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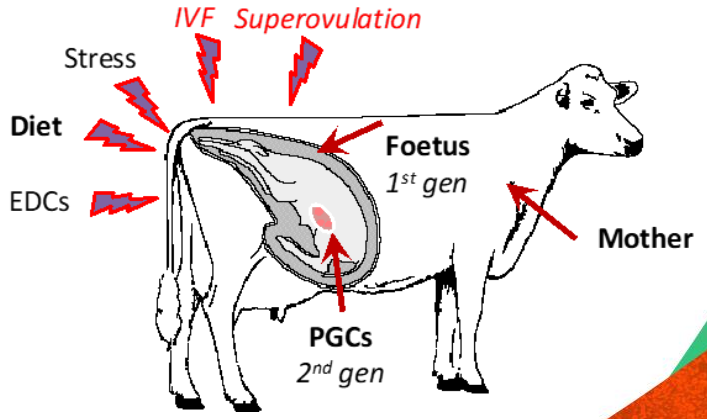
Extreme Weather Impact on Female *Offspring* Fertility

Maternal heat and nutrition stress and offspring reproduction



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Conflict of interest

- No conflict of interests to disclose

Outline

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- 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

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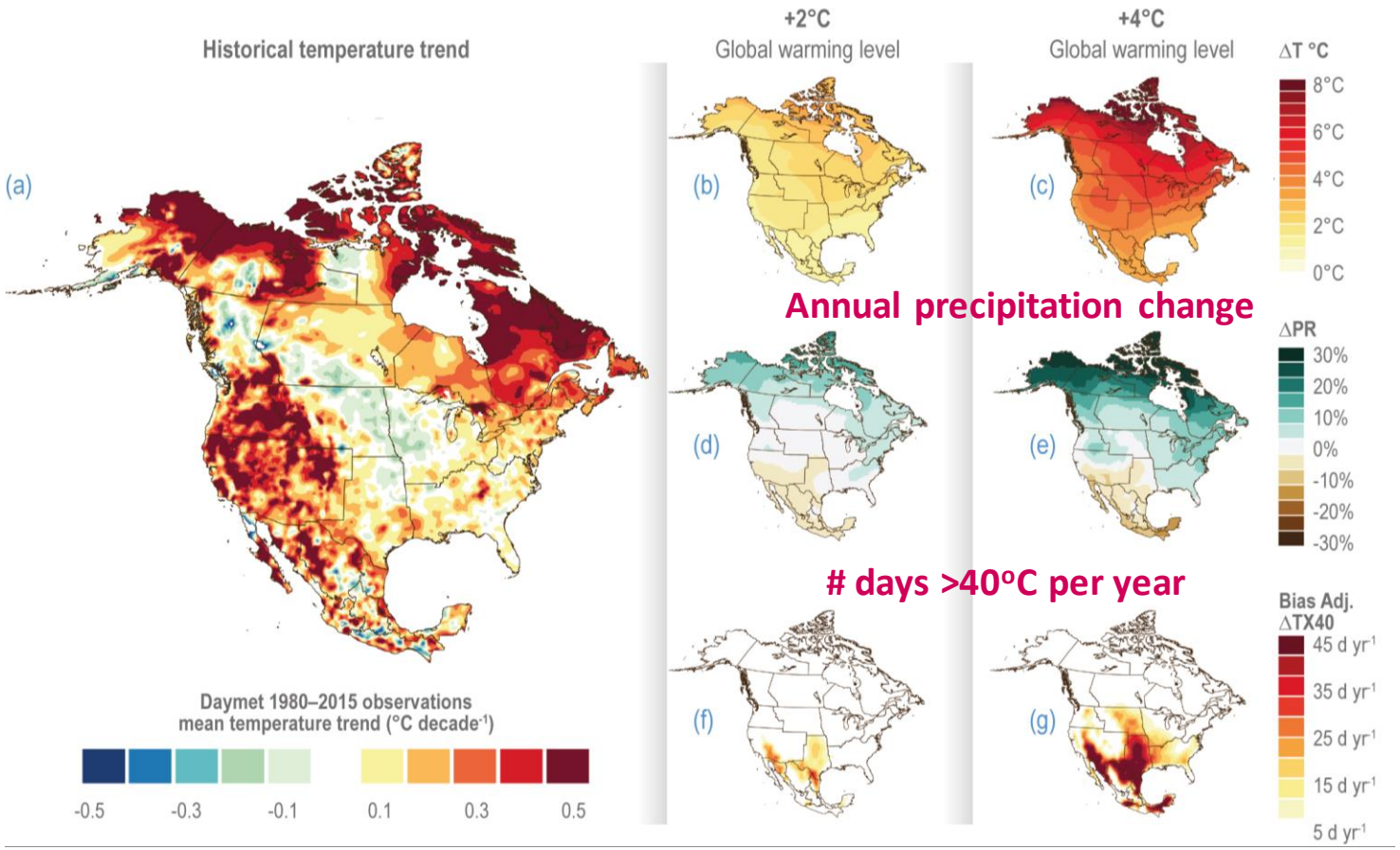
- Maternal stress occurring before conception (breeding) and during pregnancy affects placenta and organ formation with long lasting effects for offspring health, productive and reproductive performance

- 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



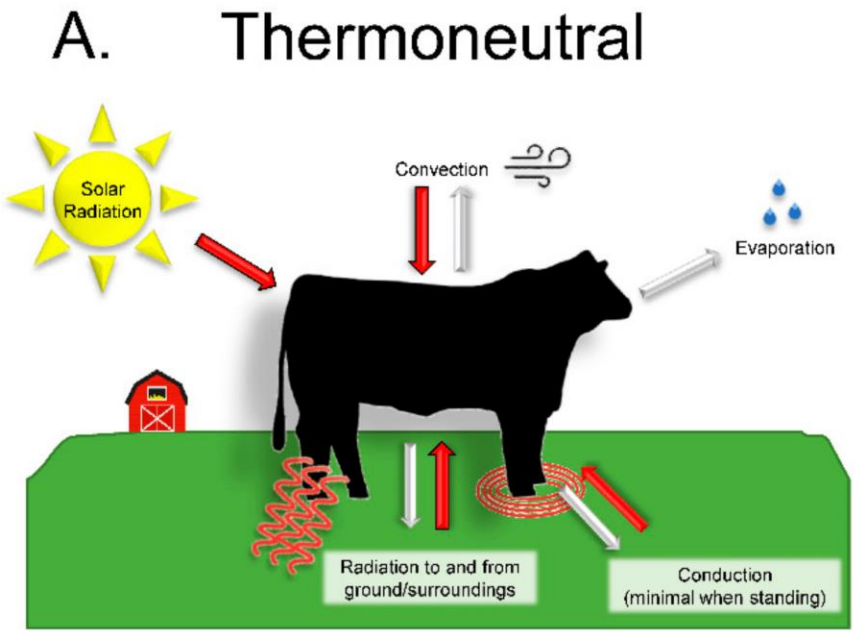
Hicke, et al 2022: North America.
In: Climate Change 2022: Impacts, Adaptation and Vulnerability. WGII – 6th Assessment IPCC

A warming thought!

- 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



Most and Yates, 2021

Effects of Heat stress

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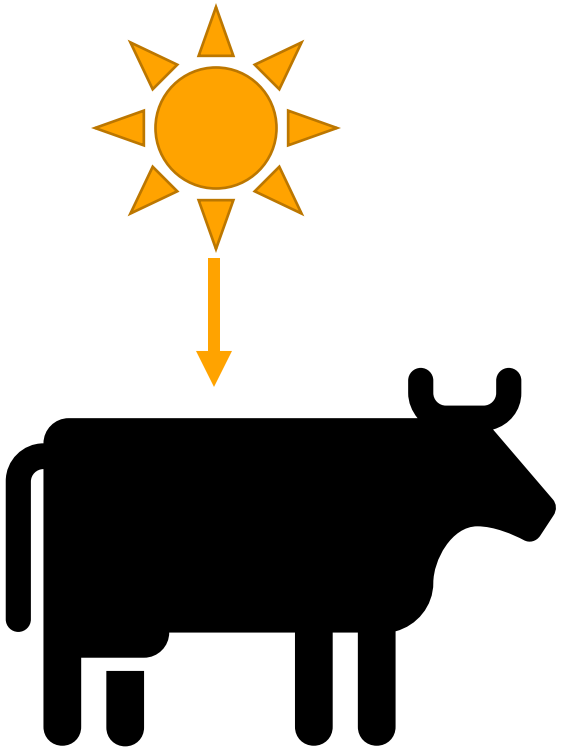

↑ rectal (core) temperature

↑ respiration rate

↓ dry matter intake, rumination

Endocrine changes

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

Reproduction - Female
↓Estrus behavior
↓Ovarian function (foll & CL)
↓Oocyte & embryo quality
↑Embryo loss
Impaired implantation
↓Uterine blood flow – Impact on fetal development?
↓ Gestation length

Reproduction - Male
Impaired spermatogenesis
↓ Sperm quality
Impaired scrotal normothermia

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

- 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

Bovine Fetal Development

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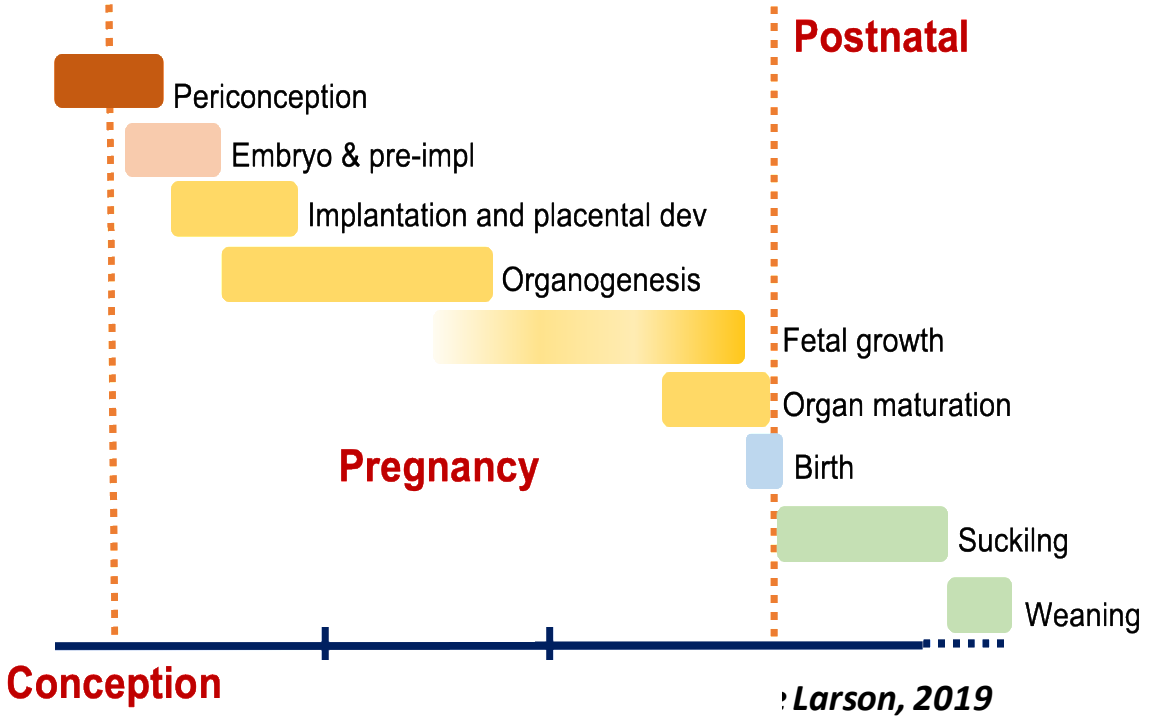
- Critical development windows for organs/tissues *(Reynolds et al., 2023)*
- Fetal growth – 2nd and 3rd trim (~80%)
- Alteration to maternal environment can affect organ/tissue formation and development: *fetal programming*



Maternal environment and fetal development (programming)

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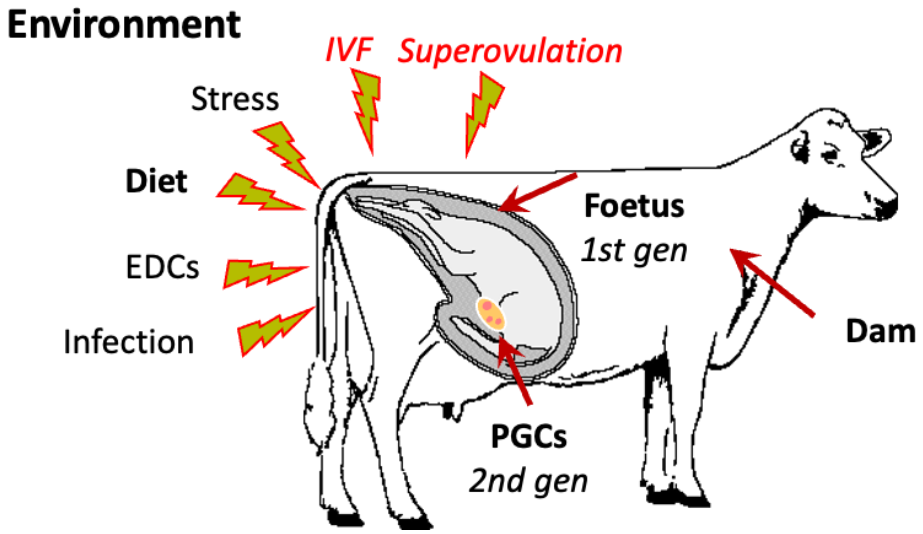
DOHaD - Developmental Origins of Health and Disease (Barker 2004)



- 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

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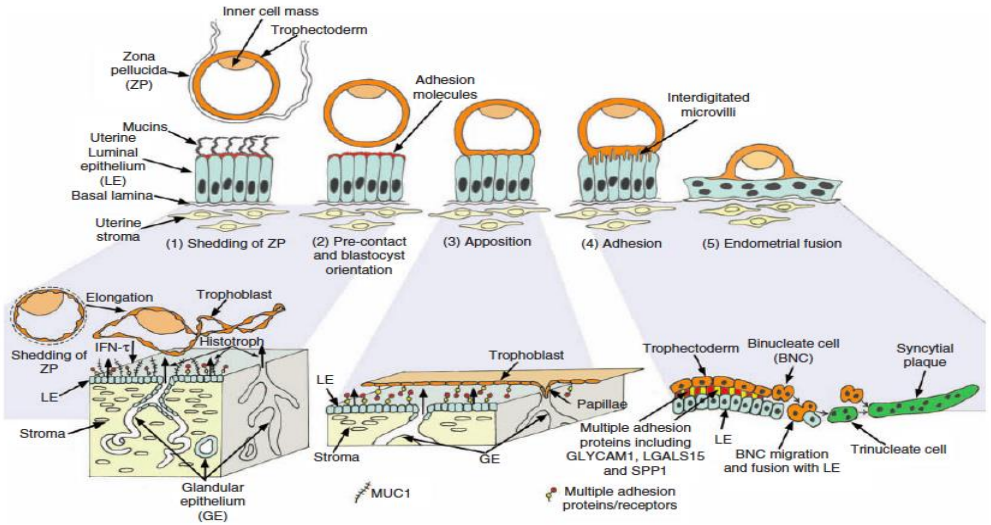
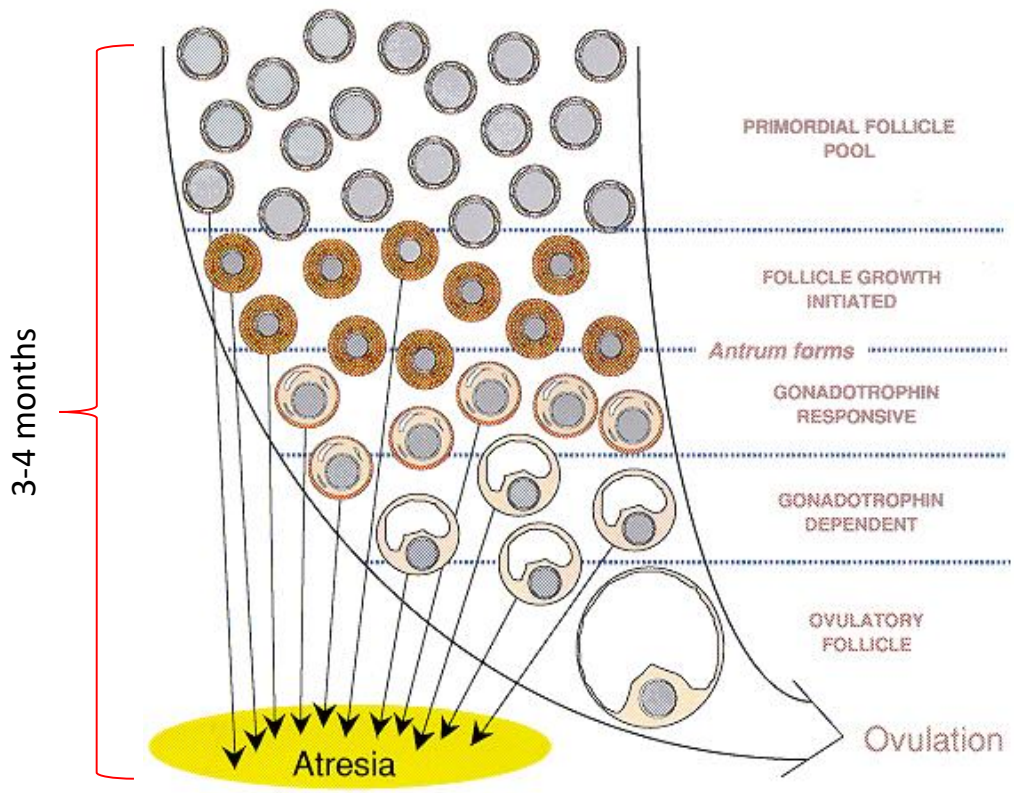
- 60d before conception (AI/service) to 1st trimester pregnancy (~60d post-conception)
  - Folliculogenesis (methylation)
  - Ovulation + Fertilisation
  - Embryo genome activation (8-16 cells)
  - Implantation (Feto-maternal comm – P4?)
  - Maternal recognition (IFNt / hCG)
  - Placental formation (initial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



Spencer et al., 2007



AMH
BMPs
GDFs
KL &c-kit
Act
etc∞

LH
FSH
E2
InhA

Campbell and Webb, 2007 & Scaramuzzi et al. 2011

Early embryo development & Implantation

So…

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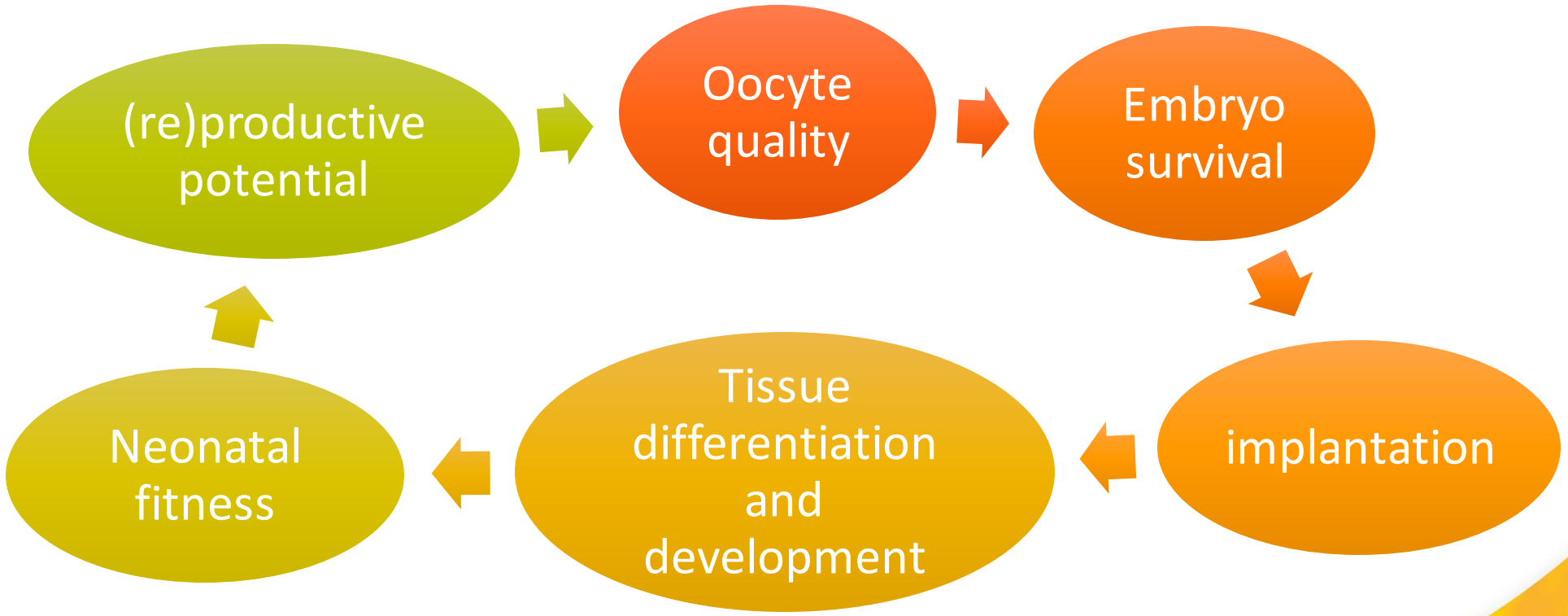
Maternal stress/interventions during fetal sensitive windows can have long-term effects



Maternal stress and fetal development

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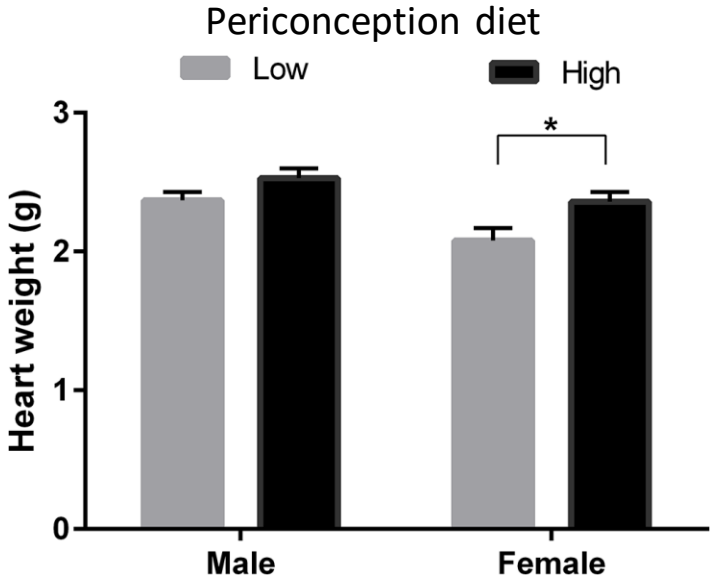

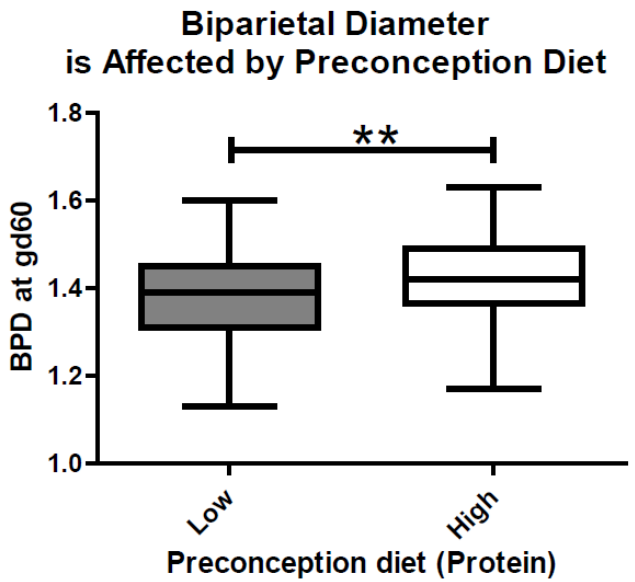

Hernandez-Medrano et al., 2015

- 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

Maternal nutrition and fetal programming - Summary of previous research (*Perry, Copping, Hernandez-Medrano in preparation)*

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Treatment Period		Diet comparison	Stage affected						
			Pregnancy Fetus	Birth	Neonate-weaning	Puberty	Adult Reproductive	Adult Productive	Carcass
Preconception		L vs H	↓ fetal & organ size ↑blood flow	= Birthweight ↓T4 (males)	↑T4 (females)	↑Age at puberty	↓ Sperm quality (motility, conc & % normal)	=ADG =LW =FCR/FE	↓ tenderness
Preconception to 1st trimester		L ⇄ H	↓ fetal & organ size		↑feed intake ↑T4 (males)			↑feed intake ↑appetite neuropeptides (gene)	
Trimester	**1st**	L vs H	↓ fetal size	↓ Placentome number ↑Placental Trophectoderm =Birth weight (m = f)	milk intake ↑(2yo) / (3yo) ↑males ADG ↑(2yo) / =(3yo) ↑colostrum Ig ↓ IFNg (males) ↑antibiotic use				muscle size ↑(2yo) steers /↓(3yo) bulls fat content ↓(2yo) / ↑(3yo) ↓ tenderness ↓EMA (bulls)
	1st to 2nd	L ⇄ H			↑IGF-1 (males)				
	2nd	L vs H		↓birth weight ↓placenta weight ↓dystocia	↓ ADG ↓weaning weight ↓ mortality		↓ovarian follicle density		

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

With information from Copping et al., 2021, Copping et al 2020a,b, Hernandez-Medrano et al.,2015, Copping et al., 2014, Copping et al., 2017, Alverenga et al., 2016, Sullivan et al., 2010, Micke et al., 2010, Micke et al., 2011., Micke et al., 2015,Miguel-Pacheco et al 2016, Perry et al 1999.

Maternal heat stress and offspring reproduction

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

- 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

***Database studies**

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

Pregnancy stage		Stage affected						
		Pregnancy Fetus	Birth	Growth	Puberty	Adult		Transgenerational*
						Reproductive*	Productive*	
Periconception								↓ lifetime milk yield
Trimester	**1st**		=birth weight			↑*CCI* ↓*CFS* ↑RB	↑culling rate	
	2nd		=birth weight			↑*SPC* ↓AMH ↑RB	↑culling rate	**= PR** **↓LBW** **(restricted vs control nutrition)** ***(Roberts et al., 2016)***
	3rd	↓pregnancy length ↓organ growth (liver, heart, thymus, adrenals, ovaries) – m ≠ f	↓birth weight ↓ immune response (cells & cytokines) ↓IgG absorption & ↑yield & IgG colostrum (parity)	↓ADG ↓weaning weight ↑/↓ *thermoregulation* ↑glucose clearance with ↓insulin clearance (sex effect) ↑cortisol ↓ mammary glands	↑*age at puberty*	↑age @ 1st calving ↓PR ↑*CCI* ↑*SPC* ↑RB ↓AMH ↓AFC ↓ovary size	↓milk yield (1st,2nd,3rd lact) ↓longevity ↑culling rate ↓ mammary alveoli + ↑connective tissue	↓ milk yield (daughters and granddaughters)

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

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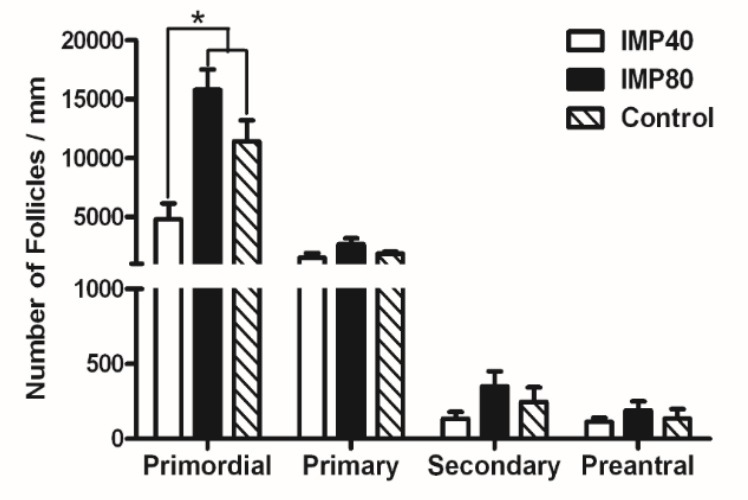
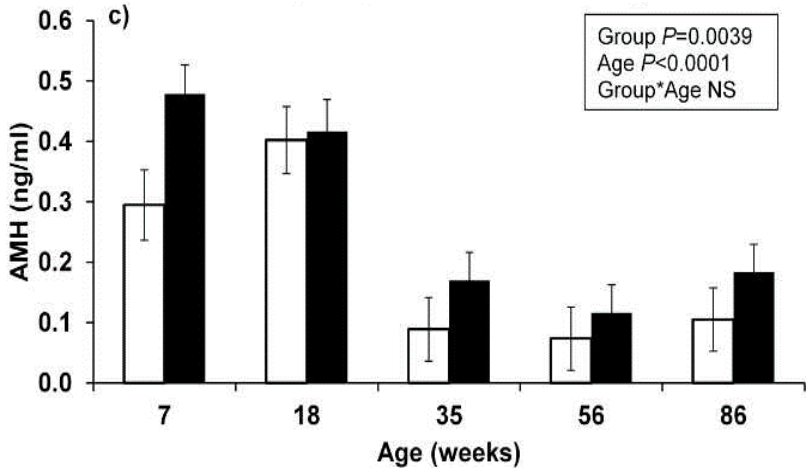


Hernandez-Medrano et al., 2012



Mossa et al., 2013

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

Conclusion

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- 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

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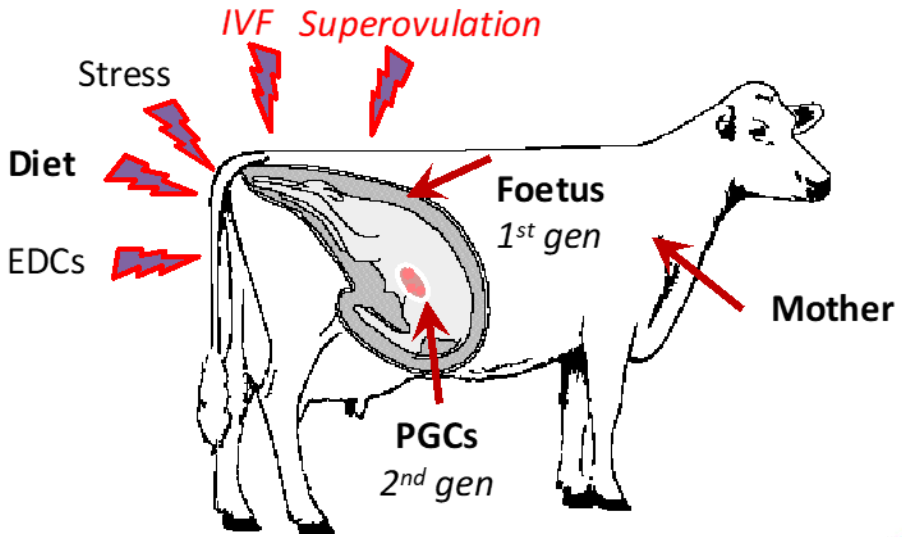
Thank you!



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