Kidney International, Vol. 68 (2005), pp. 2317–2322

Total body water volume for white children and adolescents and anthropometric prediction equations: The Fels Longitudinal Study

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Background. There are few studies of total body water (TBW) volume in children. Such studies are needed, as are new prediction equations for the clinical management of children with renal insufficiency and those receiving dialysis.

Methods. Mixed longitudinal data were from 124 white boys and 116 white girls 8 to 20 years of age. TBW volume was measured by deuterium nuclear magnetic resonance spectroscopy, and random effects models were used to determine patterns of change over time. Sex-specific TBW prediction equations were developed using regression analysis.

Results. Boys had significantly greater ($P < 0.05$) mean TBW volumes than girls at all but 3 ages. TBW was significantly ($P < 0.05$) associated with age and maturation in the boys and the girls. In boys, mean TBW/WT varied from 0.55 to 0.59, while in the girls the mean declined from 0.53 to 0.49 by 16 years of age. Boys had significantly larger means for TBW/WT than girls, who had a significant, slight negative trend with age. The prediction equations were TBW = −25.87 + 0.23 (stature) + 0.37 (weight) for boys and TBW = −14.77 + 0.18 (stature) + 0.25 (weight) for girls.

Conclusion. Means are provided for TBW in white children from 8 to 20 years of age, whose average fatness affected the percentage of TBW in body weight. These updated TBW prediction equations perform better than those available from the past.

Knowledge of total body water (TBW) volume is needed for children affected by burns, dehydration and, more so, for the management of children with renal insufficiency and those receiving dialysis [1–3]. However, measurement of TBW volume in children has not received much research or clinical attention because of concern with quantifying fat in order to treat the current pediatric obesity epidemic [4]. Estimated biannual means for TBW are available for non-Hispanic white, non-Hispanic black, and Mexican-American children from 12 to 20 years of age, but these have limited validity, in part because they were predicted from the bioelectrical impedance data in the third National Health and Nutrition Examination Survey (NHANES III) [5]. Reported age trends in TBW volume in children are from cross-sectional data [6].

The few published studies reporting deuterium measures of TBW volume in children are now several decades old [2, 7]. Measuring TBW volume in children via deuterium in saliva or urine is not difficult, but to meet the clinical need for pediatric dialysis patients, the TBW prediction equations of Mellits and Cheek from the 1960s are recommended [8]. These equations have been improved by the work of Morgenstern et al [2], but the study sample still represents the parents and grandparents of present U.S. children. The proper estimation and clinical interpretation of TBW volume necessitates, at a minimum, the availability of deuterium-measured data from current healthy children [2, 3, 9]. In addition, there is a clear need for new anthropometric TBW prediction equations applicable to children undergoing dialysis rather than reliance on equations from 40 years in the past or some assumed percentage of body weight [2]. At birth, approximately 70% to 75% of body weight is water, which is reported to decrease to an adult value of about 60% by 1 to 3 years of age [10–12].

This paper presents distribution statistics for TBW volume measured with deuterium in healthy white children, along with ratios of TBW to body weight, relationships with age and maturation, and the development of new TBW prediction equations. This study uses a set of mixed longitudinal data collected on a regular schedule over a recent 8-year period. The availability of TBW volume

Key words: total body water, children, fat-free mass, prediction equations.

Received for publication April 7, 2005
and in revised form June 14, 2005
Accepted for publication June 21, 2005

data from a current sample of children is a useful comparison for clinical interpretations. The effect of fatness on TBW volume [13, 14] is considered also due to the increased prevalence of obesity among U.S. children [4].

METHODS

The present study sample consisted of 124 white boys and 116 white girls, 8 to 20 years of age who were participants in the Fels Longitudinal Study [15]. The Fels Longitudinal Study is an ongoing study of the growth, development, and body composition of a sample of persons living predominantly in Southwestern Ohio. These healthy children were observed at regularly scheduled annual visits from 1989 through 1996. In this mixed longitudinal data set, there were 1 to 4 visits per child, for a total of 494 visits for the boys and 444 visits for the girls. The Institutional Review Board of Wright State University approved all procedures.

Stature (S), weight (WT), and TBW were measured according to standardized procedures [16, 17]. Each child provided a baseline saliva sample to determine the natural abundance of deuterium and then received 15 g of deuterium oxide (D_2O, 99.8%) in 150 cm^3 of water, and a second saliva sample was taken at least 2 hours after the deuterium dose. The deuterium concentration in the specimen samples was measured by nuclear magnetic resonance (NMR) spectroscopy and corrected for natural abundance and isotope exchange [17]. Stature and weight were used to calculate BMI (WT/S^2, kg/m^2). These procedures have been reported in detail previously [17, 18].

Statistical analysis

The present set of mixed longitudinal data was first arranged into a cross-sectional format of annual age groups from 8 to 20 years. A child's data were randomly represented only once within each annual age group, but it could be represented in adjacent age groups. Descriptive statistics, including means and standard deviations, were computed for TBW, TBW/WT, and BMI and BMI percentiles (BMI%), which are based on the current Centers for Disease Control growth charts [19].

The mixed longitudinal data set was used to test for the relationships with age and maturation, using random effect models to determine the longitudinal patterns of change for boys and girls separately. This statistical model analyzes the complete set of serial and cross-sectional data, accommodates missing values and measurements taken at varying time intervals, and allows for the inclusion of covariates [20].

TBW prediction equations

Data in the cross-sectional format of annual age groups from 8 to 20 years became the validation group for the development of the TBW prediction equations. A cross-validation group was created by randomly selecting a single visit for each available child from the remaining mixed longitudinal data set. The number of children in the cross-validation group (95 boys and 90 girls) was less than in the validation group because those children with only a single visit were in the validation group. Children in the cross-validation group were also represented in the validation group but at different ages. Regression analysis was performed using the validation group to predict TBW from weight, stature, and age. The regression model with the lowest root mean square error (RMSE) was tentatively selected as the model for predicting TBW for a group. The accuracy of the selected equation models from the validation group was confirmed by applying them to the cross-validation group and comparing the RMSE with the corresponding pure error [21]. In addition, the equations were cross-validated by the Prediction of Sum of Squares (PRESS) procedure [21, 22]. Cross-validation using the PRESS procedure is similar to applying the equation to an independent sample. The PRESS procedure involves (*1*) fitting a regression equation with one observation excluded, (*2*) obtaining the predicted value of the excluded observation, (*3*) calculating the residual for that predicted value (observed–predicted), (*4*) repeating *1* to *3* for all observations, (*5*) taking the sum of squares of all residuals, and (*6*) deriving the PRESS statistic by taking the square root of the sum of squares of the residuals divided by the total number of observations. The closer the RMSE and PRESS statistic values, the better the cross-validation (i.e., cross-validated equations have the same predictive power in independent samples as in the samples from which the equations were developed).

RESULTS

Means and standard deviations are presented by 1-year age groups in Table 1 for boys and girls from 8 to 20 years of age. Mean TBW volumes in boys are 16 L at 8 years of age, double this amount by age 14 years, and 40+ L by 16 years of age. In girls, mean volumes are about 15 L at age 8 years and increase up to about 29 L by 17 years of age. Within each age group, the boys had significantly larger mean TBW volumes ($P < 0.05$) than the girls except from 10 to 12 years of age. Also included in Table 1 are means for BMI and BMI% as indicators of fatness. Differences in mean BMI values between boys and girls were scattered between 8 and 20 years of age, and none were statistically significant. In the boys, the mean BMI% ranged between the 44th and 50th percentiles, and for the girls the mean ranged between 49th and 55th percentiles, indicating that the overall level of fatness in these children was about average compared with current national reference data [19].

Between 8 and 20 years of age, the mean TBW volumes in Table 1 increased by 26 L in the boys and by 14 L in the

Table 1. Means and standard deviations for TBW volume and TBW/WT at annual age groups with only one observation per child in each age group

Age	*N*	TBW	SD	TBW/WT	SD	BMI	BMI%[b]
Boys							
8	27	16.2[a]	2.0	0.58[a]	0.04	15.9	44.34
9	35	18.5[a]	2.4	0.57[a]	0.08	17.0	47.71
10	32	19.5	2.8	0.55[a]	0.06	17.4	47.68
11	49	21.5	3.2	0.56[a]	0.07	17.7	44.39
12	43	24.2	5.4	0.55[a]	0.05	18.6	44.93
13	40	29.2[a]	6.6	0.58[a]	0.07	19.2	45.35
14	51	32.6[a]	6.8	0.57[a]	0.07	20.3	47.90
15	50	36.7[a]	7.0	0.58[a]	0.06	21.0	46.80
16	41	40.6[a]	7.7	0.61[a]	0.08	21.1	44.26
17	46	40.7[a]	6.8	0.58[a]	0.06	22.0	45.17
18	34	41.3[a]	6.5	0.59[a]	0.07	22.2	41.87
19	20	43.1[a]	8.5	0.56[a]	0.07	24.0	49.99
20	26	42.0[a]	5.0	0.59[a]	0.07	22.2	
Girls							
8	28	14.8	1.9	0.53	0.05	16.5	51.32
9	35	16.8	3.4	0.53	0.06	16.9	49.03
10	43	19.7	3.5	0.53	0.06	17.7	52.79
11	40	21.2	4.2	0.52	0.06	18.3	49.43
12	35	24.9	4.3	0.53	0.05	19.1	53.43
13	41	25.8	3.9	0.52	0.07	19.9	53.02
14	45	27.5	3.7	0.51	0.05	20.7	55.25
15	36	27.6	3.8	0.50	0.04	20.4	50.65
16	42	28.4	4.1	0.49	0.05	21.5	51.43
17	34	29.0	3.5	0.49	0.04	21.9	54.24
18	25	29.1	4.6	0.49	0.05	21.7	51.36
19	9	29.4	3.2	0.49	0.06	22.8	53.65
20	31	29.0	3.4	0.49	0.05	21.8	

[a] Significant difference between boys and girls at the same age, *P* value < 0.05.
[b] CDC/growth charts BMI percentiles.

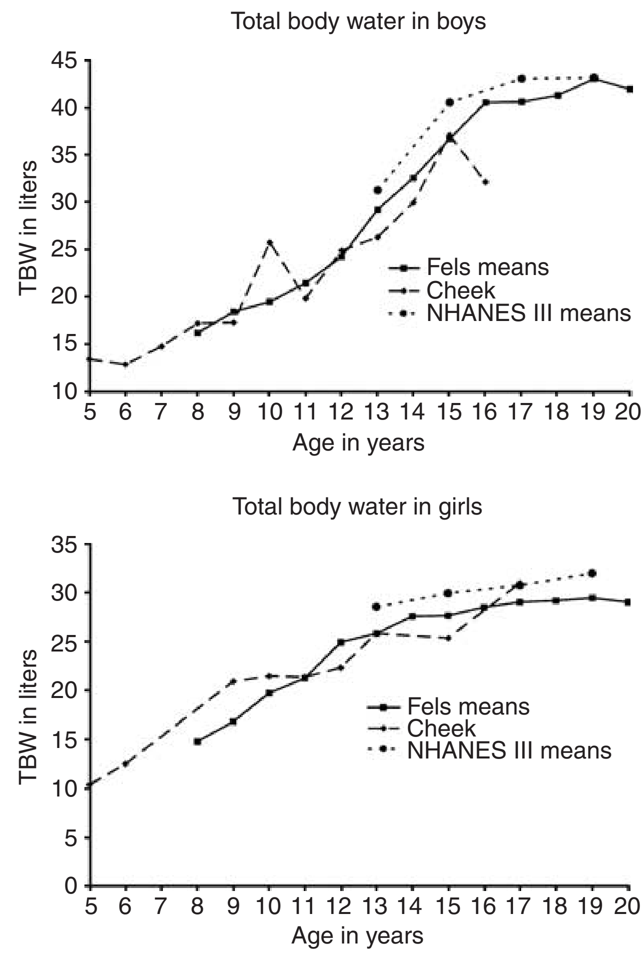

Fig. 1. Means for TBW at an age for white boys and girls from 8 to 20 years of age, with corresponding data from Cheek and from NHANES III.

girls. A random effects model was applied to the mixed longitudinal TBW data for these boys and girls to test for significance of the age-related changes. TBW volume was significantly ($P < 0.05$) associated with age, age squared (age^2), and age cubed (age^3) in the boys, and with age and age^2 in the girls. These age associations reflect the increase in TBW volume during growth and its greater increase in boys than girls after 12 years of age.

TBW volume was also significantly associated with maturational status using relative skeletal age of the hand-wrist (skeletal age-chronologic age) determined by the Fels method [23]. Relative skeletal age was divided into tertiles with the most mature children whose skeletal age was older than their chronologic age in group 1 and the least mature children whose skeletal age was younger than their chronologic age in group 3. The most mature boys had a mean TBW approximately 6 L larger ($P <$ 0.05) than the less mature boys. The most mature girls had a mean TBW approximately 1 L larger ($P < 0.05$) than the girls of average maturity, and both these groups of girls had means for TBW almost 3 to 4 L larger than the least mature girls.

Plots of the mean TBW volumes of these Fels children (Fig. 1) were similar to those reported by Cheek almost 40 or more years ago [24]. The TBW data from Cheek are similar to the means of the Fels boys at most ages, except for 10 and 16 years of age. In the girls, the TBW data from Cheek are larger than the means of the Fels girls before age 11 years and slightly below that of the Fels girls afterwards, except at 16 years of age. At the same time, the means for these Fels and Cheek children after 12 years of age are less than the estimated TBW means for the non-Hispanic white children in NHANES III [5].

In boys, the means for TBW/WT vary from 0.55 to 0.59 between 8 and 20 years of age (Table 1). In the girls, the means for this ratio decline from 0.53 at age 8 years to 0.49 by 16 years of age. The boys had significantly larger mean ratios than the girls at every age group. When a random effects model was applied to test for age-related changes using the mixed longitudinal sample, none were found in the boys, but there was a significant, slight negative trend with age in the girls.

While the mean TBW volumes from these Fels children and from the children Cheek reported [24] are similar at comparable ages, this is not true for the means for

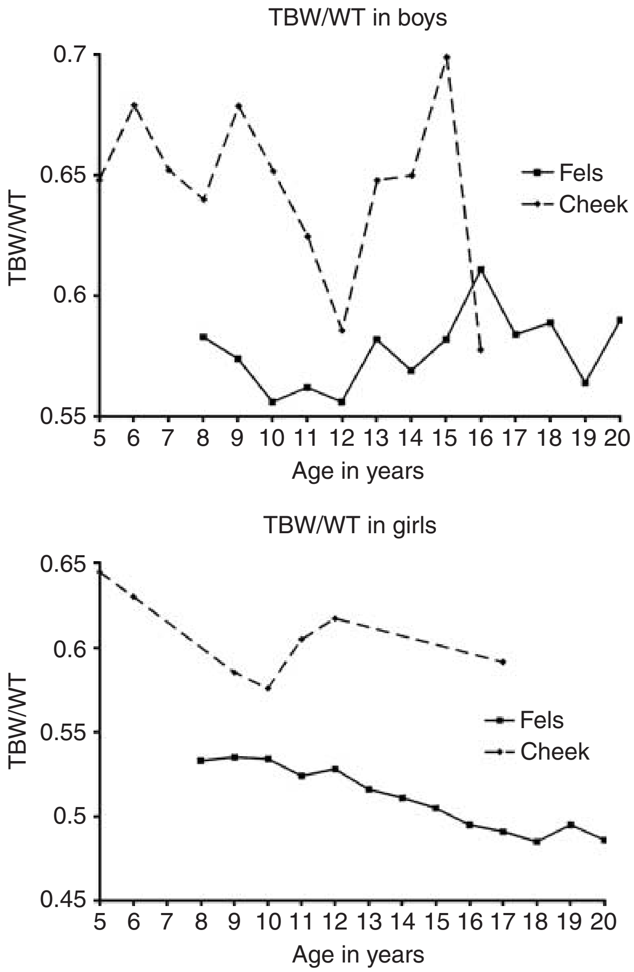

Fig. 2. Means for TBW/WT at an age for Fels boys and girls, with corresponding data from Cheek.

TBW/WT in these 2 data sets. As can be seen in Figure 2, the mean ratios are much smaller in these Fels children than in the children studied by Cheek [24], reflecting the comparatively high level of adiposity in these Fels children.

TBW prediction equations

Prediction equations for TBW are presented in Table 2. Stature and weight are the best predictors of TBW, with R^2 values of 0.92 in boys and 0.90 in girls. The RMSE is 3.53 L in the boys and 2.00 L in the girls. In developing these equations, age and age^2 were not significant variables; however, age^3 was significant in the boys, but this did not improve the R^2 and decreased the RMSE by only 0.1 L, which is less than the analytical measurement error for TBW. The final TBW prediction equations are as follows: boys, TBW = −25.87 + 0.23 (stature) + 0.37 (weight); girls, TBW = −14.77 + 0.18 (stature) + 0.25 (weight).

Table 2. Regression coefficients and standard errors for TBW prediction equations in boys and girls

Predictor variables	Regression coefficients	SE	R^2	RMSE
Boys ($N = 124$)				
Intercept	−25.87	3.95	0.92	3.53
Stature	0.23	0.03		
Weight	0.37	0.03		
Girls ($N = 116$)				
Intercept	−14.77	2.99	0.90	2.00
Stature	0.18	0.03		
Weight	0.25	0.03		

Table 3. Cross-validation results of the TBW prediction equations and comparison with published equations

Group	RMSE	PRESS	PE	PE [a]	PE [b]
Boys validation ($N = 124$)	3.53	3.64		8.75	4.62
Boys cross-validation ($N = 95$)			3.60	8.15	4.73
Girls validation ($N = 116$)	2.00	2.06		5.76	2.33
Girls cross-validation ($N = 90$)			2.43	5.87	2.87

[a] Pure error calculation using equations of Morgenstern et al [2].
[b] Pure error calculation using equations of Mellits et al [25].

The cross-validation results for these equations are presented in Table 3. For both boys and girls, the PRESS statistic is very close to the corresponding RMSE value, and the pure errors (PE) from the application of these equations to the cross-validation groups are also close to the RMSE values. We also applied the equations of Morgenstern et al [2] and Mellits and Cheek [25] to the validation and cross-validation groups of Fels children and calculated the respective pure errors. The pure errors from the equations of Morgenstern et al [2] are about 5 L greater than the RMSE of the new prediction equation for boys and about 3 L greater than that for the girls. The pure errors from the equations of Mellits and Cheek [25] are about a liter greater than the RMSE of the new prediction equations for boys but are close in value to the RMSE for the girls. Thus, the equations of Morgenstern et al [2] perform poorly compared to new predictions, and the equations of Mellits and Cheek [25] less so.

DISCUSSION

TBW volume in these children was measured by in vivo dilution using deuterium labeling and deuterium NMR analysis, as we have reported previously for adults [17, 26]. These TBW volumes across age reflect the overall growth in weight that occurs normally in children at these ages. In the girls, TBW increases linearly until about age 14 years, after which it remains relatively stable. In the boys, TBW also increases linearly until about age 12 years, then the slope increases with the onset of the adolescent growth spurt until about 16 years of age, after which it also levels off. These sex and age differences in growth and TBW volumes reflect the linear and curvilinear age relationships in these data. The association of more TBW in children with greater maturity based on relative skeletal age is similar to that reported for more sexually mature children who are taller, heavier, and have higher BMI values than their less mature peers [27].

The measured available TBW volume data are almost exclusively for white children, with the exception of the limited estimated NHANES III TBW means for non-Hispanic black and Mexican-American children from bioelectrical impedance data [5]. The mean TBW volumes of these Fels children and those of Cheek are similar as seen in Figure 1, but most of the points from Cheek's data [24] represent either a single measurement or the mean of data from only a couple of children. In addition, at 8, 9, and 10 years of age, the TBW volume means of these Fels children are also similar to corresponding means reported by Fomon et al in 1982 [7]. The means for the Fels and Cheek data sets are less than the NHANES III TBW means at comparable ages, due in part to the estimation method used to construct the NHANES III values and the fact that they represent national values.

The much lower ratio of TBW/WT in these Fels children reflects their greater adiposity compared with the children in Cheek's data (Fig. 2). It is noteworthy that one of the goals of the work by Cheek et al in the 1960s was to develop new methods to assess fatness in children because the reported prevalence of childhood obesity was as high as 20% [25]. These average ratios (percentages) from 8 to 20 years of age are much smaller than the accepted 70% to 60% for children [12, 25], especially in girls. The absence of an age trend in the ratio of TBW/Wt in the boys contradicts the positive age association also reported for boys by Heald et al 40 years ago [28]. This fact and the significant negative age trend in the girls reflect the greater level of adiposity in the general pediatric population today.

The value of the ratio of TBW/WT in these Fels children at 18 to 20 years of age is the same as that reported earlier for adults in this and other recent samples, about 55% for men and about 45% for women [5, 17]. The mean adult percentage of body water in weight has historically had a range of 55% to 65% [29], but more recent data indicate that this mean is about 58% in men and 48% women at 20 years of age, and declines to respective means of about 46% and 43% by 60 years of age [17]. Thus, the accepted ratio of TBW/WT for these children (and adults) is much lower than previously published, and these revised values should be considered for clinical use rather than those reported 30 or more years ago.

TBW prediction equations for children

In these boys and girls, TBW was predicted from stature and weight, which accounts for about 90% of the shared variance in TBW as noted earlier by Cheek et al [3, 24]. Age was not a significant variable that was due to its covariant relationship with stature, weight, and TBW during childhood [24]. These new equations have RMSE values of about 2 L in the girls and about 3.5 L in the boys, which were slightly larger than the RMSE values reported by Mellits and Cheek [25]. The equations of Mellits and Cheek [25] have been used clinically and refined by Morgenstern et al [2], but both were developed using a sample of children from almost 40 years ago whose level of adiposity was less than that of current children. This adiposity difference is evident when the equations of Morgenstern et al [2] and Mellits and Cheek [25] are applied to these Fels children and the pure errors calculated. The pure errors for Morgenstern's equations are about 5 L greater than the RMSE of the Fels boys and about 3 L greater than the RMSE of the Fels girls. The pure errors for the Mellits and Cheek equations were closer to the corresponding RMSE values of the Fels boys and girls. If this is the precision of these older equations in healthy contemporary U.S. children, then a similar level of precision in clinical cases can be expected, and the problem of sample specificity should be kept in mind also. In the cross-validation of the present equations, the PRESS statistics were close to the RMSE values, indicating that these equations should perform well in other independent samples (Table 3).

The clinical importance of prediction equations is their application. A child's predicted value will differ from the true value as a function of the difference between the measured values and the corresponding sex-specific means in Table 1. When these equations are applied to other groups or individuals, their precision will depend on how different that group or individual is from the children used to develop these equations (i.e., the greater the differences, the poorer the predictive accuracy). Good predictive accuracy, however, can only be attained using equations developed from children with renal failure.

CONCLUSION

These findings provide reference values for TBW volume measured via deuterium in a recent group of white children from 8 to 20 years of age. The degree of fatness among these Fels children is about average compared with U.S. children today, and this affects the percentage of TBW in their weight, which is much lower than that reported for children in the past. In addition, updated TBW prediction equations are provided that perform well. These data and results are from healthy children, and their application and inference to children with clinical conditions affecting their TBW should be made with caution.

ACKNOWLEDGMENTS

This work was supported by grants HD27063, DK071485, HD38356, and HD12252 from the National Institutes of Health, Bethesda, Maryland.

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