Is Protein Catabolism Nonrandom?

In an earlier study[1] it was observed that protein loss induced by underfeeding or starvation of mice was accompanied by greater specific activity of the lysine-labeled protein compared with normally fed controls. The total counts per minute (cpm) of the protein was the same in both groups, however. Among the several possible explanations, it was suggested that 'nonrandomized breakdown in protein occurs, i.e., "older" (unlabeled) protein is preferentially broken down.' However, this was rejected since there was no known basis for this.

In a study on protein metabolism in aging mice[2], an observation was made which once more raises this possibility. 54 male mice uniformly distributed in age from 320 to 750 days were available for the experiment. At approximately 320 days, growth had ceased and the carcass protein content had reached the maximum value for the total life span[3]. They were injected with 0.1 μC of ^{14}C-lysine and were killed after 48 and 120 h. It had been determined that the log-linear phase had been reached by 48 h. Only 2 time periods could be used because of the scarcity of old animals. It was observed that although carcass protein decreased by 12.4% during this interval (320 to 750 days), $t^1/_2$ increased progressively to more than 30% greater than the value at 320 days (from 146 to 194 h)[2]. During the $t^1/_2$ interval for 320 day old animals, they exhibited a net loss of 0.94 mg of protein while the oldest lost 1.28 mg of protein. The specific activity (SA) increased respectively by 0.054 cpm/mg of protein and 0.072 cpm/mg of protein during the $t^1/_2$ intervals. The total cpm of the protein extrapolated to zero time (injection time) was practically independent of age (12,600 cpm for the 320-day-old animals to 12,950 cpm for the oldest).

Results and discussion. The data were recalculated to show the net decrease in carcass protein nitrogen ($-\triangle$N) compared with the maximum value at 320 days (623.4 mg) as a function of age, and SA and cpm as a function of $-\triangle$N (Table). It is apparent that an extremely high correlation exists between the net loss of protein nitrogen and increase in SA and cpm 48 h and 120 h after injection of the ^{14}C-lysine. This is not inconsistent with the possibility that 'older' protein is broken down preferentially.

SHIMKE and DOYLE[4] commented on the possibility that nonrandom breakdown of enzymes occurs. A theory of 'aging' of protein molecules as a signal for degradation seems excluded generally since the degradation of specific proteins wherever studied in animal tissue follows first order kinetics. However, SHIMKE and DOYLE point out that protein molecules exist in a number of different thermodynamic states. A protein might be subject to degradation only when molecules assume certain conformations. The microheterogeneity of proteins is well known[5]. That of albumin has been studied extensively[6]. One aspect of the heterogeneity is associated with the nonintegral sulfhydryl content and includes nonmercaptoalbumin components. Could the latter relate to albumin which has been modified as a result of its longer history in the body? Can this material be 'recognized' and catabolized in preference to mercaptoalbumin?

With regard to the problem of aging, if this hypothesis is correct, the data suggest the following: with increasing age there is a greater net loss of protein during the $t^1/_2$ interval. Since cpm in the total carcass protein extrapolated to zero time did not change with age and SA after 48 and 120 h actually increased with age[2], more 'older' protein must have been broken down during this interval. This suggests that there is no defect in the 'recognition' mechanism with age but an increase in the rate that unlabeled ('older') protein becomes modified for recognition. This is not inconsistent with the increase in inactive enzyme molecules reported in aging nematodes[7] and the thesis of OERIU and OERIU[8] that disorders of redox control occurs in aging resulting in enhanced oxidation of functional -SH groups of proteins with an accumulation of -S-S- groups.

Zusammenfassung. Injektion von ^{14}C-Lysin in 320 bis 750 Tage alten Mäusen deutet darauf hin, dass während des Alterns alte Proteinmoleküle infolge ihrer Strukturänderung rascher katabolisiert werden als neue.

Correlation of net loss of carcass protein nitrogen ($-\Delta$N)[a] with age and of specific activity (SA) and total counts per minute (cpm) with $-\Delta$N.

Regressions[b]	No[c]	r[d]	P
$-\Delta N = 51.18 - 0.16A$[e]	54	0.31	0.02
SA_{48}[f] $= 16.211 - 0.049\ (-\Delta N)$	24	0.84	<0.001
$SA_{120} = 11.520 - 0.037\ (-\Delta N)$	30	0.87	<0.001
$cpm_{48} = 9922.1 - 11.7\ (-\Delta N)$	24	0.55	<0.01
$cpm_{120} = 7071.7 - 7.0\ (-\Delta N)$	30	0.87	<0.001

[a] $-\Delta N$ in mg = N — 623.4 (observed protein nitrogen content of skinned eviscerated carcass (N) compared with the value for 320-day-old mice). [b] Regression were calculated with a Control Data 6400 Computer. [c] No. = number of animals in each group. [d] r = correlation coefficient, [e] Age in days (from 320 to 750 days). [f] 48 and 120 refers to time in h after injection of ^{14}C-lysine.

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Lettuce Seedling Growth: Antagonism Between Gibberellic Acid and Niacin

Niacin, a member of 'B'-complex vitamins, has been found to suppress germination of seeds and seedling growth of certain monocotyledonous plants when such seeds are presoaked with the aqueous solution of this vitamin[1]. Gibberellic acid antagonism to the action of many growth substances is also well known[2,3]. There appears to be no reference in the published literature to gibberellic acidniacin interaction in seedling growth. The present report summarizes observations on the effect of gibberellic acid and niacin, alone and in combination, on lettuce seedling growth.