Extreme Weather Impact on Female Offspring Fertility

Maternal heat and nutrition stress and offspring reproduction

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Conflict of interest

• No conflict of interests to disclose
Outline

• Heat stress
  • Overview and impact on cattle production

• Maternal stress and fetal development
  • Fetal development and programming
  • Periconception period and gestation

• Effects of maternal stress (nutritional and thermal) on offspring performance

• Conclusions
Take home message

- Maternal stress occurring before conception (breeding) and during pregnancy affects placenta and organ formation with long lasting effects for offspring health, productive and reproductive performance.

- Maternal environmental stress (nutritional or thermal) in pasture-based systems is multifactorial and has a cumulative effect on fetal and placental development.
Observed and projected climate changes across North America

- Milder Winters with hotter & longer Summers (IPCC, 2022; Cohen et al., 2021)
- Increase frequency of extreme events
  - Heat waves
  - Floods
  - Droughts
  - Fires
  - Hurricanes/Tornadoes
- Combined/additive effects on pasture-based systems

Heat stress/load - cattle

- Thermoneutral zone (-5°C to 25°C) & THI
  - Dairy (lactation <68 or dry <72), beef (<74 feedlot)
  - Geography, facilities, animal factors (breed, coat color)
  - Radiation and air movement – THI adj, BGHI, HLI
- Heat waves - ↑temp day & night - ↓ heat dissipation (↑ heat load)
  - Clear hot sunny days (no clouds), high humidity and minimal wind = higher risk

A. Thermoneutral

Most and Yates, 2021
Effects of Heat stress

- Estimated costs:
  - Direct - ~US$800M / US$4-5K per dead animal (Ferreira et al., 2016; Sullivan & Mader, 2018)
  - Indirect - ~US$600M / 5-10x higher than dead loss (Laporta et al., 2020; Sullivan & Mader, 2018)

Diagram adapted from Most and Yates 2019 and Cartwright et al., 2023

- **Reproduction - Female**
  - ↓ Estrus behavior
  - ↓ Ovarian function (foll & CL)
  - ↓ Oocyte & embryo quality
  - ↑ Embryo loss
  - Impaired implantation

- **Reproduction - Male**
  - Impaired spermatogenesis
  - ↓ Sperm quality
  - Impaired scrotal normothermia

- **Endocrine changes**
  - ↑ rectal (core) temperature
  - ↑ respiration rate
  - ↓ dry matter intake, rumination

- **Health and immunity**
  - ↑ Respiratory alkalosis
  - ↑ Ruminal acidosis
  - ↑ Lymphocyte proliferation
  - ↑ ROS activity

- **DMI = ↓ metabolic heat**
  - ↓ Growth
  - ↓ Milk production and component (prot & fat)

- **↓ Uterine blood flow – Impact on fetal development?**
- **↓ Gestation length**
Bovine Fetal Development

- Critical development windows for organs/tissues *(Reynolds et al., 2023)*
- Fetal growth – 2nd and 3rd trim (~80%)
- Alteration to maternal environment can affect organ/tissue formation and development: *fetal programming*
Maternal environment and fetal development (programming)

DOHaD - Developmental Origins of Health and Disease (Barker 2004)

- Environmental factors
  - Thermal stress
  - Maternal nutrition
  - ART (cloning & superovulation)

- Linked to placental development and function
  - Blood flow and vascularization
  - Nutrient transporters
  - Compensatory adaptation to maternal stressors?

- Epigenetics
  - Methylation
  - Non-coding RNAs (e.g., miRNA)
  - Histone modification

(Fowden et al., 2006; Hernandez-Medrano et al., 2012; Reynolds et al., 2019; Perry et al., 2019; Cattaneo et al., 2023)
Periconception period

- 60d before conception (AI/service) to 1st trimester pregnancy (~60d post-conception)
  - Folliculogenesis (methylation)
  - Ovulation + Fertilisation
  - Embryo genome activation (8-16 cells)
  - Implantation (Feto-maternal comm – P4?)
  - Maternal recognition (IFNt / hCG)
  - Placental formation (initial anchoring)

Campbell and Webb, 2007 & Scaramuzzi et al. 2011
Maternal stress/interventions during fetal sensitive windows can have long-term effects.
Maternal stress and fetal development

• Maternal nutrition and heat stress can modify fetal development (Wu et al., 2006; Mossa et al., 2013; Hernandez-Medrano et al., 2012, 2015; Ferreira et al., 2016; Copping et al., 2020; Ouellet et al., 2020)
  - ↓ fetal growth
  - ↑ neonatal mortality & ↓ immune function
  - ↓ ADG and weaning weight
  - Cardio-metabolic (ins resistance) and cardio-vascular modifications, body composition (fat depot), organogenesis (gonads)

• Birth weight – not a good indicator

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**Periconception diet**

- Low
- High

![Heart weight (g)](chart)

- Male
- Female

**Biparietal Diameter is Affected by Preconception Diet**

- Low
- High

![BPD at g60](chart)

Hernandez-Medrano et al., 2015
### Maternal nutrition and fetal programming - Summary of previous research (Perry, Copping, Hernandez-Medrano in preparation)

<table>
<thead>
<tr>
<th>Treatment Period</th>
<th>Diet comparison</th>
<th>Pregnancy Fetus</th>
<th>Birth</th>
<th>Neonate-weaning</th>
<th>Puberty</th>
<th>Reproductive</th>
<th>Adult Productive</th>
<th>Carcass</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preconception</td>
<td>L vs H</td>
<td>↓ fetal &amp; organ size</td>
<td>↑ blood flow</td>
<td>= Birthweight</td>
<td>↑T4 (males)</td>
<td>↓ Sperm quality (motility, conc &amp; % normal)</td>
<td>= ADG = LW = FCR/FE</td>
<td>↓ tenderness</td>
</tr>
<tr>
<td>Preconception to 1st trimester</td>
<td>L vs H</td>
<td>↓ fetal &amp; organ size</td>
<td>↑ feed intake</td>
<td>↑T4 (males)</td>
<td>↑ feed intake</td>
<td>↑ appetite neuropeptides (gene)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st</td>
<td>L vs H</td>
<td>↓ fetal size</td>
<td>↓ Placenta number</td>
<td>↑Placental Trophectoderm</td>
<td>= Birth weight (m = f)</td>
<td>milk intake ↑(2yo) / (3yo) ↑males</td>
<td>ADG ↑(2yo) / = (3yo)</td>
<td>↑colostrum Ig</td>
</tr>
<tr>
<td>1st to 2nd</td>
<td>L vs H</td>
<td></td>
<td></td>
<td>↑IGF-1 (males)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd</td>
<td>L vs H</td>
<td>↓birth weight</td>
<td>↓placenta weight</td>
<td>↓dystocia</td>
<td>↓ ADG</td>
<td>↓weaning weight</td>
<td>↓mortality</td>
<td>↓ovarian follicle density</td>
</tr>
</tbody>
</table>

- B taurus x B indicus heifers (2 & 3yo)
- 4 separate experiments (300+ animals)

Maternal heat stress and offspring reproduction

(Birkenhagen B, Gashorn H, Hernandez-Medrano JH – preliminary results)

- Scoping review – AMH and reproductive parameters
  - HS vs non-HS
- Mostly dairy cattle - dry period
  - 2-8 wk before calving
- Transgenerational effects - dairy and beef

<table>
<thead>
<tr>
<th>Pregnancy stage</th>
<th>Stage affected</th>
<th>Adult Reproductive*</th>
<th>Transgenerational*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periconception</td>
<td></td>
<td>↑CCI</td>
<td>↓ lifetime milk yield</td>
</tr>
<tr>
<td>1st</td>
<td>=birth weight</td>
<td>↓CFS</td>
<td>= PR (restricted vs control nutrition) (Roberts et al., 2016)</td>
</tr>
<tr>
<td>2nd</td>
<td>=birth weight</td>
<td>↑SPC</td>
<td>↑culling rate</td>
</tr>
<tr>
<td>3rd</td>
<td>↓pregnancy length, ↓organ growth (liver, heart, thymus, adrenals, ovaries) – m ≠ f, ↓immunologic response (cells &amp; cytokines), ↓IgG absorption &amp; ↑yield &amp; IgGcolostrum (parity), ↓weaning weight, ↓thermoregulation, ↑/↓glucose clearance, ↓insulin clearance (sex effect), ↑cortisol, ↓mammary glands</td>
<td>↑age @ 1st calving, ↓PR, ↑CCI, ↑SPC, ↑RB, ↓AMH, ↓AFC, ↓ovary size</td>
<td>↑age at puberty</td>
</tr>
<tr>
<td>Trimester</td>
<td></td>
<td>↑culling rate</td>
<td>↓milk yield (1st, 2nd, 3rd lact)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑culling rate</td>
<td>↓mammary alveoli + ↑connective tissue</td>
</tr>
</tbody>
</table>

CCI = Calving to conception; CFS = Calving to first service; SPC = service per conception; RB = repeat breeders

*Database studies

With information from Cattaneo et al., 2023; Ahmed et al., 2021; Dado-Senn et al., 2021, 2020; Davidson et al., 2021; Laporta, 2021; Recce et al., 2021; Chavez et al., 2020; Ouellet et al., 2020; Toledo et al., 2020; Shivley et al., 2018; Akbarinejad et al., 2017; Pinedo & De Vries, 2017; Monteiro 2016a,b, 2014; Roberts et al., 2016; Brown et al., 2015; Karimi et al., 2015; Strong et al., 2015; Tao et al., 2014, 2012
Maternal stress and reproductive function

- Infertility vs low fertility
- Decrease of ovarian reserve *(Sullivan et al., 2009; Mossa et al., 2013; Akbarinejad et al., 2017)*
  - Primordial follicles
  - AMH
  - AFC

- Reproductive parameters – 1\textsuperscript{st}/2\textsuperscript{nd} vs subsequent breeding seasons *(Cattaneo et al., 2023)*
  - Age at puberty
  - Age at first calving
  - Calving to conception interval
  - Longevity/culling rate
Conclusion

• Maternal stress impacts fetal development (organs and tissues) with long-term effects on offspring performance
  • As early as peri-conception and throughout pregnancy
  • Birth weight not always affected, but other effects associated to specific organ developmental windows

• Foetal programming seems to be an adaptive strategy, preparing fetus for a challenging environment (low nutrient availability)
  • Controlled by placenta (blood flow) and epigenetics
  • Adaptive or maladaptive – Animal vs production system?
  • Transgenerational effects = advantage or disadvantage?

• Similar effects between different types of stressors (nutrition or thermal stress)
  • Additive stressor effects – pasture-based systems = simultaneous stressors?
  • Common solutions?

• Economic impact – indirect costs most important due to loss of productivity

• Beef vs dairy – unbalance in research
  • Thermal – mostly dairy and some feedlot research
Thank you!

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