Body Composition in Human Infants at Birth and Postnatally

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ABSTRACT The predictive values of anthropometric measurements, race, gender, gestational and postnatal ages, and season at birth and at study for the total body dual energy X-ray absorptiometry (DXA)-derived lean mass (LM), fat mass (FM) and fat mass as a percentage of body weight (%FM) were determined in 214 singleton appropriate birth weight for gestational age infants [101 Caucasian (60 boys, 41 girls) and 113 African American (55 boys, 58 girls)]. Gestational ages were 27 to 42 wk and the infants were studied between birth and 391 d, weighing between 851 and 13446 g. In addition, predictive value of body weight, LM and FM for DXA bone measurements was also determined. Scan acquisition used Hologic QDR 1000/W densitometer and infant platform and scans without significant movement artifacts were analyzed using software 5.64p. Body weight, length, gender and postnatal age were significant predictors of LM (adjusted $R^2 \geq 0.94$) and FM (adjusted $R^2 \geq 0.85$). Physiologic variables had little predictive value for %FM except in the newborns (adjusted $R^2 \leq 0.69$). Body weight was the dominant predictor of LM and FM, although length had similar predictive value for LM with increasing postnatal age. Female infants had less LM and more FM throughout infancy ($P < 0.01$). LM or FM offered no advantage over body weight in the prediction of bone mass measurements. DXA is a useful means with which to determine body composition, and our data are important in the design and assessment of nutritional intervention studies. J. Nutr. 130: 2188–2194, 2000.

KEY WORDS: race gender bone fat lean tissue humans

Dual energy X-ray absorptiometry (DXA) is used increasingly as the method of choice to measure various components of body composition (BC) during infancy (Koo 2000). We reported previously that body mass is the dominant predictor of bone mineral status in newborns (Koo et al. 1996) and older infants (Koo et al. 1998). This is supported by other recent reports of bone mass measurements in infants (Lapillonne et al. 1997, Rigo et al. 1998). Our findings is also consistent with the finding in adults of a positive relation of body habitus (Aloia et al. 1999, Chumlea and Guo 1999, Ravn et al. 1999) with bone mineral status, although lean body mass (Courteix et al. 1999, Ferretti et al. 1998, Valdimarsson et al. 1999) and fat mass (Courteix et al. 1999, Ferretti et al. 1998) are thought to be stronger determinants of bone mass. In contrast, little is known about the physiologic predictor of soft tissue composition during infancy, and there are no data to determine the predictive ability of soft tissue composition on bone mineral status in infants. The aim of this study was to extend our previous observation on bone mineral status (Koo et al. 1996 and 1998) in newborn infants and throughout infancy to document the differences in soft tissue composition during this period. We aimed to determine the predictive value of anthropometric measurements and other physiologic variables on soft tissue body composition measurements. In addition, the predictive value of soft tissue composition on bone mineral status was also assessed.

SUBJECTS AND METHODS

Subjects. The total study population included 214 singleton infants with birth weights from 1002 to 3990 g. The subjects’ birth weights were appropriate for gestational age (Brenner et al. 1976). Gestational ages of the subjects as determined by maternal menstrual dating and/or ultrasound were from 27 to 42 wk and within 2 wk of gestational age assessment by standard examination (Ballard et al. 1991). Eighty-five subjects were preterm with gestational age < 38 wk of these, 53 subjects had low birth weight (< 2500 g). There were 101 Caucasian (60 boys, 41 girls) and 113 African American infants (55 boys, 58 girls). For infants beyond the immediate newborn period, the type of milk and whether the infant was receiving solids were recorded. This study was approved by the Institutional Review Board for human subjects at the University of Tennessee-Memphis, and written informed consent was obtained from each subject’s parent.

Anthropometric measurements. The nude weight and length of the infant were measured at each study. The weights of the cotton blanket that swaddled the infant and the diaper, if used, were also determined. An additional blanket or a large cotton sheet was used in 22 infants to better swaddle the larger infant. A diaper was used in all infants beyond the newborn period. The study weight is the total weight including the nude weight and the weight of blanket/s and diaper. The weight in grams was determined with a digital electronic scale (Air Shields, Vickers, OH). The scales were regularly main-

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2188
tained by the hospital Biomedical Instrumentation personnel and calibrated with known standard weights. Recumbent length was the average of two consecutive measurements within 0.4 cm and was determined using a standard length board (Ellard Instrumentation, Seattle, WA).

**DXA measurements.** All infants were clinically well at the time of study, and each infant was studied on one occasion. Scan acquisition of total body (TB) was performed with a single beam whole-body scanner (Hologic QDR 1000/W densitometer, Hologic, Waltham, MA), with the use of an infant platform. With our densitometer, the typical maximum entry radiation exposure during an infant whole-body scan was 3 μSv (1 μSv = 0.1 mrem). The radiation scatter at 90 cm from the scanner was <0.3 μSv from 10 min of measurement (Koo et al. 1995a).

All scans for this study were performed with the swaddled subject placed on top of the infant platform with a cotton blanket interposed between the subject and the platform (Koo et al. 1996 and 1998). A heat lamp was used as needed to maintain a satisfactory environmental temperature. All scans were performed without sedation or additional restraint but a pacifier with nonmetallic parts was used as needed. Occasionally, the scanning procedure was interrupted if movement artifact was noted, and a repeat scan was performed when the infant had been pacified.

Scans were analyzed using the software (Version 5.64p) developed in conjunction with the manufacturer. In addition to the analysis of the total body, analyses of different regions were also performed using the same software if the position of the infant allowed adequate delineation of separate regions. Regional analyses typically involved the head and each of the four extremities. The residual region was regarded as the trunk for a total of six regions. Each scan was reviewed by one of two investigators (JW or WK) and was judged technically satisfactory if the external calibration step phantom and the skeletal outline of the subject lay within the scan region and without significant movement artifact (Koo et al. 1995b).

Quality control scans were performed daily on a manufacturer-supplied anthropomorphic spine phantom, and the long-term (≥3 y) CV for the determination of bone mineral content (BMC), bone area (Area) and bone mineral density (BMD) using an anthropometric spine phantom are <0.31% for all parameters. The average annual rate of change for each of these measurements was not significantly different from zero. The in vivo replication of TB DXA measurements in 50 infants was significantly correlated [r = 0.99 and P < 0.001 for all variables, i.e., BMC, Area, BMD, lean mass (LM) and fat mass (FM), respectively]. In our laboratory, the standard deviation (σ) of difference (Bland and Altman 1986) between paired DXA measurements for TB BMC was 3.8% at a mean of 93 g; TB Area was 2.5% difference (Bland and Altman 1986) between paired DXA measurements. The independent variables are known to have the potential to affect growth and body composition; these included race, gender, gestational age, postnatal age at study, nude weight, length and season of birth. The season variable was determined by coding the month of birth at three monthly intervals beginning at March as spring, and was transformed into dummy variables using spring as the reference season. In addition, each of the three variables, LM, FM and nude weight, was entered alone as an independent variable to determine the value of each of these three independent variables in the prediction of BMC, Area and BMD.

For each of the dependent variables, a final model predictive equation was generated, containing only significant independent variables. This represents a hierarchical modeling process that first determines the most powerful individual predictor of DXA measurements and then determines whether any other set(s) of independent variables either augmented or diminished the model's explanatory capability of the single best predictor. Percentiles were also calculated for LM, FM and %FM using Altman's method (Altman 1993) and the best-fit curves were plotted on the basis of the actual data.

For the postnatal cohort, study weight and nude weight were significantly correlated (r² = 0.99) and only nude weight was entered as an independent weight variable. Data analysis used the same procedures as described above. However, three additional variables were entered as independent variables. These included birth weight, the season at the time of study (derived from the study month and entered into regression model using the same technique described above) and, for infants beyond the immediate newborn period, the type of milk intake and use of solid food on the day of study. Milk intake was transformed into dummy variables before analyses using human milk as the reference milk.

All statistical tests were performed with SPSS 9.0 (SPSS, Chicago, IL) for Windows at an adopted significance level of 0.05. Values are means ± SD.

**RESULTS**

DXA scans were performed between birth and 391 d. The nude weight of the infants at study was between 851 and 13,446 g. The "at birth" cohort included 150 subjects (85 preterm infants; 82 boys; 78 Caucasian and 72 African American) and DXA scans were performed at 2.1 (±1.6) d after birth. Ten preterm infants were studied between 6 and 7.7 d after they had recovered from transient respiratory illnesses. The "postnatal" cohort included 129 infants born at term with 70 boys and 59 girls, 62 Caucasian and 67 African American. Of infants born at term, 64 were studied beyond the newborn period.

At birth cohort. Nude weight consistently proved to be the single best predictor of LM, FM and %FM with an adjusted R² of 0.978, 0.837 and 0.632, respectively. Gender and length were the only additional predictors that could be forced into a predictive equation for these dependent variables on the basis of statistical significance, although the additional contributions to the prediction of LM, FM and %FM were 0.5, 3.2 and 6.2%, respectively. Female infants had significantly lower LM, but higher FM and %FM (P < 0.01). The final regression equations (P < 0.001 for all models) for the prediction of TB LM, FM and %FM including all significant predictors are as follows:

\[
\text{DXA}_{\text{LM}} (g) = -714 + 0.626 \times \text{nude weight (g)} + 29.94 \times \text{length (cm)} - 39.7 \times \text{gender}
\]

Adjusted \(R^2 = 0.983, \text{SEE 70 g} \)

\[
\text{DXA}_{\text{FM}} (g) = 644 + 0.347 \times \text{nude weight (g)} - 25.9 \times \text{length (cm)} + 33.3 \times \text{gender}
\]

Adjusted \(R^2 = 0.869, \text{SEE 70 g} \)

\[
\text{DXA}_{\text{FM}} (%) = 22.0 + 6.525 \times 0.03 \times \text{nude weight (g)} - 0.581 \times \text{length (cm)} + 1.3 \times \text{gender}
\]

Adjusted \(R^2 = 0.694, \text{SEE 2.1%} \)

Where gender = 0 for male infants and 1 for female infants and SEE is the standard error of estimate.

Percentiles for DXA measurements of TB LM, FM and %FM in newborn infants based on nude weights are shown in
Figure 1 A–C. It should be noted that percentiles are descriptive, not predictive, and draw attention to the increasing variability of the dependent variables as nude weights increased. The standard error of estimate for a predictive equation is a function of the dependent variable and represents the strength of the correlation between independent and dependent variables. The adequacy of the predictive equation across the body weight range of our newborn cohort was determined by computing predictive equations based on two nude weight ranges divided approximately at the midpoint of the total weight range. The resultant \( r \) and SEE values of the prediction equations generated from the total cohort and from the two subpopulations are shown in Table 1. With increasing body weight from 1.5 to 3.5 kg, the average proportion of TB LM decreased from 90.8 to 81.8% and the average proportion of TB FM increased from 7.5 to 16.2%.

Regional distribution of soft tissue mass (upper and lower extremities, and trunk) was also well predicted by nude weight, with adjusted \( R^2 \) from 0.87 to 0.93 for LM and from 0.78 to 0.83 for FM. With increasing body weight from 1.5 to 3.5 kg (an increase of 133%), there was an average increase in LM at the upper and lower extremities, and the trunk of 121, 122 and 212%, respectively, although the trunk:extremities ratio for LM remained stable at \(-1.85\). The average increase in FM at these regions was 540, 528 and 345%, respectively, whereas the trunk:extremities ratio for FM decreased from 1.03 to 0.79.

**Postnatal cohort.** For term infants during infancy, length was the most dominant predictor of LM, with an adjusted \( R^2 \) of 0.915. However, nude weight became the dominant predictor for LM with an adjusted \( R^2 \) of 0.958 if length was excluded from the regression. Nude weight was the dominant predictor of FM with an adjusted \( R^2 \) of 0.738. There was no single predictor of %FM that resulted in an adjusted \( R^2 \) of >0.20. Gender and postnatal (study) age were the additional predictors that could be forced into a predictive equation for these dependent variables on the basis of statistical significance, although the additional contribution to the prediction of LM, FM and %FM was <3, <12 and 6.2%, respectively. Female infants had significantly lower LM but higher FM and %FM (\( P < 0.001 \)). Incorporating any other independent variable including type of milk intake (10 infants were fed human milk, 9 infants were fed homogenized whole cow’s milk and the others were fed infant formulas) and the use of solids in the diet concurrent with DXA assessment failed to improve prediction. The final regression equations (\( P < 0.001 \) for all models) for the prediction of TB LM, FM and %FM including all significant predictors are as follows:

- \( \text{DXA LM (g)} = -1319 + 0.278 \times \text{nude weight (g)} + 64.59 \times \text{length (cm)} - 307 \times \text{gender} + 2.473 \times \text{age (d)} \)
  - Adjusted \( R^2 = 0.944 \), SEE 338 g
- \( \text{DXA FM (g)} = 908.4 + 0.706 \times \text{nude weight (g)} - 53.0 \times \text{length (cm)} + 358.5 \times \text{gender} - 3.057 \times \text{age (d)} \)
  - Adjusted \( R^2 = 0.856 \), SEE 345 g
- \( \text{DXA FM (%)} = 9.57 + 0.0037 \times \text{nude weight (g)} + 4.56 \times \text{gender} - 0.0538 \times \text{age (d)} \)
  - Adjusted \( R^2 = 0.403 \), SEE 4.7%

where gender = 0 for male infants and 1 for female infants. Percentiles for DXA measurements of LM, FM and %FM in term infants during infancy based on nude weights are shown in Figure 2 A–C. Adequacy of the predictive equation across the body weight range of our postnatal cohort was determined as for the newborn cohort (Table 1). After birth, the proportion of TB LM continued to decrease, whereas the TB FM increased. The TB LM and TB FM averaged 66.3 and 31.4%, respectively, at the body weight of 10.5 kg.

Regional distribution of soft tissue mass (upper and lower
extremities, and trunk) was also well predicted by study nude weight, with adjusted $R^2$ from 0.92 to 0.96 for LM and from 0.82 to 0.96 for FM. With increasing body weight from 3.5 to 10.5 kg (an increase of 200%), there was an average increase in LM at the upper and lower extremities and trunk of 113, 194 and 155%, respectively, although the trunk:extremities ratio for LM remained stable at ~1.90. The average increase in FM at these regions was 485, 573 and 365%, respectively, whereas the trunk:extremities ratio for FM decreased from 0.82 to 0.57.

**Body weight vs. soft tissue mass prediction of DXA bone measurements.** When each of the variables (nude weight, LM and FM) was entered independently into the regression model, nude weight consistently provided the best predictive value at birth and throughout infancy for DXA bone measurements compared with LM and FM (Table 2). Details of the DXA bone measurements are reported elsewhere (Koo et al. 1996 and 1998).

**DISCUSSION**

Changes in BC can have numerous functional implications in health and in disease. For example, the amount of lean tissue mass affects positively the ventilatory function, whereas increased proportion of body fat has the opposite effect (Lazarus et al. 1997); low bone mass increases the fracture risk independently of age (Kanis et al. 1994, Koo and Steichen 1998); low body mass index associated with low body fat increases the risk for bone loss (Ravn et al. 1999) and possibly the development of osteoporosis and its complications. In contrast, the very high body mass index associated with high body fat predisposes the individual to the numerous complications of obesity (Dietz 1998). Thus, an increased understanding of the relation between physiologic determinants of BC in infants may lead to a greater understanding of the role of genetic and environmental influence on changes in BC and may be critical to the management of healthy and sick infants, particularly in the design and assessment of the role of nutritional intervention (Shetty 1999).

In infants, body weight can predict various aspects of BC during the newborn period (Koo et al. 1996 and 1998, Lapillonne et al. 1997, Rigo et al. 1998), but no data exist concerning the predictive effect of various physiologic parameters on BC beyond this period. This study demonstrated that body weight contributed heavily to the model’s explanatory power for soft tissue (LM and FM) composition during infancy. Length becomes the dominant predictor of LM with increasing postnatal age, although the predictive value of body weight on soft tissue composition remains significant throughout infancy because length and weight are colinear.

It is well documented that in children (Taylor et al. 1997) and adults (Frisancho 1993), females have more FM and less LM than males. Females are shorter and weigh less than males at birth and throughout infancy (Brenner et al. 1976, Hamill et al. 1979), but little is known about the earliest onset of gender-related difference in FM and LM. Only one report in newborn infants specifically showed greater FM in females compared with males (Rigo et al. 1998). Our data demonstrated that gender has an independent predictive effect on the amount of LM and FM at birth. In addition, the gender difference in FM and LM increased throughout infancy. The increase in FM in females was accompanied by a similar decrease in LM. In contrast, there is no gender-related difference in bone mass measurements throughout infancy (Koo et al. 1996 and 1998). The consistency and persistence of the gender-related difference in soft tissue composition is also reflective of the standardized technique in scan acquisition, including the consistency in the type and amount of covering used for each infant, thus minimizing any interference with DXA soft tissue measurements from variable types and amounts of clothing and covering.

On the basis of differences in adjusted $R^2$ values in the statistical models, our study demonstrated that the independent physiologic variables, i.e., weight, length and gender, appear to be stronger predictors for the amount of LM than for FM. The ability of physiologic variables to predict FM and in particular %FM decreases with increasing postnatal age. This
is presumably related to the increased role of environmental influences such as dietary intake (and physical activity in older children) on fat mass accumulation compared with lean mass (Barlow and Dietz 1998, Grandjean 1999, Shetty 1999). In this study, the type of milk intake and the use of solids on the day of DXA assessment did not contribute to the determination of body composition in infants. However, this study was not designed to determine the influence of dietary intake because no details on the duration or quantity of specific intake were available.

It is important to note that the large range of LM, FM and %FM at any given body weight shown in the figures represents biologic variability expressed as percentile channels rather than predictive value of body weight on these DXA measurements. However, stability of the correlations (r-values) for the prediction of LM whether from body weights of total or subpopulations supports the adequacy of our model based on the total population of subjects in each cohort. Lack of significant differences in the residuals derived from the prediction equations based on subpopulations also supports the contention that the predictive value of nude weight on LM is independent of the range of body weights within each cohort. We presented SEE in standard Z-score form to reflect the role of correlation in determining the SEE because the standard deviation of the dependent variable is unity in the Z-score measure. The observed stability of correlation across body weight ranges means that a difference in SEE between two ranges of body weights was due to the increased variability in dependent measure, not to a change in correlation. Our data support a similar conclusion for FM prediction, although the predictive ability of body weight for FM decreased somewhat in heavier postnatal infants. FM%, a calculated value, is poorly predicted by body weight especially in the postnatal cohort whether the prediction equation was based on the total or subpopulations.

In contrast to the well-defined racial differences in BC of children (Aloia et al. 1999, Chumlea and Guo 1999, Gilsanz et al. 1991) and adults (Aloia et al. 1999, Chumlea and Guo 1999, Ortiz et al. 1992), our study showed that there is no racial effect on soft tissue composition in this age group once body weight and length are taken into account. This is consistent with our previous reports on TB DXA bone measurements (Koo et al. 1996 and 1998), and other reports on skeletal weight, density and percentage of ash (Trotter and Hixon 1974), and distal radial BMC (Namgung et al. 1994) during infancy. Racial difference in BC found in older ages presumably is also related to the increasing importance of environmental influence and possibly the genetic and environmental interaction. Similarly, season did not affect soft tissue composition during infancy.

In the range of body weights studied, changes in TB LM can be represented by linear modeling but the changes in FM were represented by both linear and nonlinear models depending on the body weight range. The pattern of accumulation of TB LM and FM in our birth and postnatal cohorts reflects the rapid growth during the last trimester and after birth, particularly the accumulation of TB FM during the late in utero and postnatal periods. With increasing body weight, there was a greater range of LM and FM, especially of FM, supporting the greater biologic variability and increasingly important role of environmental influences such as differences in dietary intake in larger and older infants.

Our data are comparable to other reports using the same DXA technique for newborn (Lapillonne et al. 1997, Rigo et al. 1998) and older (Mehta et al. 1998) infants. However, strict comparison among studies is difficult because of the different populations studied. Some reports included infants
with birth weights of >4 kg, thus raising the possibility of large-for-gestational-age infants in the study cohort (Lapillonne et al. 1997, Rigo et al. 1998); additional small differences may be related to the use of different models of DXA densitometer (Abrahamsen et al. 1995) and different versions of software (Picaud et al. 1999), even those provided by the same manufacturer. Nevertheless, despite the limitations associated with all in vivo techniques of BC measurement (Koo 2000), there appears to be general agreement in the overall absolute and relative changes in the soft tissue composition among the various reports of BC based on the same DXA technique.

None of the in vivo DXA data are directly comparable with the chemical analysis of cadavers (Widdowson 1975, Ziegler 1976) because the techniques used in deriving the LM and FM are not comparable with the in vivo reports (Koo 2000). Furthermore, BC extrapolated from chemical analysis may not be truly representative of normal infants because most of the subjects reported were below the fiftieth percentile on the growth curve, the causes of death, especially those that may have affected growth and BC, were not available, and there is a lack of cadaver data beyond the newborn period.

Our data show that body weight is also a major predictor of regional DXA soft tissue composition, although its predictive ability is somewhat weaker than that for TB soft tissue. Similar to our findings for DXA bone measurements (Koo et al. 1996 and 1998), there was extensive variation in the amount of LM and FM among different regions (upper and lower extremities, trunk); the changes in these regions during in utero and postnatal growth as indicated by our "at birth" and "postnatal" cohorts, were not directly proportional to the changes in body weight or the soft tissue composition of the whole body. The relative difference in regional BC was also reflected in a proportionately greater increase in FM at the extremities compared with the trunk as body weight increases, whereas the proportion of LM between trunk and extremities remained steady throughout infancy.

Caution is required in the interpretation of DXA BMD, an areal density based on BMC divided by skeletal area (Nelson and Koo 1999, Prentice et al. 1994). The reasons for this caution include the dissimilar rate of increase in BMC and skeletal area during infancy and childhood, and the technical difficulty in obtaining an accurate TB area in a swaddled infant/child. To allow better interpretation of DXA bone mass measurements, attempts have been made to normalize the DXA bone measurements on the basis of the reports in adults that LM is a good predictor of bone mass as BMC (Ferretti et al. 1998, Valdimarsson et al. 1999) or as BMD (Courteix et al. 1999, Valdimarsson et al. 1999) and that FM is a good predictor of BMC (Ferretti et al. 1998) and BMD (Courteix et al. 1999). However, we showed that in healthy infants, LM is an independent predictor of TB BMC throughout infancy and TB Area in newborns, but is consistently weaker than the use of body weight to predict these measurements. Furthermore, LM has minimal predictive value on TB BMD, and FM has minimal predictive value for any DXA bone measurement except BMC in the newborn period. These findings suggest that weight-bearing and impact-loading exercise critical to the increase of LM and bone mass in older subjects (Courteix et al. 1999, Pettersson et al. 1999) are not well developed in younger subjects. Thus the use of LM or FM provides no advantage over body weight in the prediction of skeletal bone mineral status during infancy.

We conclude that in healthy infants, body weight is the dominant predictor of LM and FM, although length has the same or stronger predictive value for LM with increasing postnatal age. Physiologic variables have little predictive value for %FM beyond the newborn period. Gender difference in LM and FM can be demonstrated at birth and increases throughout infancy. The use of LM or FM offers no advantage over body weight in the prediction or normalization of bone mass measurements during infancy. Our data on the precision of DXA measurement and the physiologic factors that influence BC are important to the design and assessment of nutritional intervention studies in infants under various physiologic and pathologic situations.

### TABLE 2

#### Predictive value of study nude weight, lean mass (LM) and fat mass (FM) on dual energy X-ray absorptiometric bone measurements in human infants

<table>
<thead>
<tr>
<th>Variable</th>
<th>At birth</th>
<th>Postnatal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1Adjusted $R^2$</td>
<td>2Adjusted $R^2$</td>
</tr>
<tr>
<td>Bone mineral content</td>
<td>0.950</td>
<td>0.950</td>
</tr>
<tr>
<td>Bone area</td>
<td>0.946</td>
<td>0.940</td>
</tr>
<tr>
<td>Bone mineral density</td>
<td>0.840</td>
<td>0.832</td>
</tr>
</tbody>
</table>

1. Variance accounted for by the complete model including one specific independent variable (study nude weight, LM or FM) entered alone with other independent variables. (For newborn cohort: race, gender, gestational age, season of birth, study age and study length. For postnatal cohort: additional independent variables included birth weight, season at study, and type of milk consumed and intake of solids on the day of study.)

2. Variance accounted for by one specific variable: study nude weight, LM or FM.
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LITERATURE CITED


