

Editorial

Uncertainties in the Interpretation and Validity of Long-Term Balance Studies

LITTLE is known about the physiology and pathology of habitually high intakes of a number of nutrients.¹ A related field of uncertainty concerns the interpretation and validity of continuously high retentions of certain nutrients. Many balance studies reported in the literature are perplexing in this regard, and the following examples are illustrative.

Protein. In Kampala, Uganda, Holmes et al.² carried out long-term balance investigations which lasted several months on malnourished Bantu adults. Observations revealed consistently high retention of nitrogen (up to 10 gm. per diem). Such retentions, however, were accompanied usually by far lower gains in body weight from the additional tissue protein than were expected. One subject who conceivably could have gained 15 kg. in three and one-half months gained only 2 kg.

Calcium. In a series of long-term balance observations (mean, 218 days) on thirty-nine Norwegian male prisoners, Malm³ found that a mean intake of 937 mg. calcium per diem gave rise to a daily mean retention of 76 mg.; over the whole period the accumulated retentions amounted to 16.5 gm. calcium or 149 gm. fresh bone (11 per cent calcium). In one subject with mean positive balance of 281 mg. per diem, the apparent gain in bone material amounted to 557 gm. In a more recent study, Harrison and Fraser⁴ performed a protracted series of interrupted balance observations extending up

to three and one-half years on osteoporotic patients who ingested about 2 to 3 gm. of calcium daily. Observations suggested retentions of several hundred grams of calcium, equivalent to several kilograms of bone material. Wheedon,⁵ also Nordin⁶ have undertaken similar studies on osteoporotic patients; their results indicate large accretions of calcium over periods of months.

Iron. Fowler and Barer⁷ carried out pioneer studies on iron absorption in patients with hypochromic anemia. With daily intakes of 500 mg. iron (as ferrous ammonium citrates) these workers reported that one woman retained 6.7 gm. iron over a period of ninety-eight days; long after her physiologic needs had been met she was still retaining iron at a high rate.

Sodium and Chloride. Gamble⁸ has stated that "measurements of retention of sodium and chloride by growing children recorded in the literature, are so large . . . that if these measurements defined actual gains, the children would in the course of a few years approach the fate of the emigrées from Sodom and Gomorrah."

COMMENTS

Needless to say, the interpretations and validity of these sustained sometimes almost fantastically high accretions of nutrients have worried many workers. The two obvious vitiating factors are (1) unassessed avenues of loss



of nutrients (other than urine and stools), in particular losses from the skin; and (2) in certain circumstances significant changes in body composition.

In their studies on the malnourished Bantu, Holmes et al.,² while not neglectful of dermal losses of nitrogen compounds, certainly showed that marked changes in body composition occurred with rehabilitation. They concluded that a proportion of the expected gain in body weight was offset by losses of metabolized body fat, and by fluid losses, so that the accretion of tissue protein was in part a replacement process. Nevertheless, the foregoing was not regarded as adequate to explain the discrepancy between gain in tissue protein and gain in body weight.⁹

The extent of insensible dermal losses of calcium and iron incurred in everyday life are not known with certainty. Malm,³ in calculations on his results, suggested a loss of calcium of 25 mg. per diem. Moore¹⁰ indicates the loss of iron from this source to be about 0.5 to 1.0 mg. per diem. Undoubtedly, losses of both elements are much higher with excessive sweating. Yet, despite such losses, there can be little dispute that large retentions of both calcium and iron¹¹ occur under conditions of sustained high intake.

In the case of the electrolytes mentioned, Gamble⁸ has stressed that the prime source of error in balance studies is "the loss of electrolytes insensibly from the skin, which we have practically no means of measuring." In relation to one particular study, he noted that "the insensible loss produced in this instance a 300 per cent error in measurement of retention by the orthodox method. This error is very much larger for the infant than for the adult because of his relatively larger surface area." This worker considered a second source of error in such studies to be "an extensive oscillation of balance for water and electrolytes which is apparently a feature of extracellular fluid."

The foregoing examples and brief discussion emphasize a number of points. (1) The need for extreme accuracy in intake and output studies and the constant reappraisal of methodology is obvious, particularly in long-term observations which are especially liable to

accumulative errors. (2) It is clear that knowledge is inadequate in regard to losses of biochemical components from the skin and other sources (hair, nails). This particular handicap seriously prejudices confidence in the interpretation of long-term investigations. (3) Perhaps the greatest obstacle standing in the way of interpretations is our unsatisfactory knowledge of body composition in relation to race, sex, age, diet and socioeconomic state. There *must* be harmony between the broad picture indicated by long-term balance studies on particular population groups, and that revealed by body composition data. If there is disagreement, then knowledge on the former must be defective. Malm³ regards as "monstrous" the suggestion that the large accretions of calcium indicated by his study imply accretions of new bone; he prefers to believe in long-term cycles of fluctuations of positive and negative balances, a view previously put forward by German workers.¹² But until there is satisfactory data on the body composition of subjects who habitually retain high levels of calcium, the validity and significance of the long-term balance studies described must remain in doubt. In the presence of habitually high iron intake it is known that the huge accretions of iron, indicated by both long-term⁷ and short-term¹³ studies, cannot continue at the original rates indefinitely, this being amply revealed by investigations on iron "overload" and siderosis in the South African Bantu.¹¹

Knowledge of enormous value to medical science has been gained by means of balance observations, especially since the introduction of isotope technics. But interpretations will continue to be hampered until the deficiencies of knowledge of the type described are remedied.

ALEXANDER R. P. WALKER, PH.D.
South African Institute for Medical Research
Johannesburg, South Africa

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