

Estimating Total Body Water in Children on the Basis of Height and Weight: A Reevaluation of the Formulas of Mellits and Cheek

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Abstract. An estimate of total body water (TBW) has important implications in clinical practice. For patients on peritoneal dialysis (PD), the estimate is critical when determining the delivered dialysis dose. The formulas of Mellits and Cheek have been recommended to estimate TBW in children on PD. These formulas were derived from healthy children, and very few infants were included. To assess the accuracy of these formulas, the original data were obtained and additional data from a broad literature review were compiled. The majority of the new data points were in the infant age range. Data were fitted using least-squares methodology and backward elimination to obtain a parsimonious model. Best fits were obtained using age, gender, and weight

or a height \times weight term. The results of the curves are as follows:

$$\text{Infants 0 to 3 mo } (n = 71): \text{TBW} = 0.887 \times (\text{Wt})^{0.83}$$

$$\text{Children 3 mo to 13 yr } (n = 167):$$

$$\text{TBW} = 0.0846 \times 0.95^{[\text{if female}]} \times (\text{Ht} \times \text{Wt})^{0.65}$$

$$\text{Children } > 13 \text{ yr } (n = 99):$$

$$\text{TBW} = 0.0758 \times 0.84^{[\text{if female}]} \times (\text{Ht} \times \text{Wt})^{0.69}$$

When compared with the previous Mellits and Cheek formulas, the new formula fits better for infants (comparison of prediction errors, $P < 0.0004$). These newer formulas do not perform significantly better for the older two groups. Actual TBW measurement in children on PD must still be determined to verify the use of these formulas and to accurately assess dialysis delivery and adequacy.

Knowledge of total body water (TBW) has implications for many areas of clinical practice, such as parenteral fluid therapy (1), pharmacokinetic evaluations, and calculation of the delivered dose of dialysis (2). There are a number of methods used to determine TBW directly (3–6); these include the measurement of distribution of “heavy” water (either D₂O or H₂O [18]), bioimpedance analysis (BIA), and estimates from anthropometrically determined fat mass. The accepted criterion standard measurement of TBW is the use of heavy water. Although not difficult to perform and free from radiation risk because the isotopes are stable, the latter studies are time-consuming and costly. BIA has become an accepted method, but there are some important caveats to performing studies in this manner, and some significant variations in the results are inherent when compared with the heavy water (4).

The need to accurately estimate TBW in patients on dialysis has taken on great significance during the past few years (7,8). An estimate of TBW is critical for the calculation of Kt/V urea, a measure of delivered dialysis dose that has become the

accepted standard. The V component of this term represents the volume of distribution of urea, widely accepted to equal TBW. For patients on hemodialysis (HD), the V component is calculated as a part of the modeling program used to generate the term Kt/V. In contrast, for patients on PD, it is necessary to estimate V. Among children who require dialysis, many of whom receive PD, an accurate estimate of V is, in turn, clearly desirable. The National Kidney Foundation has established a series of quality of care guidelines through the Dialysis Outcomes Quality Initiative (K/DOQI). The K/DOQI guidelines for peritoneal dialysis adequacy recommend that V (TBW) in children should be estimated using the anthropometric formulas of Mellits and Cheek, because most clinicians do not have access to heavy water or BIA and because these formulas were felt to be more accurate than the simple estimates of TBW that are based on percentages of body weight (2).

Mellits and Cheek reviewed the literature through 1968 and collected all the reports delineating individual measures of TBW for healthy infants and children (9). In all cases, the TBW assessments were conducted with deuterium oxide (D₂O), and all of the data had to include the subjects' height and weight. They then graphically evaluated the distribution of the TBW measures and developed equations that estimated the actual TBW.

In light of additional data points available in the literature and newer computer-fitting algorithms, we undertook a formal reassessment of the literature. We used the original data points and more recent reports to determine the accuracy of the

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Mellits and Cheek formulas as well as the accuracy of the simple estimates of TBW (0.6 to $0.7 \times$ body weight in kg [1]).

Materials and Methods

Literature Review and Data Retrieval

Using the references from the Mellits and Cheek article, the original data points were collected and entered into a database. In addition, a MEDLINE literature search was conducted for all articles using the term “total body water.” The resulting list was limited to infants, children, and adolescents (≤ 21 yr of age). The articles were retrieved and added to the database if they met the following criteria:

1. TBW was measured using water D₂O or H₂O (18). If the former was used, the data had to be corrected for non-water hydrogen pools in the body.
2. Individual data points had to be reported, with subject gender, height, and weight.
3. The study subjects were healthy infants and children.

The references of all the articles were manually reviewed to attempt to identify additional data sets. Several recent articles used H₂O (18) in an effort to validate other TBW methods on healthy children (10–12), but efforts to obtain the individual data points from the authors were unsuccessful.

Statistical Analyses

Total body water was modeled as a linear function of age, gender, height, and weight. Parameter estimates were obtained by using the method of least squares. After reviewing initial data displays, it was evident that TBW, age, height, and weight would best be analyzed on the natural logarithmic scale ($\ln[\]$) to provide a more linear association and a more symmetric distribution of the residuals conforming to the normality assumptions needed for the percentile estimates. Previous TBW data suggest that the relationship of TBW to body size changes in early infancy and at the time of puberty (1). Accordingly, the total cohort was separated into subgroups that were 0 to 3 mo, 3 mo to 13 yr, and >13 yr of age. The estimation of the regression model was done separately for these subgroups.

The initial step in the modeling process was to fit all of the clinical variables. Backward elimination was then performed to obtain a more parsimonious model. The removal of variables was set at a significance

level of 0.05. After reviewing the reduced model, further simplifications were investigated. The percentile distribution of TBW was then estimated from the final regression model (13,14). To compare our models with those previously published, we first calculated the mean squared prediction error (*i.e.*, prediction error = (Actual TBW – Predicted TBW) [2]) for each of the proposed models on the subset of the data that was common to both our study and that of Mellits and Cheek ($n = 236$). The mean squared prediction error was then compared using the likelihood ratio statistic overall and within age subgroups. Similar comparisons were used to compare the proposed models with the simple estimates of TBW ($0.7 \times$ Body Weight in infants <1 yr of age; $0.6 \times$ Body Weight for older children) but using all the data available for the proposed model. See the appendix for further details on the statistical model.

Results

Three hundred thirty-seven subjects who met all entry criteria were identified (9,15–21). The original cohort of 236 children, 26 of whom were infants <1 yr of age, from the Mellits and Cheek report constituted the majority of the patients. Many of the newly identified patients were infants. The demographics of the patients are reported in Table 1. Note that gender was only reported for 39 of the 71 infants 0 to 3 mo of age.

0 to 3 Months

Modeling was performed three times in this group of patients. Gender, as noted, was not available for 45% of the infants. It did not appear to have a significant impact on the accuracy of the formula and was eliminated. Height also had no statistically significant association with TBW in the model ($P = 0.5$) and was likewise removed. Age and weight were significantly associated with TBW, and the R^2 of the model with the reduced number of variables was 0.98, with a residual variance of 0.004. However, for this group, the effect of age was quite small and the age group restricted (0 to 3 mo), prompting the model to be refit without the age variable. The resulting equation had an R^2 of 0.97 and residual variance of 0.005. The 50th percentile TBW can be estimated as:

$$TBW = 0.887 \times (Wt)^{0.83}$$

Table 1. Patient demographics

Patient Characteristic	Overall ($n = 337$)	Age Group		
		0 to 3 mo ($n = 71$)	3 mo to 13 yr ($n = 167$)	13 yr + ($n = 99$)
Age (yr) ^a	8 ± 7	20 ± 29 d	5 ± 4	17 ± 3
	5 (8 mo to 14 yr)	3 (1 to 30) d	5 (3 mo to 8 yr)	16 (15 to 19)
Male/Female ^b	201/104	25/14	95/72	81/18
Height (cm) ^a	112 ± 47	48 ± 7	108 ± 28	166 ± 11
	113 (68 to 157)	47 (42 to 53)	108 (85 to 126)	169 (159 to 175)
Weight (kg) ^a	28 ± 24	3 ± 2	21 ± 12	59 ± 12
	19 (8 to 48)	2 (2 to 4)	17 (12 to 27)	61 (49 to 68)
TBW (L) ^a	17 ± 14	2 ± 1	12 ± 7	36 ± 8
	12 (5 to 27)	2 (1 to 3)	10 (7 to 16)	38 (30 to 42)

^a Summarized as a mean \pm one SD and 50th (25th to 75th) percentiles.

^b Gender information was available in only 39 subjects 0 to 3 mo of age.

Figure 1 depicts the 10th, 50th, and 90th percentiles for TBW using the complete form of the modeled equation (see appendix for the full equation and the derivation of the version used here).

3 Months to 13 Years

Similar modeling was performed for the data on the children in this age group. Although gender was a significant factor, it was apparent that age did not contribute statistically to TBW estimation within this range of ages ($P = 0.4$); it was therefore removed from the model. The coefficients for height and weight in the resulting equation were similar, and a combined anthropometric parameter, $(Ht \times Wt)$, was fit into the model. This yielded an R^2 of 0.97 and a residual variance of 0.006. The 50th percentile TBW for children in this age range can be estimated as:

$$TBW = 0.0846 \times 0.95^{\text{if female}} \times (Ht \times Wt)^{0.65}$$

For males, the factor 0.95 would, of course, be omitted. Figure 2 depicts the 10th, 50th, and 90th percentiles for TBW using the complete form of the modeled equation.

More than 13 Years

For this group, like the 3 mo to 13 yr group, gender was significant but age had no impact. Dropping age as a variable decreased the R^2 from 0.898 to 0.897, with no change in the residual variance. Although height was a marginally significant factor, and the coefficients for height and weight did differ (in contrast to the younger age group), a model similar to that of the younger group, using $(Ht \times Wt)$ was fit. The R^2 for this “simplified” model was still 0.896, and the residual variance remained constant at 0.006. This model was considered the final model because of its consistency with the model for the younger age group. The 50th percentile for the children >13 yr of age can be estimated as:

$$TBW = 0.0758 \times 0.84^{\text{if female}} \times (Ht \times Wt)^{0.69}$$

The intercept for this older group is slightly different, the correction factor for TBW in females is slightly lower, but the power of the $Ht \times Wt$ parameter is remarkably consistent with the younger group. Figure 3 depicts the 10th, 50th, and 90th percentiles for TBW using the complete form of the modeled equation.

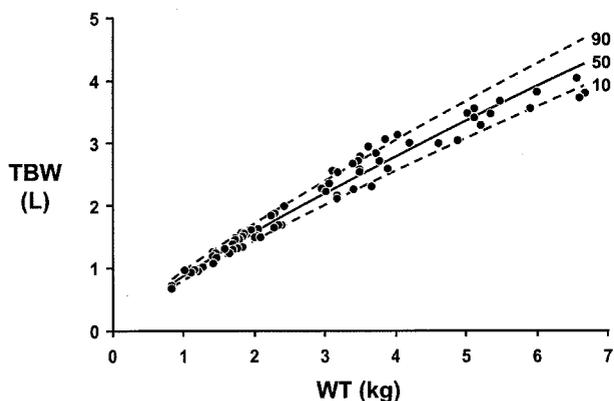


Figure 1. Total body water (TBW) plotted against body weight for infants <3 mo of age. The 10th, 50th, and 90th percentile curves generated from the equations in the text are shown.

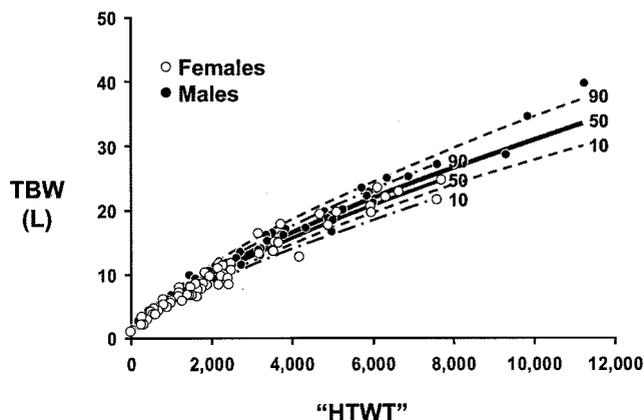


Figure 2. TBW plotted against the parameter $(Ht \times Wt)$ for children from 3 mo to 13 yr of age. The 10th, 50th, and 90th percentile curves, generated from the equations in the text are shown. The curves for both males (●) and females (○) are presented.

Comparison with Mellits and Cheek and Simple Estimates

The mean squared prediction error for each of the proposed models was compared with the Mellits and Cheek equations (9). Table 2 summarizes this comparison for each of the age groups as well as overall. For the youngest age group, the new model had a significantly lower prediction error (*i.e.*, the new model performs better) when compared with the Mellits and Cheek equations ($P < 0.0001$). For the middle age group and oldest age group, the prediction errors for the new equations were generally greater in comparison with the Mellits and Cheek equations, but they were only significantly greater for the 3 mo to 13 yr group. Overall, there was not a significant difference between the prediction errors; the new equations have a mean squared prediction error rate of 4.11 compared with 3.51 for the Mellits and Cheek model. The proposed model was similarly more accurate for infants and adolescents, as well as for the group overall (Table 2) compared with the 0.6 to 0.7 model.

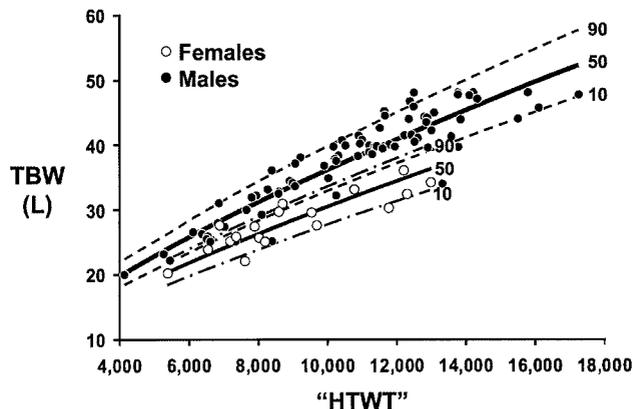


Figure 3. TBW plotted against the parameter $(Ht \times Wt)$ for children >13 yr of age. The 10th, 50th, and 90th percentile curves generated from the equations in the text are shown. The curves for both males (●) and females (○) are presented.

Table 2. Comparison of mean squared prediction errors between previous models and the current proposed model^a

A				B			
Age Group	Current Model	Mellits-Cheek	<i>P</i> value ^b	Age Group	Current Model	0.7-0.6 Model	<i>P</i> value ^b
0 to 3 mo (<i>n</i> = 26)	0.044	0.22	0.0001	0 to 3 mo (<i>n</i> = 71)	0.03	0.07	0.0005
3 mo to 13 yr (<i>n</i> = 116)	2.01	1.14	0.0028	3 mo to 13 yr (<i>n</i> = 167)	1.54	1.74	0.4300
>13 yr (<i>n</i> = 94)	7.89	7.40	0.7545	>13 yr (<i>n</i> = 99)	7.93	12.96	0.0158
Overall (<i>n</i> = 236)	4.11	3.51	0.2270	Overall (<i>n</i> = 337)	3.04	4.62	0.0001

^a These data demonstrate the comparison of mean squared prediction errors between previous models (A, the models of Mellits and Cheek; B, the 0.7-0.6 × body weight models) and the current proposed model. For the comparison with the Mellits and Cheek models, only common data points were used; for the comparison with the 0.7–0.6 model, all data available to generate the current proposed model were used.

^b Likelihood ratio *P* value versus current model.

Discussion

The formal calculation of total body water has become an infrequently performed clinical practice. Nevertheless, an understanding of the various body compartments is critical to fluid and electrolyte therapy in children, a mainstay of pediatric care (1). Rational treatment of dehydration, a common cause of pediatric morbidity, is dependent on accurate estimates of TBW and its components (22,23).

TBW estimates have also become a necessary component of the management of children on dialysis (2). The K/DOQI projects have established clear guidelines, based largely on expert opinion, for minimally adequate dialysis delivery to children. These guidelines were based on small case reports in children and extrapolation from adult studies. To calculate a Kt/V in children on PD, TBW must be estimated for use as the V component. The K/DOQI PD adequacy guidelines, lacking other options, recommended the equations of Mellits and Cheek to estimate TBW in children.

The present study developed a series of formulas using modern computer curve-fitting analyses. There are essentially three curves, with a correction for gender in the curves that were generated for the two older groups of children, presumably pre and postpubertal. The need for a gender correction in the older group has been well documented (1), but a correction for gender in the children from 3 mo to 13 yr has not been shown previously. The curves generated for the infants did a better job of predicting TBW than the Mellits and Cheek formulas. That this subset did not need a gender correction may be due to the fact that 45% of the data points in this subgroup did not have a report of gender in the original article, or there may be no physiologic reason at this point in development for the TBW compartment to differ by gender. The model for this age is of particular importance, because the children in this age range who require dialysis are virtually all on a form of PD.

The Mellits and Cheek formulas are in fact four equations that, like those derived in this report, reflect the affect of gender on TBW. They also reflect the curvilinear distribution of TBW against height. Two lines were drawn to approximate the data, with breakpoints where the linear slope of the TBW in its relation to height changed (*i.e.*, where the two lines intersected). A multivariate analysis using both height and weight was performed

after the breakpoints had been established (9). Unfortunately, this breakpoint differs for boys and girls, and the slopes also differ, leading to the following equations:

$$\text{Boys, ht} < 132.7 = -1.927 + (0.465 \times \text{wt}) + (0.045 \times \text{ht})$$

$$\text{Boys, ht} > 132.7 = -21.993 + (0.406 \times \text{wt}) + (0.209 \times \text{ht})$$

$$\text{Girls, ht} < 110.8 = 0.076 + (0.507 \times \text{wt}) + (0.013 \times \text{ht})$$

$$\text{Girls, ht} > 110.8 = -10.313 + (0.252 \times \text{wt}) + (0.154 \times \text{ht})$$

The equations derived in this report are also reflective of the curvilinear relation between height, weight, and TBW, and they also account for gender but are able to do so in essentially three equations (the correction for gender being built in) that are distinguished only by the age of the child. As noted, the model for the infants is a better predictor of measured TBW. The other two equations perform no better than those of Mellits and Cheek, but they are easily solved with modern calculators and may be simpler to use.

It is clear from the analysis that the common estimate of TBW as 60% of body weight is probably inaccurate when applied to individual children. However, with either the formulas reported here or the Mellits and Cheek formulas, the ability to factor in adiposity and its effect on TBW is also lacking. Nevertheless, the formulas presented here are significantly better at predicting TBW than 0.6 × body weight.

Importantly, these new equations demonstrate the strong correlation of TBW with the anthropometric parameter (Ht × Wt). The recent update of the K/DOQI dialysis adequacy guidelines reviews the various formulas for estimating body surface area (BSA) (24). All the equations cited contain some variation on a (Ht × Wt) parameter. Often the individual measure is raised to a separate power. A common equation for the estimation of BSA is $([\text{Ht} \times \text{Wt}]/3600)^{0.5}$. Clearly, the use of the (Ht × Wt) parameter will allow for mathematical relationships between TBW and surface area to be explored. This will likely have an effect on dialysis therapies, and it may affect pharmacologic studies in children as well.

Retrospective data collections and reanalyses such as this report have certain intrinsic weaknesses, the most critical being the patient groups/demographics. For example gender information is unavailable in 45% of the infants, and there are far fewer infants >4 kg than there are infants <4 kg. It is also possible that

laboratory analyses of the samples from the newer patient sets are more precise than those from patients studied 50 yr ago, even when the same methods were used. The science associated with the measurement of TBW has also matured, and some of the earlier articles did not, for example, report adjustments for blood water. Nevertheless, it is not likely that any of these issues would lead to clinically significant changes in the proposed models.

Finally, it should be noted that the measurements of TBW analyzed by Mellits and Cheek, as well as those added for this report, were all performed on healthy infants and children. Whether or not the resulting models are directly applicable to children on dialysis whose renal failure may have resulted in significant alterations in TBW is unknown. This issue was recognized by the DOQI workgroups (2), and it is an issue that requires further study if PD adequacy (on the basis of correlation between dialysis dose and patient outcome) in children is to be defined.

Appendix

Percentile Estimation

From standard linear regression theory, if the normality (gaussian) assumption is valid, then the p -th percentile estimate of TBW as a function of patient characteristics is given by:

$$\ln TBW_p = \ln TBW_R + z_p \times \sigma_R$$

with back transformation to the original scale given by

$$TBW_p = TBW_R \times e^{z_p \times \sigma_R}$$

Here, $\ln TBW_R$ is the predicted natural logarithm of TBW, given the clinical variables in the regression model; z_p is the p -th percentile of the standard normal distribution; and σ_R is the square root of the residual error variance from the fitted regression model.

Common z_p values that may be used depending on the required percentile to be estimated are: for the 2.5th percentile (and the 95th percentile), -1.96 ($+1.96$); for the 5th (95th) percentile, -1.645 ($+1.645$); for the 10th (90th) percentile, -1.282 ($+1.282$); and for the 25th (75th) percentile -0.674 ($+0.674$). The z_p value for the 50th percentile is zero.

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