Growth and body composition in preterm infants is altered early

Tim Donovan, Nada Al-Theyab, Barbara Lingwood, Yvonne Eiby, Paul Colditz

RBWH Neonatal Nurseries, Australia
RBWH Growth

Postnatal Growth Restriction (strong association with neurodevelopmental risk)

- FT-AGA
- PT-AGA 32.0-36.6w
- PT-AGA 28.0-31.6w
- PT-AGA <28.0w

Growth patterns in preterm infants born appropriate for gestational age

Pamela Dodrill, Geoff Cleghorn, Tim Donovan and Peter Davies

Journal of Paediatrics and Child Health
7 studies, 366 infants, Mean GA 30 wks vs Term

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>%TBF</th>
<th>Preterm</th>
<th>Term</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
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<td>SD [%]</td>
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<td>Mean [%]</td>
<td>SD [%]</td>
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<td>Atkinson 1994</td>
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<td>10</td>
<td>0</td>
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<td>Test for overall effect: Z = 3.15 (P = 0.18)</td>
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<td>Total (95% CI)</td>
<td>366</td>
<td>306</td>
<td>100.0%</td>
<td>3.06 [0.25, 5.88]</td>
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<td>Test for overall effect: Z = 2.13 (P = 0.03)</td>
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</tbody>
</table>

%FM Metabolic risk
To look earlier

• Ascertain normative body composition at birth between 32 and 36 wks gestation

Control Group

• Assess effect of ex-utero growth on body composition in infants born at <32 weeks

Study Group
METHODS

SUBJECTS

- Infants cared for at Royal Brisbane and Women's Hospital, born 2012 to 2016
- For this analysis excluded infants with BWt <10thP or >90thP

BODY COMPOSITION

- Measured by air displacement plethysmography (Pea Pod)
- BC measured: Control Group: 2-5 days post partum
  Study Group: At 32-36 wks corrected age
RESULTS
### Infant Characteristics

<table>
<thead>
<tr>
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<th>Study (exutero)</th>
<th>Control (inutero)</th>
<th>( P )</th>
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<td>( n=100 )</td>
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<td>( n=88 )</td>
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<tr>
<td>Birth GA, wk</td>
<td>29.3 ± 1.8</td>
<td>34.2 ± 1.3</td>
<td>&lt;.0001</td>
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<tr>
<td>Birth weight, g</td>
<td>1326 ± 333</td>
<td>2149 ± 349</td>
<td>&lt;.0001</td>
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<tr>
<td>Birth weight Z scores</td>
<td>0.15 ± .64</td>
<td>-0.28 ± .57</td>
<td>&lt;.0001</td>
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<tr>
<td>Male (%)</td>
<td>53 (53%)</td>
<td>45 (51%)</td>
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</table>
Full Term Control
- Term infants n=45
- RBWH cohort
- Maternal booking BMI 18.5-25.0
- Exclusions: BWt <10%le, Maternal DM, Maternal illness

Pediatric Res 2010, 68:1

**WEIGHT**

P values
- time < .001
- group .97
- time*group .66

Wt deficit 480g

![Diagram showing weight gain over post-menstrual age (wks) for study, control, and term control groups.](image-url)
Length

Lth deficit 3.5cm

P values
  time .002
  group .002
  time*group .77

Length (cm)

Post Menstrual Age (wks)

study  control  term control
% Fat Mass

P values
  time .19
  group .03
  time*group < .001

%FM excess 13.3%
Fat Free Mass

FFM Deficit
820g
DISCUSSION

Premi GRACE Study
• VPT infants have higher %FM from 32wks corrected age

• Their %FM accelerates markedly between 34wks and Term CA

• Weight gain <1 year not associated with adverse metabolic outcomes in early adolescence

• Rapid weight gain at >1yr strong association with:
  % Fat mass and waist circumference
  Higher fasting insulin, blood pressure and lower insulin sensitivity
FAT FREE MASS

- FFM decelerates from 34wks CA when compared with inutero controls
- Important FFM deficit in VPT infants at Term CA  (Mean deficit 820g)
  
  - FFM gain associated with improved cognitive/motor scores on BSID-111 at 12 mthCA  \( p=0.002 \)
  - No association between FM gain and BSID-111 outcomes at 12mthsCA
I thank my co researchers, the parents and staff from the Royal Brisbane and Women's Hospital and the University of Qld Centre for Clinical Research

Nada Al-Theyab
Barbara Lingwood
Paul Colditz
Yvonne Eiby
Fat Mass

P values
- time: 0.13
- group: 0.05
- time*group: <0.001

FM Excess
- 340g

FM (g) vs. Post Menstrual Age (wks)
- Study: Red
- Control: Blue
- Term Control: Black

Centre for Clinical Research
Munich 2016

END
## Infant Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Study (ex-utero) (N = 132)</th>
<th>Control (in-utero) (N = 109)</th>
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<tbody>
<tr>
<td>Birth GA (wk)</td>
<td>29.3 ± 1.8</td>
<td>34.2 ± 1.3</td>
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<tr>
<td>Birth weight (g)</td>
<td>1302 ± 368</td>
<td>2121 ± 406</td>
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<tr>
<td>Birth weight Z scores</td>
<td>0.13 ± 0.84</td>
<td>-0.36 ± 0.87</td>
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<tr>
<td>AGA/SGA/LGA (N)</td>
<td>118/7/7</td>
<td>88/16/5</td>
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<tr>
<td>Male N (%)</td>
<td>67 (51%)</td>
<td>65 (49%)</td>
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Greater Early Gains in Fat-Free Mass, but Not Fat Mass, Are Associated with Improved Neurodevelopment at 1 Year Corrected Age for Prematurity in Very Low Birth Weight Preterm Infants

Sara E. Ramel, MD, Heather L. Gray, MPH, Ellen Christiansen, MD, Christopher Boys, PhD, Michael K. Georgieff, MD, and Ellen W. Demerath, PhD

University of Minnesota

- 34 VLBW infants  Mean gestational age 27.4 ±2.6wks
- FFM gain associated with improved cognitive/motor scores on BSID-111 at 12 mthCA  p=0.002
- Remained significant when adjusted for BWt, GA and IVH
- No association between FM gain and BSID-111 outcomes at 12mthsCA
Catch-up growth and metabolic outcomes in adolescents born preterm
Nicholas D Embleton,1,2 Murthy Korada,1,2 Claire L Wood,1 Mark S Pearce,2

- 102 infants, Mean GA 30.8wks,
- Reviewed at median of 11.5yrs

- Trajectory of <1 year wt. gain not associated with adverse metabolic outcomes in early adolescence

- Strong association of rapid weight gain at >1yr of age with:
  1. % Fat mass and waist circumference
  2. Higher fasting insulin, blood pressure and a lower insulin sensitivity

Adiposity (%FM)
- VPT infants have higher %FM from 32wks corrected age
- Their %FM accelerates most markedly between 34wks and Term CA
Premi GRACE Study

Full Term Control

- Term infants n=45
- RBWH cohort
- Maternal booking BMI 18.5-25.0
- Exclusions: BWt <10%le, Maternal DM, Maternal illness

Pediatric Res 2010, 68:1
Premi GRACE Study

%FM

Post menstrual age (wks)

P values
- time: 0.208
- group: 0.023
- term: 0.001

%FM study ♦ %FM control ■ full term ♣
Prevalence of obesity in Australian children aged 2-18 years

Increased protein intake decreases postnatal growth faltering in ELBW babies

Barbara Elizabeth Cormack,¹ Frank H Bloomfield²,³

What this study adds

- Recommended protein intakes can be achieved using standard intravenous nutrition solutions and commercial breast milk fortifiers.
- Increasing protein intake is associated with significantly reduced downward crossing of centiles for weight, length and head circumference between birth and discharge.

Munich 2016
Munich 2016
AGA Subgroup

Munich 2016

Graph showing weight (g) against measurement gestational age (wks) for different groups:
- Wt(g) study
- Wt(g) control
- Full term

The graph illustrates the growth pattern across gestational ages, with error bars indicating variability.
AGA Subgroup

- Length (cm) control
- Length (cm) study
- Full term

Measurement Gestational age (wks) vs. Length (cm)
?AGA subgroup

Munich 2016
Obese Adult Proportion 2000-2013

OECD 2013
Current consensus on preterm infant growth up to term equivalent age:

That preterm infant’s growth mimics that of the fetus in-utero both anthropometrically and in terms of body composition.
Weight gain and Neurodevelopment

- 2006 USA
- n= 600, 500-1000g
- Wt gain quartiles
- Only 9g/day difference
- Best outcome: Neurodev by Bailey 2yr and CP rate in highest growth quartile
- Remains significant when adjusted for CNLD, IVH,PVL

VLBW preterm infants at term corrected age have:

1. **Postnatal Growth Restriction** (strong association with neurodevelopmental risk)
SUBJECTS

• Infants cared for in the Royal Brisbane and Women's Hospital, born 2012 to 2016

• For this analysis excluded infants with BWt <10thP or >90thP
Premi GRACE Study

<table>
<thead>
<tr>
<th>PMA</th>
<th>Number of infants</th>
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<td>36</td>
<td>25</td>
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<td>40</td>
<td>19</td>
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Infants measured at each gestation
Premi GRACE Study
• Confirmed that VLBW infants have a higher %FM and a lower FFM (xxxgms) at term corrected age

• VLBW infants have higher %FM from 32wks corrected age and their %FM accelerates most markedly between 34wks and Term CA

• FFM is reduced in infants delivered at <32wks gestation and continues to decelerate from 34wks CA when compared to preterm infants delivered at 32-36wks gestation

• %FM accretion in VLBW infants occurs from birth

• The rate of accretion of %FM in VLBW infants mimics that seen in Term infants over the first 5 months of postnatal life
CONCLUSION

- Postnatal FFM restriction in infants born at <32wks is evident from at least 34wks gestation
- %FM shows a rapid gain in <32wk infants from 33 wks CA
- The %FM trajectory postnatally of <32wk infants is very similar in quantum and rate to term infants in the first 4.5mths
- FFM gains and not %FM gains are associated with improved neurodevelopmental outcomes at 12mthsCA
- As early weight gain (<12mthsCA) does not appear related to worse metabolic outcomes in early adolescence, efforts should continue to improve FFM accretion in Very Preterm Infants at least till term CA
METHODS
Obese/Overweight Children 2-15 yrs by Gender
Full Term Control
• Term infants n=45
• RBWH cohort
• Maternal booking BMI 18.5-25.0
• Exclusions BWt <10%le, Maternal DM, Maternal illness

Pediatric Res 2010, 68:1
Length

P values
- time: 0.002
- group: 0.002
- time*group: 0.77

Post Menstrual Age (wks)

- • study
- - control
- - term control
% Fat Mass

P values
  time .19
  group .03
  time*group < .001

% FM

Post Menstrual Age (wks)

study  control  term control
Fat Mass

P values
  time .13
  group .05
  time*group<.001

```
FM (g)
```

```
Post Menstrual Age (wks)
```

- ○ study
- --- control
- • term control