Body water content of extremely preterm infants at birth

Gary Hartnoll, Pierre Bétrémieux, Neena Modi

Abstract

**Background**—Preterm birth is often associated with impaired growth. Small for gestational age status confers additional risk.

**Aim**—To determine the body water content of appropriately grown (AGA) and small for gestational age (SGA) preterm infants in order to provide a baseline for longitudinal studies of growth after preterm birth.

**Methods**—All infants born at the Hammersmith and Queen Charlotte’s Hospitals between 25 and 30 weeks gestational age were eligible for entry into the study. Informed parental consent was obtained as soon after delivery as possible, after which the extracellular fluid content was determined by bromide dilution and total body water by H\(_2\)O dilution.

**Results**—Forty two preterm infants were studied. SGA infants had a significantly higher body water content than AGA infants (906 (833–954) and 844 (637–958) ml/kg respectively; median (range); p = 0.019). There were no differences in extracellular and intracellular fluid volumes, nor in the ratio of extracellular to intracellular fluid. Estimates of relative adiposity suggest a body fat content of about 7% in AGA infants, assuming negligible fat content in SGA infants and lean body tissue hydration to be equivalent in the two groups.

**Conclusions**—Novel values for the body water composition of the SGA preterm infant at 25–30 weeks gestation are presented. The data do not support the view that SGA infants have extracellular dehydration, nor is their regulation of body water impaired.

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Keywords: body composition; water compartments; growth restriction; newborn; preterm; dehydration

Preterm birth is often associated with nutritional compromise and impaired growth performance. Recent epidemiological research has also suggested that poor intrauterine growth may set the scene for several diseases of adult life.1 There is therefore a legitimate interest in the composition of the preterm infant, both appropriately grown (AGA) and those small for gestational age (SGA), of whom most will have suffered intrauterine growth restriction. This study was carried out to obtain data on the body water content of preterm infants of less than 30 weeks gestation and to compare the body composition of AGA and SGA infants.

The first report of the composition of the human fetus appeared in 1857 with the work of von Bezold.2 This was followed by a number of cadaver studies,3–5 up to and including that of Widdowson and Spray in 1950.6 It is not known whether the early cadaver studies involved fetuses that were AGA or SGA, and in recent years, with the development of techniques to assess body composition in vivo, few cadaver studies have been carried out. More recent in vivo studies have largely excluded the preterm SGA infant. The only available data on the body composition of such infants is from a study by van der Wagen et al1 in which seven infants with gestations ranging from 32 to 39 weeks were investigated. To our knowledge, there are no published data on the body composition of SGA preterm infants of less than 30 weeks gestation.

**Methods**

Measurements of body water compartments at birth were made as part of a larger study investigating fluid balance in preterm infants. Inborn infants between 25 and 30 weeks gestation admitted to the neonatal units at the Hammersmith and Queen Charlotte’s Hospitals, London, UK were eligible for recruitment. The study was approved by the institutional research ethics committee, and written informed parental consent was obtained. Infants with major congenital abnormalities and obvious derangements of fluid balance such as hydrops were excluded.

SGA infants were defined as those who were below the 9th centile on the Child Growth Foundation charts (Child Growth Foundation 1996/1, 2 Mayfield Avenue, London W4 1PW, UK). Gestational age was determined from maternal dates confirmed by an early ultrasound dating examination.

Total body water (TBW) and extracellular fluid volume (ECFV) were determined as soon as possible after delivery. TBW was measured using H\(_2\)O dilution as previously described.7 Briefly, after taking a baseline sample of blood, the infant was given 1 ml/kg water enriched with H\(_{18}\)O. The exact amount of water administered was determined by weighing the syringe before and after administration of the water on a chemical balance accurate to ± 0.0001 g. The water was administered by nasogastric tube, and the tube was flushed with a further 2 ml sterile water for injection. Two further blood samples were taken as close to three and six hours after H\(_{18}\)O administration as possible, the exact time being noted (blood sampling...
was timed to coincide with clinical sampling whenever possible). The sample was spun immediately, and the serum separated and frozen at −20°C until analysed. Exact times of sampling were noted in order to extrapolate backwards to a concentration at time zero \((C_0)\). Extrapolation to time zero was performed by linear regression on the log of values of 
\(^1\)\(^8\)O concentrations (ppm). The \(^1\)\(^8\)O samples were analysed as previously described, and 'TBW calculated using the method of Schoeller et al..

ECFV was determined using bromide dilution. After a baseline blood sample had been obtained, 1 ml/kg NaBr solution containing 100 mg/ml NaBr was administered intravenously, using vascular access sited for clinical purposes. NaBr equilibrates rapidly if given intravenously. In addition, the half-life is very long, so that once equilibration is reached only a single sample is needed to calculate ECFV. We obtained two samples after baseline, at the same time as the samples for TBW estimation, to confirm that equilibration had taken place. They were then averaged to provide a single measure. After being spun, 10 µl aliquots of serum were pipetted on to 1 cm diameter filter papers. These were dried in air before being sealed in plastic cuvettes for despatch to the Centre for Analytical Research in the Environment, Imperial College at Silwood Park, for analysis by neutron activation. Assay results are expressed as µg bromide/ml serum and this value is used in the following equation:

\[
ECFV = \frac{\text{Amount of Br administered}}{\text{serum [Br]}} \times 0.90 \times 0.95 \times 0.934
\]

The amount of bromide administered was calculated as follows:

\[
\text{Bromide injected} = \text{Weight of NaBr solution given (g)} \times \text{[NaBr sol]} \times \text{conversion factor}
\]

The amount of NaBr solution given was measured by weighing the syringe before and after administration of the solution using a chemical balance accurate to ± 0.0001 g. ECFV was calculated as:

\[
ECFV (\text{ml}) = \frac{\text{NaBr solution administered (g)} \times 10^2 \times 0.777 \times 0.9 \times 0.95 \times 0.934}{\text{Serum bromide concentration \times 1.073}}
\]

where 0.90 is the correction factor for intracellular bromide, 0.95 corrects for the Donnan equilibrium across the cell membrane, 0.934 corrects for the proportion of water in serum, 0.777 is the factor to convert mg/ml NaBr to mg/ml bromide, and 1.073 is the specific gravity of NaBr solution (manufactured by the Department of Pharmacology, Northwick Park Hospital, Harrow, Middlesex, UK). The Donnan equilibrium correction is necessary because intravascular anionic proteins cause differential movement of bromide ions across the capillary membrane such that the concentration of bromide in the interstitial fluid is about 5% greater than in serum water.

Intracellular fluid volume (ICFV) was calculated by subtracting ECFV from TBW, and body solid content by subtracting TBW from body weight. We estimated the fraction of lean body mass in AGA babies as TBW for AGA babies/TBW for AGA babies based on the assumption of a 0% adipose tissue content in AGA babies. Fat content was then calculated as 1 − lean mass. We also determined whether, at this calculated fat content, there was any significant difference in lean body mass water content between the groups, as might be expected if lean body tissue hydration is the same in both groups and adipose tissue is anhydrous.

Statistical analysis was carried out using Intercooled Stata version 4.0. Unless otherwise stated, results are quoted as median and range. Comparisons were made using the Mann-Whitney two sample statistic for continuous variables and Fisher’s exact test for categorical variables.

### Results

Forty-two preterm infants were studied. Measurements were made within 18 hours of birth. Seven infants were SGA and 35 were AGA. Birth weights were 760 (420–1020) and 990 (710–1570) g and gestational ages 28 (26–29) and 27 (25–30) weeks for SGA and AGA infants respectively. There were no differences between the groups with respect to sex or gestational age (table 1).

Body composition differed between the groups (table 2). SGA infants had a significantly higher body water content, when expressed per unit body weight, than AGA infants (906 (833–954) and 844 (637–958) ml/kg respectively; \(p = 0.019\)) and therefore a correspondingly lower body solid content (94 (46–167) and 157 (42–363) g/kg respectively).

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Body composition analyses</th>
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<tbody>
<tr>
<td></td>
<td>SGA</td>
</tr>
<tr>
<td>TBW (ml/kg)</td>
<td>906 (833–954)</td>
</tr>
<tr>
<td>ECFV (ml/kg)</td>
<td>505 (311–569)</td>
</tr>
<tr>
<td>ICVF (ml/kg)</td>
<td>386 (314–463)</td>
</tr>
</tbody>
</table>

Values are median (range). *Mann-Whitney two sample statistic.

SGA, small for gestational age; AGA, appropriately grown for gestational age; TBW, total body water; ECFV, extracellular fluid volume; ICVF, intracellular fluid volume.
in SGA babies and a range of possible body fat content in AGA infants confirmed that, at an assumed 7% body fat content in AGA babies, there was no longer a significant difference in TBW per unit lean body mass between the groups (table 3).

Discussion
We have presented novel data on the body composition of the preterm infant and provided a baseline for longitudinal studies of growth after preterm birth. We are unaware of any previous studies reporting in vivo measurements of body water content of SGA babies below 30 weeks gestation. We have shown that the body composition of preterm SGA infants differs significantly from that of AGA babies of equivalent gestational age, with differences in TBW and both an absolute and a relative reduction in body solid mass.

Our measurements of body composition for AGA infants are comparable with the limited published data. Bauer et al. studied a group of infants of comparable gestational age to those in our study, although SGA babies were specifically excluded. TBW content was within our range of values. The data of Heimler et al., derived from infants of slightly longer gestation (30.7 ± 2.4 weeks), are also within the range of results of the present study. All of the published cadaver studies report values that fall within the range defined by the three in vivo studies reported here. Table 3 lists studies in which body composition was determined within the first 24 hours after birth and in which it was possible to extract values for infants below 32 weeks gestation. Results from the three cadaver studies are included for comparison.

Deuterium oxide dilution has also been used to determine TBW. However, deuterium is not anhydrous. If this is also the case in extremely immature SGA infants, then reanalysis of our data suggests a fat content of about 7% in AGA infants. This would account for the differences in the TBW measurements between the AGA and SGA babies. Petersen et al., using dual photon absorptiometry with 185Ga, detected no fat in either AGA or SGA preterm infants, between 31 and 36 weeks gestation and at term, 2% in SGA infants, and 13% in AGA infants. However, the cadaver studies of Fehling suggest a mean fat content of 2.1% in infants of 24–32 weeks gestation. This is similar to data from Iob and Swanson for gestations of between 24 and 32 weeks.

### Table 3

<table>
<thead>
<tr>
<th>Reference</th>
<th>Date</th>
<th>SGA (0% fat)</th>
<th>AGA (0% fat)</th>
<th>N/S</th>
<th>SGA (4% fat)</th>
<th>AGA (4% fat)</th>
<th>N/S</th>
<th>SGA (7% fat)</th>
<th>AGA (7% fat)</th>
<th>N/S</th>
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<tbody>
<tr>
<td><em>von Bezold</em></td>
<td>1857</td>
<td>906 (833–954)</td>
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<tr>
<td><em>Feiling</em></td>
<td>1877</td>
<td>844 (637–958)</td>
<td>0.019</td>
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<td>—</td>
</tr>
<tr>
<td>Givens et al</td>
<td>1933</td>
<td>864 (650–976)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Shaffer et al</td>
<td>1989</td>
<td>879 (664–998)</td>
<td>NS</td>
<td>—</td>
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<tr>
<td>Bauer et al</td>
<td>1989</td>
<td>908 (685–1030)</td>
<td>NS</td>
<td>—</td>
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</table>

Values are median (range). SGA, small for gestational age; AGA, appropriately grown for gestational age; TBW, total body water; ECFV, extracellular fluid volume; N/S, not stated.

### Table 4

<table>
<thead>
<tr>
<th>Reference</th>
<th>Date</th>
<th>SGA (0% fat)</th>
<th>AGA (0% fat)</th>
<th>N/S</th>
<th>SGA (4% fat)</th>
<th>AGA (4% fat)</th>
<th>N/S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fehling</td>
<td>1877</td>
<td>846 (637–958)</td>
<td>0.019</td>
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<tr>
<td>Bauer et al</td>
<td>1989</td>
<td>864 (650–976)</td>
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<td><em>Fehling</em></td>
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<td>NS</td>
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</table>

Values are median (range). AGA (7% fat) 908 (685–1030) NS.
Widdowson and Spray present their data by body weight and suggest about 2.5% body fat at 1000 g. Enzi et al. showed a 3% difference in body fat mass, measured by anthropometric means, between AGA and SGA infants at 35 weeks gestation. Summary data from Ziegler et al. show a body fat content of 0.7–4.9% for the gestational age range 25–30 weeks. Our estimated difference therefore appears reasonable.

It is notable that the ratio of extracellular to intracellular water was not significantly different. This suggests that SGA infants are not dehydrated, as has been suggested. Further, it is unlikely that SGA infants would have a greater cell volume, as it is unlikely that SGA infants would have a greater cell volume, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number. For the extracellular volume, there is a relative increase in number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible, or preservation of cell number, with the implication that catch up growth is possible. Therefore, it appears that the regulation of body water distribution is unimpaired in SGA infants.

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