Evidence for developmental programming in cattle

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‘Developmental programming’

Stimuli during critical period of early development

Permanent changes in physiology / metabolism

Short and long-term health consequences
Introduction

- Dutch famine cohort study
  - hungerwinter WWII

*Painter et al., 2005*
Introduction

**Nulliparous heifers**
- Bred at ± 15 months
- Large part of body growth during first gestation

**Dairy cows**
- Inseminated < 100 DIM
- Produce large amounts of milk while being pregnant

Demanding in terms of energy and nutrients requirements
Introduction

HUMAN
- Undernourishment during pregnancy
- Energy restriction for embryo/fetus
- Placenta
- Birth weight
- Long-term health

CATTLE
- Growth/lactation during gestation
- Energy restriction for embryo/fetus
- Placenta
- Birth weight
- Long-term health and production
Studies

PLACENTA

PRENATAL
birth size metabolism

POSTNATAL
growth fertility

LACTATION
Placental development

- **Aim**: assess effect of maternal body growth/milk yield on placental development

- Expelled fetal membranes
  - maternal growth: BB heifers ↔ BB cows
  - maternal lactation: HF heifers ↔ HF cows

*Van Eetvelde et al., 2016*
Placental development

- Expelled fetal membranes
  - weight of membranes and cotyledons
  - cotyledon number
  - cotyledonary surface area
    ⇒ exchange mother - calf

Van Eetvelde et al., 2016
Placental development

![Graph showing weight (kg) for Placenta, Membranes, and Cotyledons with different categories: Primi HF, Primi BB, Multi HF, Multi BB. Significant differences marked with * P<0.05.]

Van Eetvelde et al., 2016
Placental development

*C P<0.05

Van Eetvelde et al., 2016
Placental development

≈ nutrient-restricted ewes (Clarke et al., 1998)
≈ nuclear somatic transfer (Miglino et al., 2007)

* P<0.05

Van Eetvelde et al., 2016
Placental development

Van Eetvelde et al., 2016

* P<0.05
Placental development

- Compensation mechanisms of the placenta
  - early gestation: developing more cotyledons
    - survival of pregnancy
  - late gestation: expansion of cotyledonary surface
    - increasing nutrient demand of fetus

Van Eetvelde et al., 2016
Studies

PLACENTA

PRENATAL

POSTNATAL

LACTATION
Studies

birth weight
± 1500 calves

metabolism
± 500 calves

growth & fertility
± 100 heifers

lactation
74 heifers
Studies

PLACENTA

PRENATAL

POSTNATAL

LACTATION
Birth weight

- **Aim**: assess effect of maternal body growth/milk yield on fetal development

- Birth weight of 1,594 HF calves
  - 540 primiparous dams
  - 1,054 multiparous dams

*Kamal et al., 2014*
Birth weight

- Maternal factors:
  - parity / age
  - body measurements / body condition
  - lactation features (Milkbot)
    - during gestation
      - 6,193 kg milk
      - 446 kg glucose
      - 217 kg proteins

(Ehrlich, 2011)

Kamal et al., 2014
Birth weight

- Birth weight ↓:
  - female calves
  - primiparous dams
    - younger age at calving
  - multiparous dams
    - higher milk yield of dam during gestation
    - shorter dry period

Kamal et al., 2014
Birth weight

High milk yield
Birth weight

High milk yield and high persistency!
Calf metabolism

- **Aim:** assess effect of maternal body growth/milk yield on metabolism calf

- 481 HF calves
  - basal glucose/insulin levels
  - glucose stimulation (150 mg/kg BW)

*Kamal et al., 2015*
Calf metabolism

• ↑ basal insulin levels:
  o female calves
  o multiparous dams
    • higher milk yield of dam during gestation
    • longer dry period

Kamal et al., 2014
Prenatal development

• Effect of high maternal milk yield / dry period
  o on birth weigh
  o on glucose and insulin metabolism of calf

• Further research necessary:
  o metabolic state of the dam?
  o long-term consequences for the offspring?

Kamal et al., 2014
Birth season

- Born during ‘hotter’ months
  - larger cotyledonary surface of placenta
  - lower birth weights
  - lower insulin levels in newborn calves

- Decreased nutrient supply during end of gestation?

Kamal et al., 2014 and 2015; Van Eetvelde et al., 2016
Body growth

Intra Uterine Growth Retardation

SGA infants

↓ insulin levels

catch-up growth

reduced insulin sensitivity at early age

↓

longterm health risks

associated with high insulin levels

Hales et al., 1991; Barker et al., 1993; Ibanez et al., 1998
Body growth

- Hypothesis:
  - catch-up growth in cattle
    - associated with low insulin at birth
    - can lead to adiposity/ health problems in later life

*Van Eetvelde, unpublished data*
Body growth

- 3 groups (daily growth during first 6 months)
  - slow: <750 g/day (n=6)
  - moderate: 750-950 g/day (n=40)
  - fast: >950 g/day (n=5)

<table>
<thead>
<tr>
<th></th>
<th>slow</th>
<th>moderate</th>
<th>fast</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Birth weight (kg)</strong></td>
<td>39 ± 1.8</td>
<td>39 ± 4.6</td>
<td>42 ± 2.2</td>
<td>0.32</td>
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<tr>
<td><strong>Glucose (mMol/L)</strong></td>
<td>6.5 ± 0.70</td>
<td>6.0 ± 0.60</td>
<td>5.9 ± 0.81</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Insulin (mU/L)</strong></td>
<td>12.9 ± 9.10</td>
<td>7.2 ± 4.76</td>
<td>4.4 ± 2.39</td>
<td>0.08</td>
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*Van Eetvelde, unpublished data*
# Body growth

<table>
<thead>
<tr>
<th></th>
<th>Growth rate</th>
<th></th>
<th></th>
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<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>slow</td>
<td>moderate</td>
<td>fast</td>
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<tr>
<td><strong>FIRST AI</strong></td>
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<tr>
<td>Age (d)</td>
<td>445 ± 38</td>
<td>454 ± 51</td>
<td>455 ± 30</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>378 ± 29&lt;sup&gt;a&lt;/sup&gt;</td>
<td>414 ± 41&lt;sup&gt;a&lt;/sup&gt;</td>
<td>473 ± 45&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.003</td>
<td></td>
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<tr>
<td><strong>CONCEPTION</strong></td>
<td></td>
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<tr>
<td>Age (d)</td>
<td>480 ± 88</td>
<td>474 ± 69</td>
<td>528 ± 58</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>406 ± 82&lt;sup&gt;a&lt;/sup&gt;</td>
<td>425 ± 45&lt;sup&gt;a&lt;/sup&gt;</td>
<td>506 ± 41&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.007</td>
<td></td>
</tr>
</tbody>
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*Van Eetvelde, unpublished data*
Body growth

≈ Human: precocious pubarche and ovulatory dysfunction (Ibanez et al., 1999)

Van Eetvelde, unpublished data
## Body growth

<table>
<thead>
<tr>
<th>CALVING</th>
<th>Growth rate</th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>slow</td>
<td>moderate</td>
</tr>
<tr>
<td>Age (d)</td>
<td>755 ± 87</td>
<td>739 ± 62</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>627 ± 69(^a)</td>
<td>616 ± 72(^a)</td>
</tr>
<tr>
<td>BFT (mm)</td>
<td>16 ± 6.5</td>
<td>15 ± 5.3</td>
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*Van Eetvelde, unpublished data*
Body growth

• FAST growing heifers
  o lower basal insulin levels at birth
  o larger body weight at calving
  o higher adiposity at calving

≈ Human catch-up growth

• Low fasting insulin levels in newborns
  o forecast of catch-up growth during early life?
    • consequences for fertility and health?

Van Eetvelde, unpublished data
Studies

PLACENTA

PRENATAL

POSTNATAL

LACTATION
1st lactation

- **Aim**: assess factors influencing first lactation milk yield

- 305-d milk yield of 74 HF heifers
  - maternal factors
  - environmental factors
  - heifers development

*Van Eetvelde, unpublished data*
1st lactation

- ↓ first lactation milk yield associated with
  - younger age at first parturition
  - lower body weight at first parturition
  - birth during winter
    - nutrition?
    - photoperiod?
    - temperature?

Van Eetvelde, unpublished data
1st lactation

- Relation birth season – metabolism

Van Eetvelde, unpublished data
1st lactation

- Born during hotter months
  - ↓ basal insulin level

- Potential consequences:
  - Development of insulin resistance in early life?
  - Higher milk yield during first lactation?

Van Eetvelde, unpublished data
Conclusion

Environmental events during gestation

Impact on development (size and metabolism) of newborn dairy calves

Consequences for health and productivity
Conclusion

- Fundamental studies necessary to
  - decipher the underlying mechanisms
  - develop preventive and curative strategies to increase productivity, health and life expectancy in dairy cattle
Thank you!

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