Some producers goals for their calves...

- To keep them alive?
- To spend the least amount of resources on them?
- To have better looking calves than my neighbor?
- To breed and calve them sometime

Are they feeding the future?

Bridging the gap between now and the future with strategic goals

- Plasma protein levels <5.5 g/dl at 24 to 48 hours post birth
- Double birth weight by weaning
- Calf mortality less than 5%
- Calf morbidity less than 10%
- AFC of 22 - 23 months

Phenotype = Genotype + Environment
Epigenetics

- A term historically attributed to Conrad Hal Waddington - 1940’s
- Same inherited traits, phenotypic differences not due to nucleotides sequence differences
- Are due to changes in chromatin (DNA + associated proteins) or other factors affecting gene expression.
- Variable, stable, often reversible

Control differentiation during development.
- Epigenotypes can persist through mitosis
- Fine tune gene expression levels.
- Maintain genome integrity.
- Protect us from damaging effects of transposons.
- Allow us to respond to changing environmental conditions:
  - Epigenetic variation can be selected
  - An alternative to mutation and genetic selection
  - Epigenotypes can allow you to survive selection
    - You can "date" a phenotype (by epigenetic means) without having to "marry" it (by undergoing mutation).
    - Epigenotypes can be transmitted to the next generation (stable thru meiosis).

Epigenetic has been linked to homeostatic regulation.
- In glucose depressed cells, the histones associated with rDNA genes are deacetylated and dimethylated at Lys9 when glucose is reduced

Epigenetic affects the stress response and it is modified by maternal behavior (Weaver, et al., 2004)
- Behavioral issue can cause life-long effects in the new born through epigenetic changes
- Pups liked and groomed more by their mother had higher methylation status of the first exon of the promoter region for glucocorticoid receptor
- Adult rats, mothered by high suckling mothers, had higher H3 acetylation and a threefold greater affinity for NGFI-A

The "Silver Spoon" effect

Queen and workers share their genome
- From the larva stage, the future queen is fed royal jelly and 10x more food than workers
- Rapid growth (200 mg vs. 100 mg)
- Longer life span (20x - 3 to 4 years)
- Maturation of its reproductive organs
Post-natal in rats

- Early post-natal feed restriction (25 days) by enlarging the litter size
- At 6 and 12 months of age, restricted rats:
  - Acute growth restriction
  - Incomplete catch-up in BW and body length
  - Lower energy remaining for growth and reproduction
- Energy balance can be programmed by early nutrition

(Remmers et al., 2008)

Pre-natal in humans

"Dutch Hunger Winter"

1944
1945
1946

Exposure
- Early
- Mid
- Late

Exposure to famine during early gestation:

- No changes in birth weight
- Most marked effects on health observed (age range from 48-53 years)
  - 3 fold ↑ coronary heart disease
  - ↑ obesity
  - Altered blood coagulation
  - More atherogenic lipid profile

(Ravelli et al. 1998; Roseboom et al., 2000)

What's to come new?

Longitudinal study at Kempenshof

- Identify the pathways altered by preweaning nutrition that can impact later life performance
- 86 calves
- Blocked: colostrum and parity
- Ad libitum: water, starter feed and straw
- Weaning: 56d of age
- Group housed: 70d of age

Conventional: 0.6 kg/d MR
LifeStart: 1.2 kg/d MR

Metabolic development (PCA analysis)

- Microbial-associated
  - volatile fatty acid metabolism
  - glucose metabolism and TCA cycle
- Liver-associated
  - bile acid and heme metabolism
- Energy metabolism
  - fatty acid and amino acid

Metabolomics at 11 months

- Heat map indicates biochemical differences between the LS and CON groups
- Smaller differences between LS and CON at 11 months when compared with d49
- Differences can be the result of a sustained metabolic change

<table>
<thead>
<tr>
<th></th>
<th>d49</th>
<th>d330</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total metabolites with P&lt;0.05</td>
<td>426</td>
<td>19</td>
</tr>
<tr>
<td>Metabolites (↑↓)</td>
<td>147</td>
<td>279</td>
</tr>
<tr>
<td>% of metabolites with P&lt;0.05</td>
<td>47%</td>
<td>3%</td>
</tr>
</tbody>
</table>

(Kool et al., in preparation)
Let's talk Dairy...

What's colostrum?

- Colostrum is the “first milk”
- It contains more total solids, higher fat, and more protein than regular milk. It is also a good source of Vitamin A and Vitamin E
- The importance of colostrum was thought to be primarily its immunoglobulin content

Colostrum – why have we given it?
Transfer of adequate passive immunity

- Important to improve mortality and morbidity of dairy calves

- Calves with < 10 mg/ml IgG in plasma (5.2 g/dl protein) had higher pre-weaning morbidity and mortality (AABP Proceedings 2002, 35:168)

Colostrum – why have we given it?
The delivery of pathogenic bacteria to the gut whether from environmental exposure or through the feeding system can alter the absorption of Ig’s

Bacteria will attach to the same channel that Ig’s move through – the gut senses the bacteria and it closes

Colostrum – Why should we care?
Dairy calves:
- Decreased average daily gain to 180 days (J. Dairy Sci., 1988, 71:1283)
- Decreased milk and fat production at first lactation (J. Dairy Sci., 1989, 72:552)
- Delayed time to first calving (Can Vet J., 1986, 50:314)

Beef Calves:
- Decreased weaning weight at 180 days (Am. J. Vet. Res. 1995, 56:1149)
### Colostrum – Why should we care?

Grouping was made according to serum IgG on d 3 of life. Calves with serum IgG < 1,000 mg/dL to the Poor group. Calves with serum IgG > 1,000 mg/dL to the Good group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conventional</th>
<th>Intensified</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Poor</td>
<td>Good</td>
</tr>
<tr>
<td># of calves</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Serum IgG, mg/dL</td>
<td>558\textsuperscript{a}</td>
<td>1.793\textsuperscript{b}</td>
</tr>
<tr>
<td>ADG, lb/d</td>
<td>1.17\textsuperscript{a}</td>
<td>1.09\textsuperscript{a}</td>
</tr>
</tbody>
</table>

Osorio and Drackley, personal communication.

### Colostrum – Is it IgGs?

Calves fed colostrum or a serum derived colostrum replacement demonstrated differences in feed efficiency from 0 to 29 d - no differences in IgG status.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Colostrum</th>
<th>Colostrum Replacement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>P</td>
</tr>
<tr>
<td>24-h IgG, g/L</td>
<td>13.7</td>
<td>13.8</td>
</tr>
<tr>
<td>Total DMI, kg</td>
<td>15.7</td>
<td>15.0</td>
</tr>
<tr>
<td>Milk replacer DMI, kg</td>
<td>10.7</td>
<td>11.0</td>
</tr>
<tr>
<td>Feed efficiency, (gain/feed)</td>
<td>0.43\textsuperscript{*}</td>
<td>0.36\textsuperscript{*}</td>
</tr>
</tbody>
</table>

Jones et al., 2004.

### Long term effects of colostrum feeding

Faber et al., 2005

**Brown Swiss calves were fed 2 L or 4 L of colostrum at first feeding**

<table>
<thead>
<tr>
<th></th>
<th>2 L</th>
<th>4 L</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>37</td>
<td>31</td>
</tr>
<tr>
<td>Daily gain, lb/d</td>
<td>1.8\textsuperscript{a}</td>
<td>2.2\textsuperscript{b}</td>
</tr>
<tr>
<td>Age at conception, mo</td>
<td>14.0</td>
<td>13.5</td>
</tr>
<tr>
<td>Survival through 2\textsuperscript{nd} lact.</td>
<td>75.7</td>
<td>87.1</td>
</tr>
<tr>
<td>Milk yield through 2\textsuperscript{nd} lact. (lb)</td>
<td>35,313</td>
<td>37,578</td>
</tr>
</tbody>
</table>

2,265 lbs

### What's in colostrum that is so important?

- Ig’s – Immune system (transient and not necessary; 60:1 cow)
- IGF-I – local gut effects (155:1 cow)
- IGF-II – local gut effects (7:1 cow)
- Epidermal growth factor – local gut effect (2:1 cow)
- Lactoferrin – local immunity effect in gut
- Prolactin – little data but good candidate for calves (18:1 cow)
- Insulin – local gut effects (100:1 cow)
- Leptin – could affect the hypothalamic pituitary axis (90:1 humans)
- Relaxin – humans, dogs, pigs – reproductive development (>19:1 pig)
- TGF α and TGF β
- Essential and non-essential amino acids
- Fatty acids – wide profile of fatty acids

W. Shi and Zhijun Cao, 2015.
Can we learn something from other species?

Long term effects of colostrum feeding

Lactocrine Hypothesis:
• It describes the effect of milk-born factors (including colostrum) on the epigenetic development of specific tissues or physiological functions.

Bartol et al., 2008

Long term effects of colostrum feeding

Intestinal development
• Thivend et al., 1980 – Small intestinal development represent 60% of GIT growth during suckling period
• Burrin et al., 1992 – Piglets had a 300% increase in jejunal protein synthesis when fed colostrum or milk vs. water, and a 33% increase in protein synthesis in ileal of calves fed colostrum vs. milk
• Burrin et al., 1995 – Used a milk base formula with similar nutrient content than colostrum; colostrum accentuated skeletal muscle, and jejunal protein synthesis

Long term effects of colostrum feeding

Reproductive performance
• Bartol et al., 2008 – Neonatal piglets that consume sows milk during first 3 days of life have improved reproductive performance later in life vs. milk replacer
  • Relaxin is a milk-born factor, present in colostrum, that has specific receptors in uterine and cervical tissues. Induces estrogen receptor differentiation and proliferation

Long term effects of colostrum feeding

Uterine development

• Gland depth and endometrial thickness

Miller et al., 2012
Long term effects of colostrum feeding

Glucose regulation

- Steinhoff-Wagner et al., 2010 – Glucose absorption is greater in colostrum fed calves than in formula fed calves
  - Glycogen reserves were higher in colostrum fed calves as evident by decrease protein catabolism and increased blood glucose concentration after 15 h feed deprivation

Conclusions

- Colostrum is important to achieve proper passive transfer of immunoglobulins
- Colostrum contains a lot more “goodies” than just IgG’s (leptin, insulin, growth hormone, relaxin, IGF-I, TGF α, etc)
- The long-term effect of feeding colostrum suggests there is a switch in the metabolism of the calves
- The concept of fetal programming is now extended to newborn mammals
- Colostrum is crucial in the “lactocrine” system of cattle
- No compensatory mechanism for the lack of such stimulus

What about sickness pre-weaning

Calves that were treated with antibiotics, produced 1,087 lb less milk in the first lactation (P > 0.01) than calves with no record of being treated.

Regardless of antibiotic treatment, the effect of ADG on first lactation milk yield was significant in all calves (P < 0.05).

Calves that were treated with antibiotics produced 623 kg more milk per kg of pre-weaning ADG while calves that did not receive antibiotics produced 1,407 kg more milk per kg of pre-weaning ADG.

Can other studies confirm this?

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Enhanced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at calving (mo)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>25.4</td>
<td>26.5</td>
</tr>
<tr>
<td>Year 2</td>
<td>24.0</td>
<td>24.4</td>
</tr>
<tr>
<td>Calving BW (lb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>1,277</td>
<td>1,338</td>
</tr>
<tr>
<td>Year 2</td>
<td>1,279</td>
<td>1,215</td>
</tr>
<tr>
<td>ME milk* (lb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 1</td>
<td>20,385</td>
<td>23,322 (2,937)</td>
</tr>
<tr>
<td>Year 2</td>
<td>19,395</td>
<td>20,149 (754)</td>
</tr>
</tbody>
</table>

Drackley et al., 2007

What do we need to do a great job?

Need to be systematic, need to consider:
- Age at First Calving
- Facilities and management
- Herd growth needs/wants

Age at first calving is a conscious management decision
- Should be made in early life
- Should be based on optimum performance under herd management conditions
- Younger is more profitable on a lifetime basis

Growth rates should reflect AFC goals

Find out more at: www.lifestartscience.com