Maternal Environment Impacts Fetal and Offspring Outcomes in Sheep

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NDSU Animal Nutrition and Physiology Center

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OUTLINE

• What is developmental programming?

• What is happening at NDSU…
  – A reproductive biologist’s perspective…
  – Understanding the biology…
  – Can we come up with tools to help….
Phenotype

Classic Animal Breeding Example

Phenotype = Genotype + Environment

Eg. Milk production = Holstein genetics + Mastitis
Phenotype

Future Animal Breeding Example

Phenotype = Genotype + Environment

Eg. Carcass quality = Genetics + Uterine environment
Programming

• The process through which a \textit{stimulus} or \textit{insult} establishes a \textit{permanent} response

• Developmental programming hypothesis
• Exposure during a \textit{critical period} in development may influence later metabolic or physiological functions in adult life
10 PRINCIPLES OF DEVELOPMENTAL PROGRAMMING

1) During development in the womb, there are critical periods of vulnerability to suboptimal conditions.

Vulnerable periods occur at different times for different tissues.
5) The placenta plays a key role in programming.
6) **Compensation carries a price.** In an unfavorable environment, the developing baby makes attempts to compensate for deficiencies. However, the compensatory effort often carries a price.
What’s Happening at NDSU?

“Healthy Offspring through Optimal Nutrition”

Center for Nutrition and Pregnancy
North Dakota State University
College of Agriculture, Food Systems, and Natural Resources
Fargo, ND 58105-5727
Global Nutrition and Selenium
NDSU Sheep Studies

High Selenium (n=42)
- (n=14) 140% NRC
- (n=14) 100% NRC
- (n=14) 60% NRC

Breeding to 50dGA

Parturition

Normal Selenium (n=40)
- (n=13) 140% NRC
- (n=13) 100% NRC
- (n=14) 60% NRC

(n=81)
All lambs placed on identical nutrition scheme until market weight
48 h after birth to weaning = Bucket Teat Unit
Weaning to Market
Maternal intake and BW changes

Day of gestation

Weight, kg

- 60% NRC
- 100% NRC
- 140% NRC

*Diet – P<0.01, (d90-145, all diets differ)
EFFECT OF MATERNAL NUTRITION ON MAMMARY WEIGHT IN EWE LAMBS

Swanson et al., 2008
EFFECT OF MATERNAL NUTRITION ON COLOSTRUM PRODUCTION IN EWE LAMBS

CON vs. RES, CON vs. HIGH
P < 0.01

Swanson et al., 2008
EFFECT OF MATERNAL NUTRITION ON TOTAL IgG PRODUCTION

Colostral IgG (g/L)

CON vs. RES, P = 0.06
CON vs. HIGH; P = 0.06

Swanson et al., 2008
Nutrition during pregnancy impacts on milk yield

![Graph showing milk yield over day postpartum with different nutrition levels and statistical significance](image-url)

- Milk yield, g
- Day postpartum
- P < 0.001
Selenium during pregnancy effects on milk yield

P < 0.001
POSTNATAL RESPONSES
Maternal nutritional intake

Birth weight, kg

Males
Females

Nut*sex; $P = 0.02$

Maternal nutritional intake

RES
CON
HIGH

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EFFECT OF MATERNAL NUTRITION ON LAMB IgG CONCENTRATION

Hammer et al., 2010

Nutr. X Se;
P < 0.05
a, b, c; P ≤ 0.04
EFFECT OF MATERNAL NUTRITION ON LAMB MORTALITY FROM BIRTH TO WEANING

Hammer et al., 2010

P < 0.02
Lamb weaning wt, 57d

Nutritional group

<table>
<thead>
<tr>
<th>Weight, kg</th>
<th>0</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>a</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td></td>
<td>b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>140</td>
<td></td>
<td></td>
<td>ab</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nutritional group

Weight, kg: 60, 100, 140

Values marked with different letters (a, b, ab) indicate statistically significant differences.
Other Economic Factors
Process of Wool Follicle Development

- **Primary follicles are initiated.**
- **Primary follicles are completed and wool fiber is produced.**
- **Secondary follicles are initiated.**
- **Secondary follicles are matured.**

Conception

- Day 60
- Day 80
- Day 100

Pregnancy

Birth

1 to 3 weeks

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Six Month Old Lambs

![Graph showing fiber > 30 µm, % for different nutritional intakes.](image)

Nutrition: $P < 0.08$

- **RES**: Fiber > 30 µm, %: a
- **CON**: Fiber > 30 µm, %: b
- **OVR**: Fiber > 30 µm, %: ab

Side fiber comfort factor for:
- **RES**: b
- **CON**: a
- **OVR**: ab

Maternal nutritional intake

<table>
<thead>
<tr>
<th>Maternal nutritional intake</th>
<th>Fiber &gt; 30 µm, %</th>
<th>Fiber comfort factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>RES</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>CON</td>
<td>b</td>
<td>a</td>
</tr>
<tr>
<td>OVR</td>
<td>ab</td>
<td>ab</td>
</tr>
</tbody>
</table>
Six Month Old Lambs

Se*Sex: $P = 0.03$

Maternal selenium supplementation

Side staple length, cm

ASe

HSe

Female

Male

a

ab

b

ab

Maternal selenium supplementation

Se*Sex: $P = 0.03$
Carcass data
Carcass Results

• Hot carcass weight:
  – Singletons > Twins (25.9 vs 21.6 ± 1.1 kg)

• No differences:
  – Body wall thickness
  – Fat depth
  – Yield grade
  – Leg Score
  – Maturity
## Carcass data

<table>
<thead>
<tr>
<th></th>
<th>ASe</th>
<th>HSe</th>
<th>SE</th>
<th>Se</th>
<th>#</th>
<th>Se*#</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone, g</strong></td>
<td>Single</td>
<td>Twin</td>
<td>Single</td>
<td>Twin</td>
<td>SE</td>
<td>Se</td>
</tr>
<tr>
<td></td>
<td>2556.8\textsuperscript{a}</td>
<td>2774.7\textsuperscript{a}</td>
<td>2560.8\textsuperscript{a}</td>
<td>2275.0\textsuperscript{b}</td>
<td>153.5</td>
<td>0.85</td>
</tr>
<tr>
<td><strong>Lean, g</strong></td>
<td>4651.8</td>
<td>3387.9</td>
<td>4738.4</td>
<td>4126.0</td>
<td>456.0</td>
<td>0.15</td>
</tr>
<tr>
<td><strong>Bone:Lean</strong></td>
<td>0.56\textsuperscript{a}</td>
<td>0.80\textsuperscript{b}</td>
<td>0.54\textsuperscript{a}</td>
<td>0.56\textsuperscript{a}</td>
<td>0.05</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
Maternal nutritional plane

Rib eye area, cm²

Singleton
Twin

RES                    CON                     HI

a a

Nut x fetal no.: $P = 0.03$
Nut: $P = 0.08$
Fetal no.: $P = 0.03$

Flank streaking

Singleton
Twin

Nut x fetal no.: $P = 0.05$
Nut: $P = 0.08$
Fetal no.: $P = 0.03$

Rib eye area, cm²

RES                    CON                     HI

a a a

Nut x fetal no.: $P = 0.03$
Nut: $P = 0.01$
Fetal no.: $P < 0.01$

Maternal nutritional plane
Semimembranosus, g

Maternal Nutritional Plane

RES  CON  OVR

ab  a  b
Reproduction?

- Onset of puberty was similar
- Uterine size was similar
- Female lambs from HSe ewes had an increased adiposity
Antral Follicles, % labeling index

Theca interna cells

Nutritional Treatment

60 100 140

A

Se: $P = 0.16$
Nut: $P = 0.42$
Se*Nut: $P = 0.07$

B

Se: $P = 0.20$
Nut: $P = 0.44$
Se*Nut: $P = 0.14$
Umbilical Blood Flow in Pregnant Ewes

Lekatz et al., 2013
Umbilical Blood Flow

Umbilical BF, mL/min

Gestation, d

ADQ (n = 15)
RES (n = 16)

Nut*Day; P < 0.0001

Lemley et al., 2012
Can Melatonin Help?
Umbilical Blood Flow

Trt*Nut*Day; P = 0.15

Lemley et al. (2012) AJP.
Protein Supplementation During Late Pregnancy

• Martin et al., 2008
## Reproductive Performance

<table>
<thead>
<tr>
<th>Item</th>
<th>Treatment</th>
<th>Prot</th>
<th>NoProt</th>
<th>SEM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Puberty, d</td>
<td></td>
<td>339</td>
<td>334</td>
<td>10</td>
<td>0.70</td>
</tr>
<tr>
<td>Cycling at beginning of breeding season, %</td>
<td></td>
<td>61</td>
<td>67</td>
<td>-</td>
<td>0.45</td>
</tr>
<tr>
<td>Calved in first 21 d, %</td>
<td></td>
<td>77</td>
<td>49</td>
<td>-</td>
<td>0.005</td>
</tr>
<tr>
<td>Overall pregnancy rate, %</td>
<td></td>
<td>93</td>
<td>80</td>
<td>-</td>
<td>0.05</td>
</tr>
<tr>
<td>Calving date, Julian d</td>
<td></td>
<td>71</td>
<td>75</td>
<td>3</td>
<td>0.15</td>
</tr>
<tr>
<td>Calf birth wt, kg</td>
<td></td>
<td>33</td>
<td>33</td>
<td>1</td>
<td>0.94</td>
</tr>
<tr>
<td>Unassisted births, %</td>
<td></td>
<td>78</td>
<td>64</td>
<td>-</td>
<td>0.24</td>
</tr>
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</table>
Reproductive Performance

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<td>64</td>
<td>-</td>
<td>0.24</td>
</tr>
</tbody>
</table>
How about protein supplementation in sheep??

Table 1. Diet composition

<table>
<thead>
<tr>
<th>Item, % DM Basis</th>
<th>Treatments&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LOW</td>
</tr>
<tr>
<td>Pellets</td>
<td></td>
</tr>
<tr>
<td>Corn</td>
<td>18.5</td>
</tr>
<tr>
<td>Dried Distillers Grain</td>
<td>7.0</td>
</tr>
<tr>
<td>Soyhulls</td>
<td>9.5</td>
</tr>
<tr>
<td>Trace Mineral</td>
<td>0.49</td>
</tr>
<tr>
<td>Hay</td>
<td>64.51</td>
</tr>
</tbody>
</table>

<sup>1</sup>LOW = ewes fed to 75% of MOD; MOD = Ewes fed to perform within NRC (2007) guidelines (100% treatment); HIGH = Ewes fed to 125% of MOD.
## Ewe lambs

<table>
<thead>
<tr>
<th></th>
<th>60</th>
<th>80</th>
<th>100</th>
<th>SEM</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Birth wt, kg</strong></td>
<td>4.5&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.14</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>Wean wt, kg</strong></td>
<td>18.2</td>
<td>19.9</td>
<td>19.2</td>
<td>0.98</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>ADG, kg/d</strong></td>
<td>0.192</td>
<td>0.217</td>
<td>0.207</td>
<td>0.13</td>
<td>0.37</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>60</th>
<th>100</th>
<th>140</th>
<th>SEM</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Birth wt, kg</strong></td>
<td>4.5</td>
<td>4.5</td>
<td>4.7</td>
<td>0.21</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Wean wt, kg</strong></td>
<td>14.7</td>
<td>16.9</td>
<td>16.0</td>
<td>.73</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>ADG, kg/d</strong></td>
<td>0.178&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>0.202&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.165&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.010</td>
<td>0.03</td>
</tr>
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</table>
## Fertility of Ewe lambs

<table>
<thead>
<tr>
<th>% bred first 17 d</th>
<th>60</th>
<th>80</th>
<th>100</th>
<th>SEM</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>50&lt;sup&gt;b&lt;/sup&gt;</td>
<td>84&lt;sup&gt;a&lt;/sup&gt;</td>
<td>67&lt;sup&gt;ab&lt;/sup&gt;</td>
<td>9.1</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lamb birth wt, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>% bred first 17 d</th>
<th>60</th>
<th>100</th>
<th>140</th>
<th>SEM</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>100</td>
<td>73</td>
<td>13.4</td>
<td>0.99</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lamb birth wt, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.7&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Mechanisms for changes?

- No change in placental weight
- BUT, perhaps change in function may be the key
Bradykinin dose response curve in fetal placental arteries

Bradykinin (M)

1e-8  3e-8  1e-7  3e-7  1e-6  3e-6  1e-4  3e-4

% constriction

LOW

CON

HIGH

$P = 0.05$

$P = 0.09$ *
MP during Last Third of Gestation in Ewes

Uterine Blood Flow

Blood flow, mL/min

RES

CON

HIGH

P = 0.07

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Future Directions

• Time period of supplementation
• Specific nutrients that are important
• Maternal efficiencies and maternal age
• Factors that impact
  – Uterine and placental blood flow
  – Mammary gland development
Developmental Programming

• IMPORTANT TO ANIMAL HEALTH AND PRODUCTIVITY:
  – Growth and nutrient transfer
  – Reproductive capacity
  – Aging and lifetime productivity
Goal: Healthy Offspring!!!
Goal: Healthy Offspring!!!
Acknowledgements

United States Department of Agriculture
National Institute of Food and Agriculture

NDSU Animal Nutrition and Physiology Center

Image of a group of people standing together, likely staff or students associated with the mentioned institutions.