Loss of body nitrogen on fasting[1,2]

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ABSTRACT An analysis of the change in total body nitrogen during fasting shows that it declines exponentially, a small fraction being lost rapidly ($t_{1/2}$ of a few days), and the remainder being lost slowly ($t_{1/2}$ of many months). The obese faster loses N, and weight, at a slower relative rate than the nonobese; and the ratio of N loss to weight loss during an extended fast is inversely related to body fat content, being about 20 g/kg in the nonobese and about 10 g/kg in those with body fat burdens of 50 kg or more. The loss of body N on a low protein-calorie adequate diet can also be described in exponential terms, and this function allows an estimate to be made of the N requirement. *Am. J. Clin. Nutr.* 32: 1570–1574, 1979.

There are a number of studies of urinary nitrogen excretion during fasting. The loss rate, both in animals and man, is rapid at first, and then gradually declines as the fast continues (1–4). Pütter (5) suggested that the decline in urine N excretion was semilogarithmic in nature, and both Martin and Robison (6) and Rand et al. (7) found this to be true in short-term studies of subjects consuming a "protein-free" calorie-adequate diet.

In a previous publication (8) the rate of weight loss during prolonged fasts was examined and found to be exponential, i.e., the rate is proportional to weight itself.

We propose now to examine the rate at which body nitrogen is lost during a fast, and to relate this to total body N. The establishment of a very good correlation between urinary creatinine excretion and lean body mass (9) provides a means for estimating total body N in man.

Subjects and methods

The obese adult males were studied at the Veterans Hospital in Los Angeles. They were 30 to 51 years old, and ranged in height from 163 to 188 cm and in weight from 133 to 244 kg. They were allowed only a potassium chloride supplement, a multivitamin tablet and medication to prevent hyperuricemia during the fast, which lasted for at least 60 days. Data for nonobese "professional" fasters were taken from publications by Benedict (2), van Hoogenhuyze and Verploegh (10), Cathcart (11), and Watanabe and Sassa (12). Only those subjects who fasted at least 2 weeks were included. The first author made detailed observations on a 40-year-old man (171 cm, 60.6 kg) who fasted for 31 days; the others reported on fasts of 14 to 37 days' duration. Daily urine samples were analyzed for creatinine and total N; fecal excretion was negligible.

Total body N at the start of each fast was estimated from urinary creatinine excretion in the following manner (9, 13):

$$\text{lean body mass (kg)} = 0.0291 \text{ urine creatinine (mg/day)} + 7.38 \quad (1)$$

$$\text{total body N (g)} = \text{lean body mass (kg)} \times 33 \quad (2)$$

Having estimated body N at the start of the fast, daily urine N values were successively subtracted, and the results expressed as a percentage of the initial body N.

An analysis was also made of N losses sustained by a male subject (28 years old, weight 64.8 kg) who ate a very low protein diet for 26 days (14). Calculated nitrogen intake averaged 0.6 g/day and cal 3150/day; during this period body weight gradually fell to 63.0 kg on the 13th day and then gradually rose to 65.5 kg on the 26th day. Urine and stools were analyzed for N; the loss of body N was calculated as (urine N + fecal N) − diet N.

At the start of the experiments estimated total body N ranged from 1875 to 2842 g for the obese fasters; from 1287 to 1552 g for the nonobese fasters, and was 1947 g for the subject who ate the low protein diet. In the immediate prefast period the obese fasters excreted an average of 18 g N per day, the nonobese fasters about 14 g/day, and the low protein diet subject 12 g/day.

With the aid of a computer the time course of calculated body N was fitted to a two-component exponential equation:

$$N(t) = N(0)[F_1 \exp(-\lambda_1 t) + F_2 \exp(-\lambda_2 t)] \quad (3)$$

where F_1 and F_2 stand for fractions of body N content, and t is time in days.

The time course of body weight was analyzed in

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similar fashion, by substituting weight for N in equation (3).

Since the rate of N loss varies somewhat among individual subjects, perhaps due to variations in acid-base status, or even variations in water intake (1), the data for each group of subjects were pooled for analysis.

There are in addition a number of reports in the literature that give data on the total N loss during fasts of at least 2 weeks' duration, thus permitting a calculation of the amount of N lost per kilogram of weight lost.

In all instances urinary N was assayed by the Kjeldahl method and creatinine by the Folin-Jaffé reaction.

Results

Figure 1 presents the data in graphic form, initial body N and initial body weight each being set at 100%. The curvilinear character of the losses is clearly evident, and it is obvious that the relative loss of body weight is greater than that of body N. Relative losses of both weight and N are greater in the nonobese than in the obese fasters, and body N was lost at a very slow rate in the subject taking the low protein diet.

The coefficients and exponents of the derived equations are listed in Table 1. For the obese fasters it appears that 6% of body N is lost with a half-time of 10.6 days, and the remainder with a half-time of 433 days. The fractional loss rate for the nonobese fasters is greater, 1% of body N being lost with a half-time of 2.4 days and the remainder with a half-time of 116 days. The SD's from regression indicate the goodness of fit. The parameters of the equations describing weight loss are similar to those found in a previous study (8).

The subject who ate the protein-free diet lost 2% of his body N with a half-time of 5.6 days, and the remainder (98%) with a half-time of 660 days. There was no significant change in weight.

Table 2 lists data on the ratio of body N loss to body weight loss for these fasting subjects (one nonobese faster is missing; see footnote to Table 1) plus a number of others for whom there was insufficient detail to permit an exponential analysis. The subjects listed in the upper portion of Table 2 are those for whom estimates of body fat content are available, and whose fasts were strictly controlled. The nitrogen content of the lost weight for the duration of the fast is only about half as great in the obese subjects as in the nonobese, so the former appear to be more efficient at conserving body N.

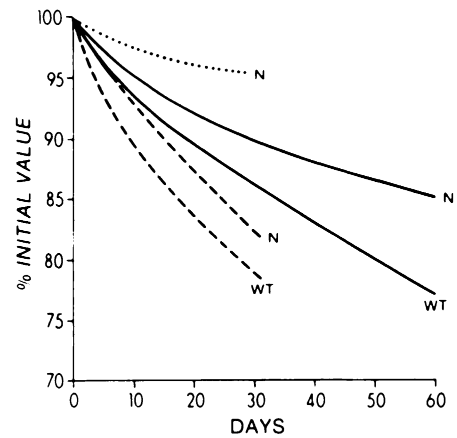

FIG. 1. Decline in body N and body weight (both as percentage of initial values) during fasting: (——), nine obese subjects; (----), four nonobese subjects; (. . . . . .), one subject on protein-free diet.

The values in the lower part of Table 2 are confounded by minor deficiencies of one sort or another (see footnotes to Table 2), and estimates of body fat content are not available for these subjects, although those studied by Owen et al. (19) and Spencer et al. (20) were obviously obese. The women studied by Vollmer and Berning (21) and Bönninger and Mohr (22) both appeared to have a N loss/weight loss ratio in the obese range; however, the former is described as an "etwas adipöse Frau" and the latter as possessing a "Fettpolster reichlich entwickelt." Moreover, in the case of the former subject there are some irregularities in the graphed values for urinary N excretion, suggesting incomplete collections, and the latter took 40 g amino acids during the course of her fast.

Discussion

The exponential equations set forth here appear to describe satisfactorily the loss of body N during fasting as well as loss of body weight (8). While the fit is not perfect, and while it is obvious that other, nonexponential equations could also be derived from these data, the exponential method offers some conceptual advantages. This approach suggests that body N exists in two pool groups, a small one with a rapid turnover rate and a large one which turns over much more slowly. The former may correspond to what others

TABLE 1
Parameters of the exponential equations

	F_1	λ_1	F_2	λ_2	SD regression
Obese subjects (9)[a]					
Body N	0.06	0.0655	0.94	0.00160	0.10 g
		(10.6d)[b]		(433d)	
Body wt	0.04	0.152	0.96	0.00368	0.20 kg
		(4.6d)		(188d)	
Nonobese subjects (4)					
Body N	0.01	0.284	0.99	0.00599	0.08 g
		(2.4d)		(116d)	
Body wt[c]	0.05	0.356	0.95	0.00643	0.11 kg
		(2.0d)		(108d)	
Protein-free diet (1)					
Body N	0.02	0.123	0.98	0.00105	0.03 g
		(5.6d)		(660d)	

[a] No. of subjects. [b] Half-time. [c] Three subjects; daily weights were not recorded for the female subject reported by Van Hoogenhuyze and Verploegh (10).

TABLE 2
N and weight loss in fasting

No. of subjects/sex	Age	Duration of fast	Initial wt	wt loss	N loss	g N lost/kg wt lost	References
	yr	*day*	*kg*		*g*		
2/F	20,48	315,231	131,118	66,46	915,670	13.8,12.1	15
9/M	30–51	60	133–244	28–48	242–434	9.6 ± 1.6[a]	Present data
2/M;1/F	35–40	20	93–112	10–13	154[b]	13.3	16
4[c]	Adult	16	102–155	11–15	102–147	10.0 ± 2.9	17
1M	40	31	61	13	273	21.0	2
2/M	31,40	14	51,66	6.8,7.8	153–145	22.6,18.6	12,11
1/F	8	15	25	3.9	72	18.5	18
1/M	49	38	134	23	275[d]	12.1	19
2/F	19,30	24,20[e]	106,134	13,12	155,128	11.9,10.6	20
1/F	58	37	63	14	139[d,f]	10	21
1/F	48	16[g]	56	8.1	108	13.3	22

[a] SD [b] Average; individual data not reported. [c] Age and sex not specified. [d] Calculated from graphed data. [e] Intake 30 kcal, 0.42 g N daily. [f] ?Incomplete urine collections. [g] Intake 6.4 g N, 160 kcal.

have called "labile protein" (23). The data of Table 1 also suggest that the pool of "labile" N is larger in the obese than in the nonobese; however, the fact that the latter were excreting somewhat larger amounts of N just before fasting may account for some of this difference.

The loss of body N in other subjects given protein-free diets has been shown to be exponential during the first few days (6, 7), but neither study was continued long enough to permit identification of a long-term exponential component. However, a plot of "steady state" urine N excretion (i.e., after the 1st week) against body cell mass (by ^{40}K counting) shows a linear relationship for the 22 subjects reported by Rand et al. (7) and Huang et al. (24). Included were nine women, and four Chinese and nine Caucasian men, with a range of body cell mass from 14 to 42 kg, and steady state urinary N excretion of 1.1 to 3.8 g/day. The correlation coefficient is 0.845. Since the body cell mass is considered to have a relatively constant N content, this relationship says in effect that N excretion during the steady state is proportional to body N content, thus implying exponential behavior for the long-term component.

There are a number of reports which show that urinary N excretion during a fast falls off in a curvilinear fashion with time and continues to decline slowly for many days (1, 4, 19, 25). The graph in the data of Runcie and Hilditch (26) shows a curvilinear decline in body K content.

It may not be generally appreciated that body N content varies among adults. Earlier reference was made to the fact that calculated body N ranged from 1287 to 1552 g for the four nonobese fasters and 1875 to 2842 g for the nine obese fasters whose data appear in Figure 1 and Table 1. Rand et al. (7) found a 3-fold range of body cell mass in their group of subjects which included elderly women and young adult males. Compilations of data on lean body mass as determined by several techniques show a wide range of values (9). If as our study suggests the urinary N excretion during periods of protein deprivation is proportional to body N content, then the magnitude of the "endogenous nitrogen" excretion will show a similar range of variation.

The data in Figure 1 and Table 2 show that the obese are more efficient at conserving body N during a fast than are the nonobese. Many years ago in studies on fasting animals Voit (27) "found that the greater the amount of fat in the body, the less is the protein metabolism" (3). Lusk (3) also compiled data that showed that longevity during starvation in animals is proportional to body fat content. Figure 2 shows that the conclusion of Voit (27) also applies to man: the ratio of N loss to weight loss for the duration of the fast is an inverse function of body fat content, up to about 50 kg of body fat, larger body fat burdens offering little if any additional advantage in this respect.

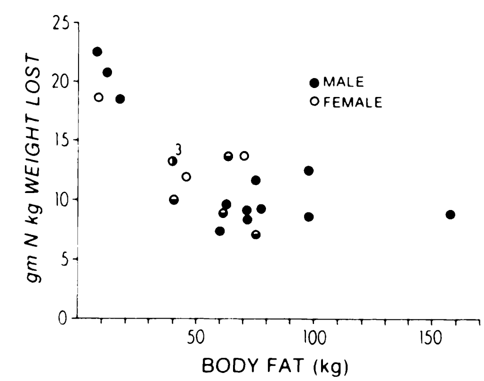

FIG. 2. Ratio of total N loss to weight loss (g/kg) plotted against initial body fat content, the latter calculated as weight minus lean body mass (from equation (*1*), except for subjects studied by Ball et al. (17) and Barnard et al. (15) who had measurements of total body water). Males (●), females (○), sex not stated (⊖): individual points for nonobese fasters (2, 11, 12, 18), present group of obese fasters, and those studied by Barnard et al. (15) and Ball et al. (17); ◑³, average of three subjects (16)."

The exponential technique applied to the data of Smith (14) can be used to generate an estimate of the daily retention of nitrogen needed to maintain N equilibrium, i.e., the requirement. From equation (*3*) the rate of change of body N content (dN/dt) is $F_1 (I - \lambda_1 N) + F_2 (I - \lambda_2 N)$, where I is intake and N is body nitrogen. Setting dN/dt equal to zero (i.e., N equilibrium), $I = F_1\lambda_1 N + F_2\lambda_2 N$. Smith's body N content at the start of his protein-free diet was estimated to be 1947 g, F_1 is 0.02 and F_2 is 0.98, λ_1 is 0.123 and λ_2 is 0.00105 (Table 1). Hence the required N intake is

$$0.02 \times 0.123 \times 1947 = 4.78 \text{ g/day.}$$

$$0.98 \times 0.00105 \times 1947 = 2.00 \text{ g/day}$$

$$6.78 \text{ g/day.}$$

It should be noted that this value represents the instantaneous loss rate of body N (in this case the negative N balance) at the very start of the experiment. This is about twice the average daily N loss for the entire 26 days (total N loss 87 g, or 3.35 g/day), and about three times the average daily loss (2.2 g) during the last week of the experiment. Despite being a minor fraction of the total, F_1 by virtue of its rapid turnover rate contributes a disporportionate share to body N loss, and hence to the estimated daily requirement.

Perhaps this approach could be of help in evaluating the effects of various low calorie diets in the treatment of obesity, and in the evaluation of N losses in other situations. ■

Addendum

Through the courtesy of Drs. Charles E. Driscoll and L. J. Filer, Jr. I have obtained data on an additional nonobese individual who recently completed a fast of 36 days. This 41-year-old male (initial weight 68.2 kg, height 173 cm), who was ambulatory and took water only, lost 15.2 kg and excreted a total of 289 g nitrogen during the 36 day fast. The ratio of N loss to weight loss, namely 19 g N/kg, is similar to the values for the nonobese fasting subjects depicted in Figure 2 and Table 2 of the present report.

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