

Fetal programming of reproduction, what we know and how we manage it

Robert A. Cushman¹, Jack H. Britt², Chadwick C. Chase Jr.¹,
Andrea S. Cupp³, George A. Perry⁴, Harvey C. Freetly¹

¹USDA, ARS, U.S. Meat Animal Research Center
²North Carolina State University
³University of Nebraska-Lincoln
⁴South Dakota State University

We are really discussing developmental programming

- Fetal programming
- Nutritional programming
- Events that occur both before and after birth
- If we are going to use it for management, it is important that we understand this

The Barker Hypothesis

“Numerous animal experiments have shown that poor nutrition during periods of rapid growth in early life may permanently change the structure and physiology of a range of organs and tissues.”

Barker and Fall , 1993. Arch. Dis. Child. 68:797

Changes in epigenetic mechanisms

DNA
attagacacggc

↓

RNA
uaaucugugccg

↓

protein

Changes in epigenetic mechanisms

DNA
attagacacggc

↓

RNA
uaaucugugccg

↓

protein

Nutrition
Heat Stress

↪

Disease

Changes in epigenetic mechanisms

DNA
attagacacggc

↓

RNA
uaaucugugccg

↓

protein

Nutrition
Heat Stress

↪

Disease

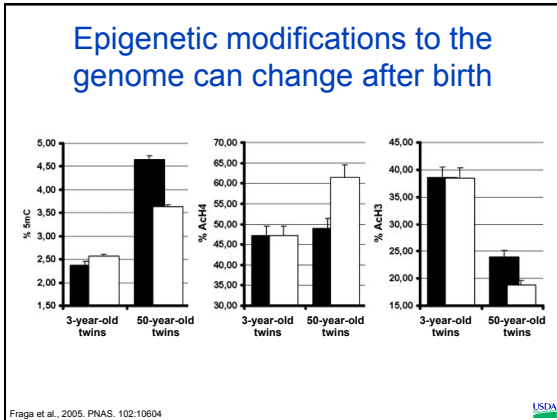
DNA
attagacacggc

↓ Methylation
Histone acetylation

RNA
uaaucugugccg

↓ MicroRNAs

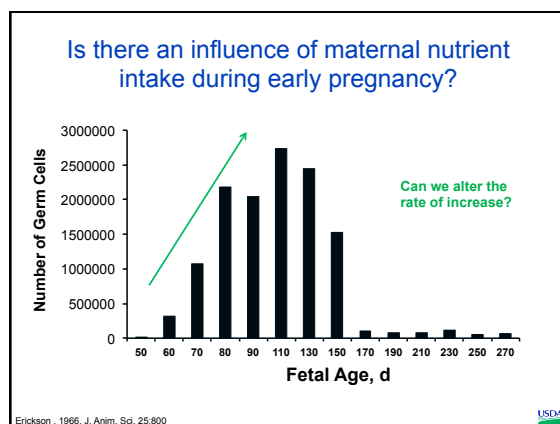
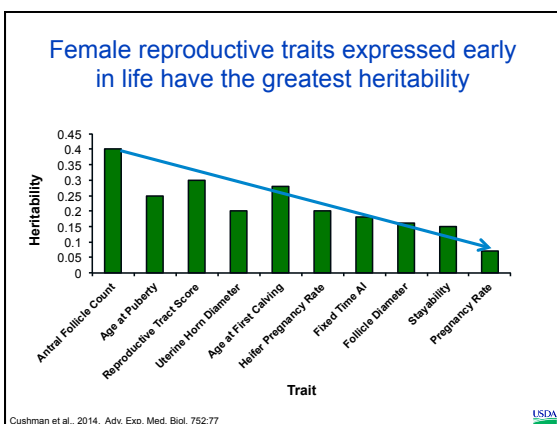
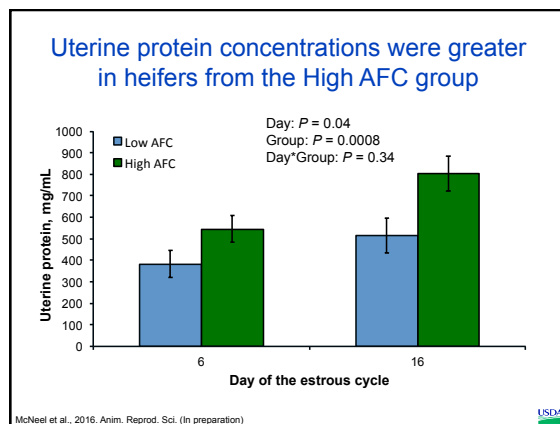
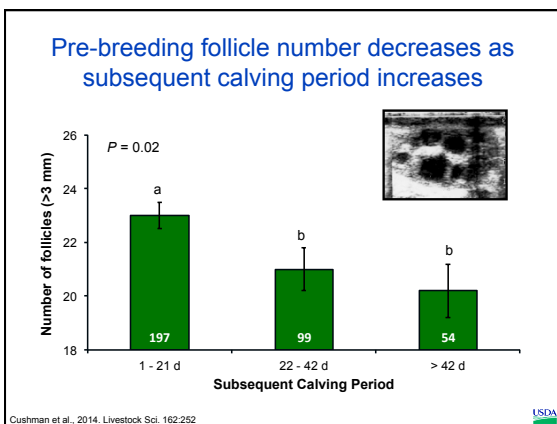
protein
or
protein

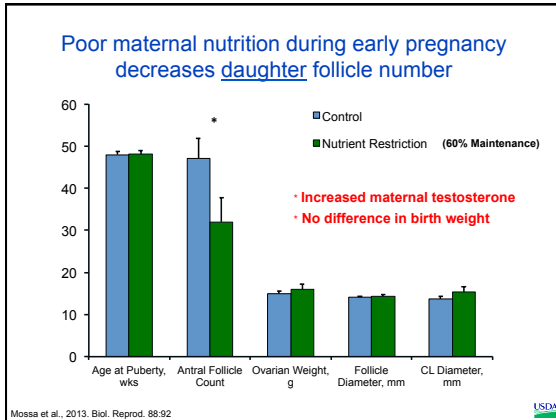


Too many times we focus on the negatives...

The other way to look at this is: "Can we apply developmental programming to improve management?"

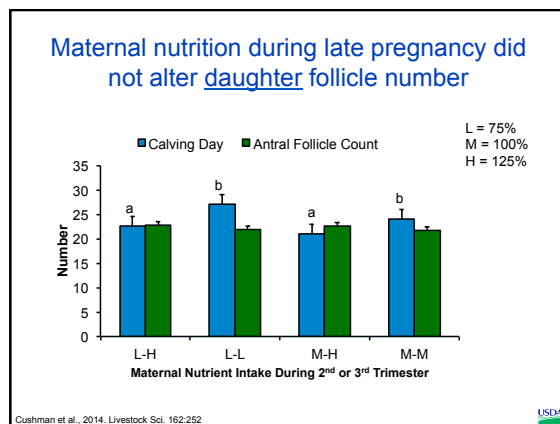
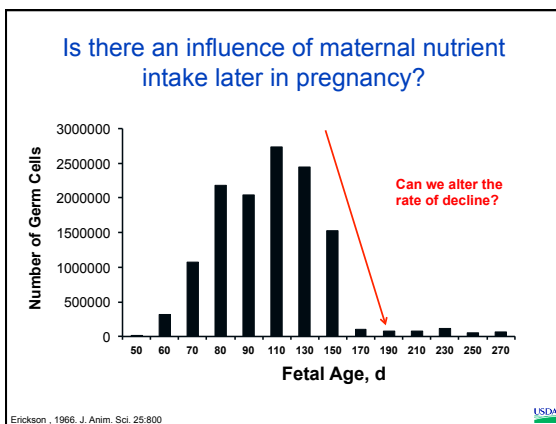
- ♦ Health
- ♦ Productivity
- ♦ Reproduction





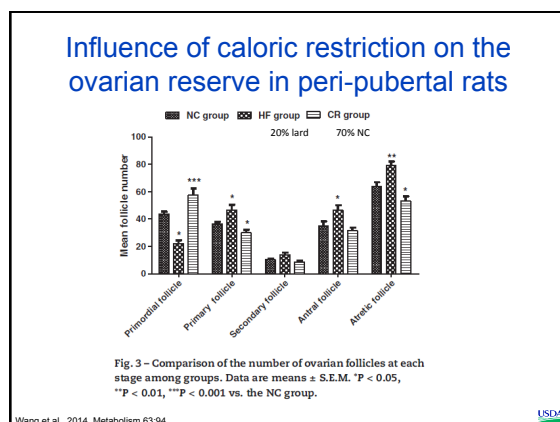
Implications

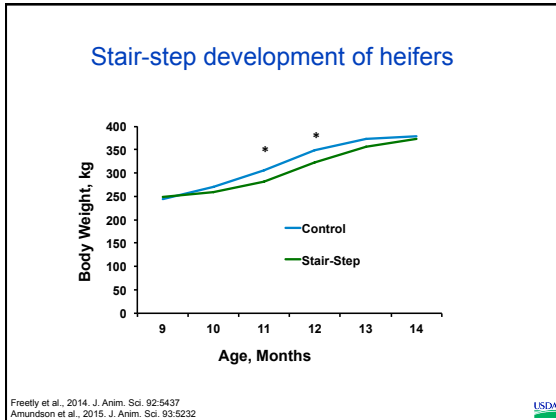
- Drought or other negative environmental impacts during the first trimester could negatively impact daughter ovarian development
- In theory, there may be ways to feed the dam during the first trimester to increase daughter germ cell numbers



Implications

- Third trimester maternal nutrient intake can positively influence heifer conception date, but it does not alter numbers of antral follicles
- Thus far, this does not help us if a drought during the first trimester has potentially decreased daughter ovarian reserves
- May not matter, because the earlier calving day could lead to increased reproductive longevity in the absence of a change in follicle number





The way we feed heifers after weaning can change the ovarian phenotype

And weaning weights were increased for the first 3 calves!!!

Diet	n	Preantral Follicle Stage		
		Primordial	Primary	Secondary
Control	6	52.4 ± 14.0	22.2 ± 4.6	3.9 ± 0.8
Stair-Step	6	112.5 ± 14.0	25.8 ± 4.6	5.6 ± 0.8
P-value		0.004	0.58	0.13

Freelty et al., 2014. J. Anim. Sci. 92:5437
Amundson et al., 2015. J. Anim. Sci. 93:5232

Implications

- Maybe the peri-pubertal period is the time when we could counter-act negative effects of limited nutrient intake during the first trimester

USDA

Oocyte quality is influenced by the environment in which it grows

Preantral follicles isolated from the ovaries of post-partum dairy cows in negative energy balance grew more slowly in a 5 day culture and resulted in fewer morphologically normal follicles than those isolated from ovaries at other stages of the production cycle

Figuerido et al., 1994. Theriogenology. 42:1303

USDA

Nutrients can change the epigenome during in vitro embryo production

- Large offspring syndrome
- Differences in muscle development
- Influence of nutrients on epigenetic mechanisms
- Instead of being afraid, can we harness this?

Crosier et al., 2002. Biol. Reprod. 67:401
Van Hoek et al., 2013. Reproduction. 145:33

USDA

How we manage it

- Change a trajectory
- Targeting an animal toward their niche in the production system
 - Sexed semen
- Programming the epigenome in embryos

USDA

Why it is challenging

- Age of the dam can influence daughter follicle number
 - Uterine or lactational?
- Another environmental input can come along and change the settings
- Can we do it consistently?



If we can...

- Then managing the epigenome could become as important as the sire we select



Questions



bob.cushman@ars.usda.gov

