Effects of Heat, Diet and Hormones on Total Body Protein Turnover Rate in Young and Old Rats[1,2] (35139)

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Most proteins in the body are in a state of flux, being continually synthesized and degraded (1). This dynamic state of the body proteins suggests that nitrogen metabolism can be influenced by various factors (2)—the endocrine system (2, 3), growth (4, 5), diet (6), and ambient temperature (7, 8). Most of the available data were obtained using conventional nitrogen balance techniques and amino acid turnover rates in various isolated tissues and cell-free preparations. Data on total body protein turnover rate are rather scarce. The objectives of the following report are to assess the effects of high ambient temperature (34°), restricted diet, thyroidectomy, and adrenalectomy on total body protein turnover rate in young and old male rats.

Materials and Methods. Normal, thyroidectomized (Thx), and adrenalectomized (Adrx) male albino rats of the Holtzman strain were received and placed in the climatic laboratory at about 23 days of age. Half the rats were exposed continuously to 28° and 50–60% relative humidity (RH) and the other half were exposed to 34° and 30–40% RH. The rats in each chamber were subdivided into: *ad libitum* fed, restricted diet (RD), Thx, and Adrx groups.

The Adrx rats in the 28 and 34° chambers were given 0.9% salt water and injected subcutaneously with 300 μg of corticosterone every second day. The injection of corticosterone was necessary for survival of the rats and to minimize regeneration of the adrenal tissue throughout the experimental period (about 600 days).

The restricted diet group (RD) in the 28° chamber were fed at the level of the thermally stressed *ad libitum*-fed rats in the 34° chamber. An equal percentage feed reduction was imposed on the 34° RD group. Thus, the level of food intake of the RD groups in the 28 and 34° rooms was reduced below their respective control group level by approximately the same percentage.

All rats were kept in suspension cages with six rats to a cage. Water was available at all times and food, Rockland Rat Ration, was available *ad libitum* for all rats except those on a restricted diet. Sulfamerazine was added to all drinking water as a precaution against respiratory diseases. Hanova germinicidal lamps and fluorescent lights remained on continuously in both chambers.

Determination of ^{75}Se-selenomethionine as an index for protein metabolism was essentially the same as previously described (3, 7). Each group was measured at the young age of 47–49 days and at the old age of 572–605 days. The data were analyzed statistically using Student's *t* test.

Results. Data on the effects of restricted diet, Thx, Adrx, and age on total body ^{75}Se-selenomethionine turnover rate (K), body weight, rectal temperature, and feed consumption on rats kept at 28 and 34° temperatures are shown in Tables I and II. The K is defined as the fraction of the body's protein pool turnover per day. Data were evaluated on the basis of (a) treatment effects

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TABLE I. Effects of Restricted Diet, Thyroidectomy, Adrenalectomy, and Age on Protein Turnover Rate in Rats Kept at 28°.

Treatment	Age (days)	Body weight (g)	No. of rats	$K^a \times 10^2$	Rectal temp.	Feed consumption (g/day)
Control	47	250	10	5.4 ± 0.08	37.9	19.6
RD	47	175	10	4.1 ± 0.10	37.8	13.2
Thx	49	164	10	3.8 ± 0.05	37.1	10.6
Adrx	49	206	12	5.2 ± 0.05	37.2	19.4
Control	572	654	9	3.8 ± 0.09	36.6	23.2
RD	605	409	10	3.9 ± 0.11	36.7	14.2
Thx	605	325	10	3.2 ± 0.09	36.6	15.1
Adrx	588	627	9	4.0 ± 0.11	36.5	26.3

[a] K is the fraction of body's protein turnover rate per day. RD = restricted fed, Thx = thyroidectomized, Adrx = adrenalectomized.

(RD, Thx, and Adrx) by comparing treated groups with untreated, *ad libitum*-fed groups kept at the same environmental temperature; (b) temperature effects by comparing groups kept at 34° with similar groups kept at 28°; and (c) age effects by comparing the young (47–49 days) and old (572–605 days) rats.

Control groups. Comparison of the 28 and 34° control groups show that exposure to heat for a short period of 24 days (age 47 days) significantly decreased K, but continuous exposure for a long period (549 days) had no effect. The old rats kept throughout their life at 28 and 34° had a significantly slower protein turnover rate than the young animals. Rats kept at 34° had an elevated rectal temperature and a depressed body weight and feed intake. The old rats at 28° had a lower rectal temperature than the young at 28°. The age effects on rectal temperature were not evident at 34°.

Restricted diet groups. Restriction of diet below *ad libitum* levels significantly decreased K in the young rats raised at 28 and 34° and had no appreciable effect on the old rats when compared to the control group. Exposure to heat did not significantly effect K of the RD groups. Body weight was decreased in all the RD groups.

Thyroidectomized groups. Body weight and protein turnover rate were depressed in all the Thx groups regardless of age and temperature when compared to their respective controls. Exposure to heat had no effect on K of the Thx rats. Thx rats had a lower rectal temperature at 34° than any other group.

Adrenalectomized groups. Protein turnover rate was similar in the Adrx and control

TABLE II. Effects of Restricted Diet, Thyroidectomy, Adrenalectomy, and Age on Protein Turnover Rate in Rats Kept at 34°.

Treatment	Age (days)	Body weight (g)	No. of rats	$K \times 10^2$	Rectal temp.	Feed consumption (g/day)
Control	47	195	10	4.2 ± 0.06	38.2	13.5
RD	47	157	10	3.7 ± 0.05	37.6	9.0
Thx	49	162	10	3.6 ± 0.05	37.3	7.4
Adrx	49	196	12	4.1 ± 0.08	37.6	15.8
Control	572	375	7	3.7 ± 0.12	38.1	14.2
RD	605	289	10	3.5 ± 0.11	38.0	9.2
Thx	605	349	10	3.1 ± 0.08	37.4	11.0
Adrx	572	393	1	3.8	37.7	16.0

groups kept in 28 and 34°. The Adrx rats at 34° had a lower rectal temperature than the control group. Exposure to heat significantly decreased K in the Adrx young rats. Similar statistical comparison in the old Adrx rats was impossible since only one rat survived the 549 days of continuous exposure to 34°. Body weight of all the Adrx groups was approximately similar to the control groups at 28 and 34°.

Discussion. In broad terms, diet, ambient temperature, and hormones are known to influence growth and longevity of animals as a result of radical changes in the dynamic equilibrium of many coordinated physiological and biochemical reactions. The data on hand (Tables I and II) deal exclusively with the effect of these factors on the metabolic pool of protein in the whole body. Evidence from earlier studies showed a high correlation between food intake and nitrogen excretion (9, 10). Also a slower plasma protein turnover rate was found when dogs were deprived of protein (11). Results on total body protein turnover rate (K) confirm data obtained using different techniques (9, 11). In this connection, diet restriction at 28 and 34° caused a decrease in K associated with lower body weight in the young rats. This is not surprising since these animals had a lower metabolic rate (12) and thyroxine secretion rate (13). When diet restriction at 28 and 34° continued for a long term the K values of the RD groups were similar to that of the control. The discrepancy in the effect of diet restriction in young and old rats is due to the fact that growth has ceased in the old rats and most of their caloric requirements are used for activity and tissue renewal. Similar to the control groups, feed intake per unit of body weight in the RD groups was no greater at 28 than at 34° and it decreased with advancing age.

The effects of Thx on K extend our previous findings (3) to include rats at different ages and kept at different temperatures. The mechanisms responsible for the changes in K due to Thx or injection of thyroid hormones were discussed elsewhere (3).

The adrenalectomized rats maintained on a reduced corticosterone therapy, salt, and fed *ad libitum* duplicate the growth rate and protein turnover rate of normal control groups. Studies on the effect of adrenalectomy and replacement therapy on protein metabolism and growth rate have produced inconsistent results (2). It has been shown that administration of small doses of corticosterone or cortisone maintain normal metabolic rate, body weight (12), and thyroid function (14), although Ingle (15) failed to restore normal functions in Adrx rats even with very large amounts of cortisone.

Exposure to heat for a short duration (23 days) resulted in a decline in K, whereas long duration of exposure had no significant effect. When the RD group at 28° was fed the same amount of feed consumed by the control group at 34° protein turnover rate was similar in both groups. This finding suggests that the voluntary feed restriction induced by hyperthermia may be a determining factor in decreased protein turnover rate.

With the exception of the RD groups, when young and old rats of all other treatments are compared it is evident that aging decreased K regardless of the ambient temperature. This confirms our recent report (5) indicating that nitrogen expenditure is decreased when growth rate ceases.

Summary. The effects of diet restriction, thyroidectomy, adrenalectomy, and ambient temperature (28 and 34°) on protein turnover rate (K) were studied in young (47–49 days) and old (572–605 days) male rats. The data indicate that thyroidectomy decreased K under all treatments. Adrenalectomized rats supplemented with salt and 300 μg corticosterone every second day had a similar K and growth rate as the control rats. Exposure to heat and restriction of diet decreased K significantly only in the young rats. The effect of heat is suggested to be associated with the voluntary reduced feed intake as a result of hyperthermia and depressed appetite.

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