Contributions of the doubly labeled water method to studies of energy balance in the Third World

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ABSTRACT Of >250 studies on energy metabolism using the doubly labeled water (DLW) technique, 12 full papers describe work performed in the Third World. Unfortunately, the term “Third World” is imprecise and the focuses of individual studies were too varied to allow much comparison among the data. There is a need to develop a more uniform approach. Useful investigations will allow comparisons of energy metabolism to be made in a consistent way across a variety of socioeconomic groups within the same country, and between the Third World and the developed world, with a commitment to the long term. In this way, the DLW method, if combined with other measurements of activity, energy intake, and body composition, will provide useful information on energy requirements and the consequences of inadequate or excessive energy intakes for the individual. Such investigations should be done, with standard protocols where possible, not just for the DLW method but also for those methods with which DLW should be integrated. Only if these suggestions are followed will real “value for money” be obtained from DLW studies in the Third World or elsewhere. In the context of these criteria, studies in the Third World using the DLW method have been only partly successful. Am J Clin Nutr 1998;68(suppl):962S–9S.

KEY WORDS Doubly labeled water, Third World, basal metabolic rate, total energy expenditure, physical activity level

INTRODUCTION

Since Schoeller and van Santen’s (1) first human application of the doubly labeled water method, many hundreds of infants, children, adults, and elderly persons have been studied in this way. These are represented in >250 studies that, when subjected to meta-analysis, show a great deal of internal consistency, and in many instances have provided answers or at least clues to the answers of pressing nutritional questions on energy requirements, the adequacy of alternative procedures, and energy metabolism.

In contrast, a database on Third World studies comprises only 12 published papers. There is no reasonable scientific explanation for the scarcity of work. A noninvasive technique of this type is highly suited to the Third World; no high technology devices are required for the field work and the sophisticated equipment can be kept in the laboratory where it belongs. Indeed, it can be reasonably argued that although there may be adequate alternative procedures to use in the developed world, Third World studies demand the use of the DLW method. Given the absence of scientific reasons for the lack of work, one possible conclusion is that Third World research is not, generally speaking, a priority for Western sources of scientific funding, except when comparative studies are likely to provide information applicable to Western problems, eg, obesity. It is hoped that lack of interest among scientists is not a natural corollary of this, but if there are few opportunities for work, young scientists may not have the chance to develop a familiarity with the Third World and its problems and ambitions.

Given this scenario, it is hardly surprising that within the work to be reviewed, it is difficult to discern a particular pattern or plan with respect either to scientific questions or long-term developmental goals. We must go to more general issues to see if the work can be bound together in some meaningful way.

A useful starting point is the recently published review of our understanding of the energy requirements of humans that was produced as the outcome of an International Dietary Energy Consultancy Group (IDECG) meeting in 1996 (2). It has interesting aspects in respect to DLW studies. Whereas it is clear that some members of the group embraced DLW concepts and methodologies with enthusiasm, others saw it as a limited and expensive specialist’s tool at best. However, several recommendations and needs were defined (3), including the following:

1) The energy requirement of an individual is the intake from food that will both balance expenditure when an individual’s body size and composition and level of physical activity is consistent with long-term good health and allow for the maintenance of an economically necessary and socially desirable level of physical activity.

2) Estimates should be based on measures or estimates of energy expenditure (actual or desirable). All currently available information should be considered.

3) The basal metabolic rate (BMR) factorial approach [physical activity level (PAL) = total energy expenditure (TEE)/BMR] should be used as the basis for estimating requirements worldwide.

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4) BMR × 1.4 can be regarded as a minimum acceptable maintenance level, but more data are needed before further defining levels for individuals with light, moderate, and heavy physical activity.

5) Metabolic adaptation to under- and overfeeding is discounted in making allowances for healthy populations.

6) Multiple approaches to estimating energy expenditure are needed.

To determine whether Third World studies using the DLW method have helped in any aspect of measuring energy expenditure we can ask: 1) Have Third World studies provided reliable measures of energy expenditure and is the information available capable of translation into PAL values? 2) Is the information useful in defining PALs for a variety of activities? 3) Is there any evidence for metabolic adaptation available from Third World DLW studies? 4) Do Third-World measurements of energy expenditure with DLW provide indications as to the suitability of other methods?

OVERVIEW OF THIRD WORLD ESTIMATES OF ENERGY EXPENDITURE

In presenting comparative data, it is best to adopt an approach that allows the simultaneous representation of BMR, TEE, and PAL. This is easily accomplished by plotting TEE versus RMR on a log scale. This tactic is amply justified (4, 5) because an analysis of data from 574 free-living adults and children (4) showed that

\[
\log \text{TEE} = \text{intercept} + \text{power} \times \log \text{RMR} \tag{1}
\]

where intercept = 0.514 = log(1.67) and the power term has a value of 1. Thus, TEE/RMR has a geometric mean of 1.67.

Plotting log TEE (y) versus log BMR (x) as shown in Figures 1–3 thus allows an easy comparison between individual values for TEE, BMR, and recommended PAL; these appear as parallel lines with positive slopes.

DLW data from normal European men and women are displayed in this way in Figure 1. For comparative purposes, FAO/WHO/UNU recommendations (6) for light and heavy occupational work are also shown (men: light, 1.55; heavy, 2.10; women: light, 1.56; heavy, 1.82). Given that the basis of the recommendations involved no isotopic work, the correspondence of observations to recommendations is quite good, but the data shown in Figures 2 and 3 and summarized in Figure 4 bring to light a major difficulty with the present topic. To state the obvious, not all third World countries are the same; the descriptor of the distribution of energy expenditure (burden of activity, requirement, respectively, and for the high PALs in men described as Gambian laborers (16) an exceptional financial reward was postulated as a significant factor.

What conclusions can be drawn from all this? We might conclude that current estimates of energy requirements based on other measures look about right, but this is not the investigative requirement, which should be to increase the database from which the prediction of energy requirements is drawn so that it becomes more secure in a wider variety of circumstances. We may conclude, for example, that in the time of high agricultural activity in the village of Keneba, Gambia, a subsistence farmer’s energy requirement is ≈2.4 × BMR, but the utility of this information is more specific than general; clearly there is a need to examine studies in more detail, where the information is available.

INDIVIDUAL STUDIES: DETERMINANTS OF ENERGY REQUIREMENTS

The work of Kashwazaki et al (10) is a detailed examination of the distribution of energy expenditure (burden of activity,
work, and energy requirement) within family groups of native Andeans living in Bolivia. The population studied consisted of 15 females and 8 males between 5 and 65 y of age. Mean PAL values for adults (2.00 \pm 0.21) were significantly different from those of adolescents (1.76 \pm 0.34) and children (1.60 \pm 0.22), but there were no differences between men and women. This study was carried out in the preharvest season and suggests a fairly equitable division of work and similarity of energy needs for the adults at the time. At the time of writing, the study is being repeated with the same individuals at harvest time, and it is expected that this continuity will substantially increase the value of the work.

As already indicated, the study in Mexican building workers (12) is the most thorough available and suggests a generic protocol for further work, if it can be achieved in less contrived circumstances. Briefly, in an 8-d program, typical work activities were simulated. The energy costs within the experiment were assessed by keeping activity diaries and monitoring oxygen consumption during work, TEE was measured by using the DLW method, and BMR was measured rather than estimated from regression equations. Energy intake was assessed from weighed diet records. This protocol allowed discretionary activity to be calculated on the assumption that energy expenditure during sleep was the same as BMR. Summaries of the data are shown in Figure 5. The overall conclusions from this work were that there was 1) no relation between discretionary and occupational energy expenditure overall and 2) no evidence to support the suggestion that subjects with low body weight compensate for energy spent on work with reductions in discretionary expenditure.

The same sort of detailed data are not available from the work of Diaz et al (16) or Riumallo et al (13), the focus of which was somewhat different. These investigations were intended to show whether dietary supplementation altered activity and improved work performance. In the former study, subjects moved earth by wheelbarrow to build a road. In a crossover design, subjects had to work for 2 wk at the end of a 6-wk period, during which supplemented groups received an extra 16 MJ/d. The salient features of the study were that there were no significant differences in TEE–BMR between supplemented and unsupplemented groups, nor was there evidence either from direct measurements of work performance that extra output was achieved or from heart rate monitors that the low postwork activity was different between the groups. Significantly, however, unsupplemented subjects lost weight and supplemented subjects gained weight (see Table 1). In the study, the incentive to work was considerable; the subjects were paid the equivalent of the earnings they would receive from selling the year’s cash crop.

The maintenance of high work performance at the expense of weight loss was also observed by Kraut and Muller (17) in coal
workers given incentives. Despite more modest supplements, less demanding work, and trivial incentives, Riumallo et al (13) showed similarly that increases in energy intake from 11.2 to 14.2 MJ over a 60-d period produced not an increase in activity as measured by DLW and factorial methods, but a 1.8-kg weight gain and significant fat deposition (2.70 kg).

Weight losses, as observed in the unsupplemented Gambian subjects, or weight gains, as observed in supplemented Chilean subjects, are not likely to be desirable in the long term. We cannot speculate from the experiments at what stage chronic malnutrition and weight loss might have effects on an individuals ability to work, but one must suspect that there will be many circumstances in which the economic needs of the family and broader community are considerable factors that will be difficult to control in any experimental design. Conversely, the absence of activity increments with supplementation, if persistent (such a situation could arise with gradual increases in affluence in the Third World), may predicate the development of obesity.

Studies in infants using the DLW method formed a significant part of Butte et al's (18) report to an IDECG meeting on energy and protein requirements. Comparisons between measured energy intake and estimates of requirements based on the energy cost of growth and estimates of energy expenditure based on DLW data showed good agreement but produced values for requirements that were lower than the previous FAO/WHO/UNU estimates (see Figure 6). The limited data from Third World studies are also shown in Figure 6 (19, 20). Data for absolute values (kJ/d) is difficult to interpret. In both studies, weight was significantly correlated with TEE, but the Mexican infants were marginally malnourished and growing only slowly; the Gambian infants were also stunted (67% were < 90% weight-for-age and 36% were <90% weight-for-height). The inference, therefore, is that energy intake in these populations is insufficient to meet the requirements for growth and expenditure combined; we need to try to ascertain whether this inadequacy arises out of a requirement for growth and maintenance that is similar to that of Western children or if exposure to a harsh climate increases this requirement. The data available are not adequate to answer that question. When expressed per kilogram body weight, the energy expenditure of Mexican infants looks only marginally higher than average western data (see Figure 6), although Butte (18) showed that the values were greater than those of a cohort of well-nourished, breast-fed Houston babies ($\bar{x} \pm SD$ 314 ± 46 compared with 268 ± 29 kJ·kg$^{-1}$·d$^{-1}$) and that the Gambian and Mexican data combined (331 ± 16.7 kJ·kg$^{-1}$·d$^{-1}$) provides a significantly higher value than the average of all Western infants measured (303.7 ± 33.8 kJ·kg$^{-1}$·d$^{-1}$). However, it has not been possible to show significant differences in the regressions of

**Figure 3.** Total energy expenditure (TEE) and basal metabolic rate (BMR) for Third World men. The parallel lines show physical activity level (PAL) values of 1.55, 1.78, and 2.10 for light, moderate, and heavy occupational work for men. □, Identified group; +, the rest of the data set. PAL values ($\bar{x} \pm SD$) were: Bolivians, 1.96 ± 0.25 ($n = 6$) (10); Cameroonian, 1.87 ± 0.12 ($n = 8$) (14); Chileans, 1.79 ± 0.14 ($n = 6$) (13); Gambians (farmers), 2.1 ± 0.41 ($n = 8$) (15); Gambians (laborers), 2.96 ± 0.66 ($n = 16$) (16); Mexicans, 1.78 ± 0.21 ($n = 13$) (12).
energy expenditure per kilogram body weight on age for these groups. A more adequate view of the true situation will emerge only with more studies.

The link between energy expenditure and energy requirement in infants is the energy needed for growth. Butte’s (18) calculated values for this are incorporated into Figure 6 to provide the requirement from the energy expenditure data, but it is pertinent to remember that although the requirement for growth is 35% of the total at 1 mo, it is only 3% at 12 mo, except in the circumstance of catch-up growth in children recovering from malnutrition.

The DLW method has also been used to estimate the energy requirements for maintenance and activity in a study of catch-up growth in malnourished children (21). Values for energy expenditure were plotted against weight gain (1.7–16 g/d) in children aged 15 mo. The predicted zero weight gain value of 323 kJ·kg\(^{-1}\)·d\(^{-1}\) compares well with energy expenditure measurements for this age group as compiled by Torun et al (22) from a variety of sources. More interestingly, the energy costs of synthesis of tissue deposited were obtained from the slope of the regression, and these combined with measurements of the composition of the weight gain (50% fat) provided a value of 26.4 kJ/g wt gain. This value is well within the range of reported values used to develop a figure of 23.4 kJ/g (6).

The DLW method has been used in 2 other studies addressing the question of adaptation to energy intake. Stein et al (9) distinguished 2 groups of Guatemalan women on the basis of socioeconomic status and showed a significant difference in total energy expenditure of \(\sim 14\%\). About half of this was accounted for by differences in lean body mass, but because BMR was not measured it is not possible to say whether the remaining difference is an 18% reduction in BMR or an 11% reduction in activity; the latter, however, was thought unlikely.

Pasquet et al (14) concentrated their experimental study around the effects of massive overfeeding (28.2 MJ/d) of high-carbohydrate diets in young Cameroonian men with the intention of trying to provide evidence for facultative thermogenesis. In the community studied, such feeding is a traditional annual event called “Guru Walla” that lasts \(\sim 2\) mo and, in this study, produced weight gains of 17 kg, of which 70% was fat.

FIGURE 4. Group physical activity level (PAL) values and percentage of national population engaged in agriculture. See legends for Figures 2 and 3 for means, SDs, and n values.

FIGURE 5. The partitioning of daily total energy expenditure in Mexican construction workers. DEE, discretionary energy expenditure; OEE, occupational energy expenditure; SEE, sleeping energy expenditure. Data from reference 12.
PAL values fell significantly from (x ± SD) 1.87 ± 0.12 to 1.45 ± 0.085 because measured RMR increased and TEE remained the same (Figure 7). Unfortunately, evidence for any adaptive process could not be obtained because the energy balance equations did not add up for the entire fattening season, with 20.7% of the energy intake unaccounted for.

The relation between the components of energy expenditure and infection is an important issue for the Third World, but with only one reported piece of work, the issue as to whether infection is a cause or consequence of negative energy balance or weight loss in unlikely to be resolved. Valencia et al (23), however, in the case of mild giardiasis and its treatment, showed that although BMR remained unchanged with treatment, TEE and TEE – RMR increased substantially though not significantly (Figure 8). The change in PAL values was from (x ± SD) 1.37 ± 0.2 to 1.54 ± 0.25. Given that the subjects were well nourished, the infections had not produced weight loss, and there were no effects on appetite, significant changes in energy metabolism may have been expected to be unlikely. In patients infected with HIV, reductions in TEE were only seen during periods of weight loss (24).

ALTERNATIVE APPROACHES TO THE MEASUREMENT OF ENERGY EXPENDITURE

Only 2 reported studies, both in Gambia, have compared alternative methods directly in the Third World. Combining the data from adult men and women (15, 25) gives similar values for both methods (heart-rate monitor: DLW = 1.067 ± 0.18, x ± SD), lending support to the high PAL values found in this community even though the limits of agreement are rather large. It may also be deduced from Haggarty et al’s work (12) in which energy expenditure during work was measured by using a portable oxygen consumption meter, that on average this measurement was compatible with simultaneous estimates of TEE using DLW.

CONCLUSIONS

The general purpose for the papers presented at this symposium was to address the question, “What have we learned from studies using the DLW method?” It would be wiser perhaps to ask, “What can we learn from studies using the DLW method in the Third World?” and “What are the best ways to design experiments?” As far as experimental design is concerned, the DLW method should not be used in the expectation that it will provide all the answers. There is little point in spending money on 18O without measuring RMR, and it is reasonable to try to further partition TEE – RMR by using devices that will adequately measure the energy cost of particular activities. Energy intake should also be measured so that, when combined with changes in body composition estimated from isotopic data, it will be possible to completely balance expenditure against intake. It may well be that in the first instance, balances of this type may merely point up the inadequacy of one or more of the methods (probably the measurement of food intake), but there must be a concerted approach to getting a combination of methodologies (not just a single methodology) right for the Third World and elsewhere.

TABLE 1
Effect of dietary supplementation on work performance in Gambian laborers

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<tr>
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<th>Group 1 (n = 8)</th>
<th>Group 2 (n = 8)</th>
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<tr>
<td></td>
<td>Weeks 0–6</td>
<td>Weeks 7–12</td>
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<tr>
<td></td>
<td>Weeks 0–6</td>
<td>Weeks 7–12</td>
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<tr>
<td>Weight change (kg)</td>
<td>1.26</td>
<td>-3.4&lt;sup&gt;4&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>-1.5&lt;sup&gt;4&lt;/sup&gt;</td>
<td>0.9</td>
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<tr>
<td>BMR (MJ/d)</td>
<td>6.9</td>
<td>6.3</td>
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<td></td>
<td>5.8</td>
<td>6.3</td>
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<tr>
<td>TEE – BMR (MJ/d)</td>
<td>13.9</td>
<td>13.4</td>
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<tr>
<td></td>
<td>10.4</td>
<td>11.6</td>
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<tr>
<td>Postwork heart rate</td>
<td>76.2</td>
<td>73.5</td>
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<tr>
<td>(beats/min)</td>
<td>74.9</td>
<td>70.3</td>
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<tr>
<td>Loads/d</td>
<td>163</td>
<td>179</td>
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<td></td>
<td>158</td>
<td>175</td>
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</tbody>
</table>

<sup>1</sup>BMR, basal metabolic rate; TEE, total energy expenditure. From reference 16.

<sup>2</sup>Supplemented 0–6 wk, unsupplemented 7–12 wk.

<sup>3</sup>Unsupplemented 0–6 wk, supplemented 7–12 wk.

<sup>4</sup>Significantly different from supplemented period, P < 0.001.
After protocols for studies are developed, they must be applied logically. It must be accepted that this aspect of published work is not completely satisfactory. None of the Third World studies published to date provide comparisons with well-nourished groups of the same or even different ethnicity in the same country. Also, comparisons between data from developing countries and the developed world are difficult because the former has focused mainly on the relatively poor, laboring classes and there are no examples of these in the latter. Improving the basis for comparison must have high priority.

It is possible to suggest several ways in which the DLW method could be usefully applied to investigate Third World problems. Comparisons of the DLW method with methods for measuring energy intake in developing countries have shown the limitations of food intake measurements, and this question needs to be addressed for developing countries. It is difficult to see how interventions designed to improve food supply and security can be monitored unless there are valid methods for measuring food intake in individual subjects. When reliable intake methodologies are developed, we can begin to investigate how seasonality in food availability relates to seasonality in energy requirements and how the work load is distributed through the community in subsistence economies, and the relation of work load to individual food intakes. However, the greatest significance of the DLW method is that the results it provides should not be influenced by subject- or operator-specific effects; provided that analytic methods are adequate and calculation procedures remain unchanged, data obtained through use of the DLW method should be universally comparable. This suggests that its most powerful application will be in multicenter and long-term studies where information is needed on the etiology diseases related to nutrition. The transition from rural subsistence to relative urban affluence is, in many regions, bringing with it the familiar problem of obesity in later life, and is thus an area in which prospective longitudinal studies using the DLW method could be used to great advantage.

REFERENCES