Lean-Body Mass Creatinine-Coefficient Deficit and Urinary Steroids

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THE PROBLEM of determining the degree of protein depletion in individuals of advanced age or following periods of chronic debilitation is probably the most basic in the clinical management of such patients. Nitrogen balance studies are impractical and often unrewarding—especially when changes in nitrogen metabolism take place slowly.

A great need exists therefore for the establishment of a practical technic for the determination of the status of nitrogen equilibrium. One of the proposed technics which is under investigation in this laboratory will be reported here.

The quantity of creatinine excreted in the urine in 24 hours is usually considered to be a function of muscle mass. Although the constancy of this quantity is not absolute, within wide ranges it is usually a function of the weight of the individual. Thus the term *creatinine coefficient* refers to milligrams of creatinine per kilogram of body weight. Aside from a variety of pathologic events, the most important variables which reduce the utility of the creatinine coefficient are those of fat and water contents.

Behnke, Osserman, and Welham[1] derived the following approximate equation for estimating the lean-body-mass (L.B.M.) for young men who were not athletes:

$$\text{L.B.M. (g)} = 2 \times (\text{Ht. [cm.]})^2 \qquad (1)$$

With the use of this equation, it is possible to calculate a L.B.M. creatinine-coefficient, thus:

$$\frac{\text{24-hour creatinine value}}{\text{L.B.M. (kilo)}} = \text{C.C.}_{\text{L.B.M.}} \qquad (2)$$

$\text{C.C.}_{\text{L.B.M.}}$ should be a much more reliable index of muscle mass than the usual creatinine-coefficient. If now a mean $\text{C.C.}_{\text{L.B.M.}}$ is established, deviation from this value should reflect a loss in muscle mass, thus:

$$\text{C.C.}_{\text{L.B.M.}} \text{ observed} - \overline{\text{C.C.}}^{*}_{\text{L.B.M.}} = -\Delta\text{C.C.} \qquad (3)$$

Another feature of this investigation pertains to the well known fact that with aging the excretion of ketosteroids and androgens diminish markedly while that of the corticoids is less affected.[2] This would lead to the expectation that the antianabolic† influence of the gonadal-adrenal axis might increase. Certain evidence suggests that illness advances the imbalance in the production of these steroids.[3,4] The metabolic consequences of these changes should therefore be observed sooner in individuals who are chronically ill.

A study was therefore made of $\text{C.C.}_{\text{L.B.M.}}$ and the urinary ketosteroids and corticoids in individuals who were well and those who were chronically ill.

METHODS

In an attempt to reduce disuniformity of population selection, the patient load was drawn mainly from the Veterans Administration Center and consisted of males from 23 to 80

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* The line over the C.C. signifies the mean value.

† Antianabolic is used here in the sense that it describes a category of events which are opposite to the anabolic. It should not be implied that the author has taken sides on the issue of whether the disturbances in nitrogen metabolism are related to antianabolic or catabolic influences.

years of age. Random complete 24-hour collections of urine were made without previous preparation of the patient. The urine was refrigerated during collection. No preservatives were added. Creatinine and hormonal determinations were made as soon as possible and the urines were refrigerated until this was done. Creatinine was determined by the procedure of Bonsnes and Taussky,[5] ketosteroids by the procedure of Drekter *et al.*[6] and corticoids by the method of Porter and Silber.[7]

individuals with multiple illnesses. The total number was 51 patients.

RESULTS

The mean $C.C._{L.B.M.}$ for 36 normal men was 27.1. All values of 27.0 or above were assigned to the group with $-$C.C. of 0 (Table I). This category included 21 men. The mean $-\Delta$C.C. of the remaining 15 normal subjects was 4.6. This group was then subclassified into individuals above or below this average. Thus,

TABLE I

Lean Body Mass Creatinine Coefficient Deficient ($-\Delta$C.C.) and Urinary Ketosteroids (K) and Corticoids (C)

Number	Age		$-\Delta$C.C.	K mg	C mg	K/C	K^2/C
	Range	Mean					
36 normal male adults							
21	23–72	44	0	13.8 ± 0.9*	8.9 ± 0.6	1.62 ± 0.10	22.9 ± 2.2
6	35–77	58	2.0 ± 0.3	11.5 ± 1.0	6.7 ± 0.5 (P = <0.02)	1.75 ± 0.15	20.5 ± 0.5
6	44–77	62	8.4 ± 0.4	7.9 ± 1.0 (P = <0.01)	5.7 ± 0.6 (P = <0.01)	1.39 ± 0.09	10.3 ± 1.4 (P = <0.01)
51 chronically ill males							
25	29–80	54	0	13.2 ± 0.7	9.8 ± 0.6	1.43 ± 0.09	19.1 ± 1.8
11	40–70	52	3.3 ± 0.1	11.6 ± 1.1	8.3 ± 1.0	1.48 ± 0.13	18.0 ± 3.1
15	42–71	59	8.4 ± 0.7	8.3 ± 0.8 (P = <0.01)	6.3 ± 0.4 (P = <0.01)	1.32 ± 0.11 (P = <0.02)	11.9 ± 2.1 (P = <0.01)

All data based on 24-hour values. Only statistically significant P values are given.
* Standard error.

The control group of 36 men was chosen from staff members, associates, other workers, and patients with minor dermatologic ailments.

Patients with clinical evidence of muscular, renal or hepatic disease were excluded from this study. In addition, individuals whose height could not be correctly measured due to deformity or bone disease were not included, nor were patients with acute illnesses accepted. The major causes of illness were as follows: 18, various manifestations of atherosclerosis and its sequalae; 9, chronic cutaneous disease; 8, chronic pulmonary disease; 2, valvular disease; 3, gastrointestinal ulceration; 4, neurologic diseases; 3, psychologic disorders; 5, hypertension; 12, arthritis; 2, resections for cancer; 1, a blood dyscrasia. These included nine men had an average $-\Delta$C.C. of 2.0 and six men, four of them over 60 years of age, had an average $-\Delta$C.C. of 7.4. The significance of these ratios will be discussed below.

The chronically ill group was similarly classified. Twenty-five patients had a $-\Delta$ C.C. of 0. In 26 $-\Delta$C.C. averaged 6.3; 11 had values less than this and 15 exceeded it. The average of the former group was 3.3, the latter 8.4. Thus 29 per cent of the chronically ill individuals exhibited large $-\Delta$C.C. values in contrast to 17 per cent of the well subjects.

Table I reveals that statistically significant differences in urinary ketosteroids and corticoids were found in the group which deviated the most from the mean lean body mass creatinine coefficient, i.e., with the greatest $-\Delta$C.C

This held true for both the chronically ill and the control groups. The possible significance of this observation is discussed forthwith.

DISCUSSION

The limitations in the use of creatinine excretion as a function of muscle mass are quite well known. These include the presence of renal, hepatic, and muscular disease. Furthermore, constancy of excretion is not absolute. Perhaps the most important reason for the failure to put creatinine coefficient into more frequent use in clinical medicine is related to the absence of a device heretofore for measuring lean body mass. The equation of Behnke, Osserman, and Welham[1] represents an important step forward in this direction. If the early observations reported here are confirmed, the determination of $-\Delta$C.C., with suitable refinements, may prove to be useful in estimating degree of protein depletion, in evaluating the influence of anabolic steroids, and in nutritional management.

The use of urinary steroid determinations in the evaluation of metabolic disturbances induced by the mixture of endogenous steroids produced by the adrenals and gonads involves the usual suppositions. It must be assumed that the urinary excretion reflects the situation in the circulation, that end-organ sensitivity is similar from individual to individual, and that the biologic activity of the mixture of steroids as it occurs in the blood may be known from a knowledge of their individual activities. The steroids were not subfractionated and consequently the findings may have a limited utility in attempts to evaluate the biologic activity of these materials or their precursors in regard to the antianabolic-anabolic influence exerted by them. Nevertheless in a broad sense the decrease in urinary 17-ketosteroids reflects decreases in the production of androgenic and therefore anabolic precursors.

The K/C ratio attempts to show the disturbance in the relative amounts of anabolic steroids to the antianabolic corticoids. It also should be interpreted to represent the activity of 1 mg of "androgens" in the presence of corticoids. The ratio K^2/C was contrived in an attempt to represent the 24-hour equivalence of the activity of the "androgens." Thus since K C represented the activity of 1 mg of "androgens," K × K/C would represent the 24-hour value. The finding that statistically significant differences occur would seem to make the use of this ratio justifiable.

Investigations in the field of aging which have been carried out in this laboratory emanate from the hypothesis that with aging, such disturbances in gonadal-adrenal-steroid production occur that increasing antianabolic influences are exerted, and that this phenomenon is accelerated by "usage."[4] The ensuing changes seem to advance certain other aspects of aging such as those related to the connective tissue.[8]

The observation that large $-\Delta$ C.C. values occur more frequently in persons who have been chronically ill and that K, K/C, and K^2/C values are lower in those individuals is consistent with the concept stated above. However, the possible coincidental occurrence of two age-associated phenomena, consequent to more fundamental aging processes must not be overlooked.

SUMMARY

The Lean Body Mass Creatinine Coefficient ($-\Delta$C.C.) is proposed as a device for evaluating nitrogen deficits in individuals who are free of renal, hepatic, and muscular disease and whose correct height is determinable. In a group of men with a variety of chronic illness, large $-\Delta$C.C. values were observed in 29 per cent of the cases in contrast to a similar group of normal men in whom large deficits occurred in only 17 per cent. A relevant finding was the presence of an increased antianabolic influence as determined by urinary steroid studies in patients with large $-\Delta$C.C. values.

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