.67$).

Calculation of the ratio of S (expressed as grams of protein per day) to BMR (kilocalories per day) allows a comparison to be made between our results and those from previous studies of the relationship of energy expenditure to protein synthesis in humans at various ages (35). In the 18 studies reported here, the mean and variation of the ratio were the same when calculated for the entire group or only for the eight studies of acutely burned children. The overall mean was 0.10 ± 0.03 g protein synthesized/kcal basal energy expenditure.

There was a significant ($P < 0.01$) positive correlation between calorie intake and S ($r = +0.70$). Protein intake did not correlate significantly with S, nor did whole body protein breakdown correlate with protein or calorie intakes.

For the 18 studies of oxygen consumption in burned patients, BMR correlated significantly with percent of total BSA burned ($r = +0.66$; $P < 0.01$) and with age ($r = -0.57$; $P < 0.05$), but did not correlate with either percentage of BSA with third-degree burns or percentage with open wounds. Furthermore, patient age did not correlate with the percentage of total BSA burned.

For those studies in which whole body protein turnover was also measured, BMR correlated significantly ($P < 0.01$) with both calorie intake ($r = +0.88$) and protein intake ($r = +0.75$). In this group, there was also a significant ($P < 0.01$) negative correlation of age with BMR ($r = -0.69$). Cautious interpretation of this latter finding is necessary, because the two youngest patients were also the most severely burned.

DISCUSSION

The present findings in children extend our previous observations in healthy adults and further show that the metabolic rate in burn patients is closedly related to the size of the burn wound (32). Furthermore, these data, when considered together with our recent studies of the dynamic aspects of whole body nitrogen metabolism in burned children (19, 20), indicate that a highly significant, positive correlation exists between the increased energy expenditure in burned children and the rate of whole body protein synthesis.

Based on a small number of children, statistical analysis of the relationship between whole body protein synthesis and basal energy expenditure ($r = 0.73$) indicates that protein synthesis accounts for approximately 50% of the variation in resting energy expenditure. A larger number of subjects would be required to substantiate the quantitative validity of this conclusion, particularly since our study includes data from three patients with marked elevations in both protein synthesis rates and energy expenditure. In addition, resting energy expenditure could be estimated more precisely if measurements of oxygen consumption and carbon dioxide production could be made over longer periods without disturbance to the subjects (11). One might anticipate that improved estimates of metabolic rate would produce an even closer relationship between altered rates of protein synthesis and heat production.

Young *et al.* (35) have computed the measured whole body protein synthesis rate in relation to the determined or standard values for BMR in healthy human subjects at various ages. Their results imply that a relatively constant proportion of resting energy expenditure is associated with the energy requirements for protein synthesis. These previous studies showed that the rate of protein synthesis per unit of resting or basal energy expenditure (expressed as grams of protein per kcal) varied little among the newborn (0.15), young adult (0.11), and elderly (0.11) subjects. Our data yield the same quantitative relationship for children and adolescents whose resting energy expenditure was determined from measurements of oxygen consumption.

Thus, thermal injury appears to have no modifying effect on the relationship between the intensity of protein synthesis (grams of protein per kg body wt per day) and the intensity of energy expenditure (kilocalories per kg per hr). However, it must be recognized that the present data are too limited to permit a separate analysis of the relationships between protein synthesis and basal energy expenditure and, therefore, the foregoing conclusion must be regarded as tentative. Nevertheless, these observations may be important in relation to the proposal made by Wilmore and associates (32) that altered catecholamine output is responsible for the increased heat production that follows burn injury. The present data suggest that the significance of changes in the balance between catecholamines and other hormones (such as insulin and glucagon), in relation to altered rates of heat production, may lie in their effect on tissue protein metabolism. A final point here is that our burn patients were studied at least 2 weeks postburn and were in various stages of recovery. The two patients (*12* and *13*) with the largest burns were in marked positive nitrogen balance, and their high rates of whole body protein synthesis and breakdown were consistent with rapid tissue protein repletion (20). Catecholamine-induced energy expenditure associated with ion pumping (17) may not be significantly different from

the normal state at this time after burn injury in medically well managed children.

In planning rational nutritional intervention for sick patients, an important goal is to provide sufficient calories, as well as protein, to support a rate of body protein synthesis that equals or exceeds the catabolic rate. Energy requirements are more difficult to determine, and, at times, there are limitations in our ability to provide adequate calories to severely burned patients. With more extensive data on the correlation between protein synthetic rates and energy expenditure, it might be possible to exploit this relationship in order to estimate the energy intakes required to achieve a synthesis rate that equals or exceeds the measured breakdown rate. Whole body protein breakdown can be determined relatively easily when nitrogen intake is controlled. The synthetic rate necessary to maintain body nitrogen or a given rate of gain in body protein could be calculated, and the energy requirement could be estimated from the established relationships between energy expenditure and synthesis rate. This hypothesis, as well as an assessment of the distribution of protein synthesis and breakdown rates among the organs, would be worth exploring because the preservation of specific protein pools is crucially important from the standpoint of prognosis (2, 16).

REFERENCES AND NOTES

1. Ashworth, A.: Metabolic rates during recovery from protein-calorie malnutrition: The need for a new concept of specific dynamic action. Nature, *223:* 407 (1969).
2. Bistrian, B. R., Blackburn, G. L., Scrimshaw, N. S., and Flatt, J. -P.: Cellular immunity in semistarved states in hospitalized adults. Amer. J. Clin. Nutr., *28:* 1148 (1975).
3. Blaxter, K. L.: Methods of measuring the energy metabolism of animals and interpretation of results obtained. Fed. Proc., *30:* 1436 (1971).
4. Brooke, O. G., and Ashworth, A.: The influence of malnutrition on the postprandial metabolic rate and respiratory quotient. Brit. J. Nutr., *27:* 407 (1972).
5. Calloway, D. H.: Nitrogen balance of men with marginal intakes of protein and energy. J. Nutr., *105:* 914 (1975).
6. Calquhoun, D.: Lectures on Biostatistics (Clarendon Press, Oxford, 1971).
7. Cuthbertson, D. P.: Injury and its effects on protein metabolism. In: H. N. Munro and J. B. Allison: Mammalian Protein Metabolism, Vol. II, pp. 373–414 (Academic Press, New York, 1964).
8. Energy and Protein Requirements: Report of a Joint FAO/WHO Ad Hoc Expert Committee. (Technical Report Series 522) (World Health Organization, Geneva, 1973).
9. Folin, D., and Bell, R. D.: Applications of a new reagent for the separation of ammonia. J. Biol. Chem., *29:* 329 (1917).
10. Garlick, P. J., Millward, D. J., and James, W. P. T.: The diurnal response of muscle and liver protein synthesis in vivo in meal-fed rats. Biochem. J., *136:* 935 (1973).
11. Garrow, J. S.: Energy Balance and Obesity in Man (American Elsevier Publishing Co., New York, 1974).
12. Garza, C., Scrimshaw, N. S., and Young, V. R.: Human protein requirements: the effect of variations in energy intake within the maintenance range. Amer. J. Clin. Nutr., *29:* 280 (1976).
13. Gemmill, C. L., and Brobeck, J. R.: Energy exchange. In: V. B. Mountcastle: Medical Physiology, Vol. I, pp. 473–497 (C. V. Mosby Co., St. Louis, 1968).
14. Halmagyi, D. F. J., and Kinney, J. M.: Metabolic rate in acute respiratory failure complicating sepsis. Surgery, *77:* 492 (1975).
15. Hawk, P. B., Oser, B. L., and Summerson, N. H.: Practical Physiological Chemistry, Ed. 13 (McGraw-Hill, New York, 1954).
16. Hay, R. W., Whitehead, R. G., and Spicer, C. C.: Serum albumin as a prognostic indicator in oedematous malnutrition. Lancet, *2:* 427 (1975).
17. Himms-Hagen, J.: Cellular hermogenesis. Ann. Rev. Physiol., *38:* 315 (1976).
18. Inoue, G., Fujita, Y., and Niiyama, Y.: Studies on protein requirements of young men fed egg protein and rice protein with excess and maintenance energy intakes. J. Nutr., *103:* 1673 (1973).
19. Kien, C. L., Rohrbaugh, D. K., Burke, J. F., and Young, V. R.: Elevated rates of protein synthesis after thermal injury [Abstr.]. Pediat. Res., *10:* 355 (1976).
20. Kien, C. L., Young, V. R., Rohrbaugh, D. K., and Burke, J. F.: Increased rates of whole body protein synthesis and breakdown in children recovering from burns. Ann. Surg. (In press).
21. Kien, C. L., Young, V. R., Rohrbaugh, D. K., and Burke, J. F.: Whole body protein synthesis and breakdown rates in children, before and after reconstructive surgery of the skin. Metabolism, *27:* 27 (1977).
22. Milligan, L. P.: Energetic efficiency and metabolic transformations. Fed. Proc. *30:* 1454 (1971).
23. Millward, D. J., Garlick, P. J., Stewart, R. J. C., Nnanyelugo, D. O., and Waterlow, J. C.: Skeletal-muscle growth and protein turnover. Biochem. J., *150:* 235 (1975).
24. Munro, H. N.: General aspects of the regulation of protein metabolism by diet and by hormones. In: H. N. Munro and J. B. Allison: Mammalian Protein Metabolism, Vol. 1, pp. 382–481 (Academic Press, New York, 1964).
25. Olson, R. E.: The effect of variations in protein and calorie intake upon rate of recovery and selected physiologic response in Thai children with PCM. In: R. E. Olson: Protein Calorie Malnutrition, pp. 275–297 (Academic Press, New York, 1975).
26. Payne, P. R., and Waterlow, J. C.: Relative energy requirements for maintenance, growth and physical activity. Lancet, *2:* 210 (1971).
27. Picou, D., and Taylor-Roberts, T.: The measurement of total protein synthesis and catabolism and nitrogen turnover in infants in different nutritional states and receiving different amounts of dietary protein. Clin. Sci., *35:* 283 (1969).
28. Schimke, R. T.: Regulation of protein degradation in mammalian tissues. In: H. N. Munro: Mammalian Protein Metabolism, Vol. IV, pp. 178–228 (Academic Press, New York, 1970).
29. Spady, D. W., Payne, P. R., Picou, D., and Waterlow, J. C.: Energy balance during recovery from malnutrition. Amer. J. Clin. Nutr., *29:* 1073 (1976).
30. Steffee, W. P., Goldsmith, R. S., Pencharz, P. B., Scrimshaw, N. S., and Young, V. R.: Dietary protein intake and dynamic aspects of whole body nitrogen metabolism in adult humans. Metabolism, *25:* 281 (1976).
31. Wannemacher, R. W., Jr., Dinterman, R. E., Pekarek, R. S., Bartelloni, P. J., and Beisel, W. R.: Urinary amino acid excretion during experimentally induced sandfly fever in man. Amer. J. Clin. Nutr., *28:* 110 (1975).
32. Wilmore, D. W., Long, J. M., Mason, A. D., Skreen, R. W., and Pruitt, B. A.: Catecholamines: mediator of the hypermetabolic response to thermal injury. Ann. Surg., *180:* 653 (1974).
33. Wilson, D. W., Nier, A. O. C., and Reimann, S. P. (eds.): Preparation of Isotopic Tracers (Edward Brothers, Ann Arbor, 1946).
34. Young, V. R.: Energy metabolism and requirements in the cancer patient. Cancer Res., *37:* 2336 (1977).
35. Young, V. R., Steffee, W. P., Pencharz, P. B., Winterer, J. C., and Scrimshaw, N. S.: Total human body protein synthesis in relation to protein requirements at various ages. Nature, *253:* 192 (1975).
36. Young, V. R., Taylor, Y. S. M., Rand, W. M., and Scrimshaw, N. S.: Protein requirements of man: efficiency of egg protein utilization at maintenance and submaintenance levels in young men. J. Nutr., *103:* 1164 (1973).

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