Maternal Plane of Nutrition: Impacts on Fetal Outcomes and Postnatal Offspring Responses

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University of Wyoming
Ruminant Nutrition Research

Purpose

- Objectives of this review are:
  1. Summarize the current information regarding effects of maternal nutrition on fetal outcomes and postnatal offspring performance.
  2. Provide a platform to assist in the formation of additional hypotheses regarding relevant aspects of developmental programming in grazing ruminant livestock species.

Maternal Nutritional Plane and Developmental Programming

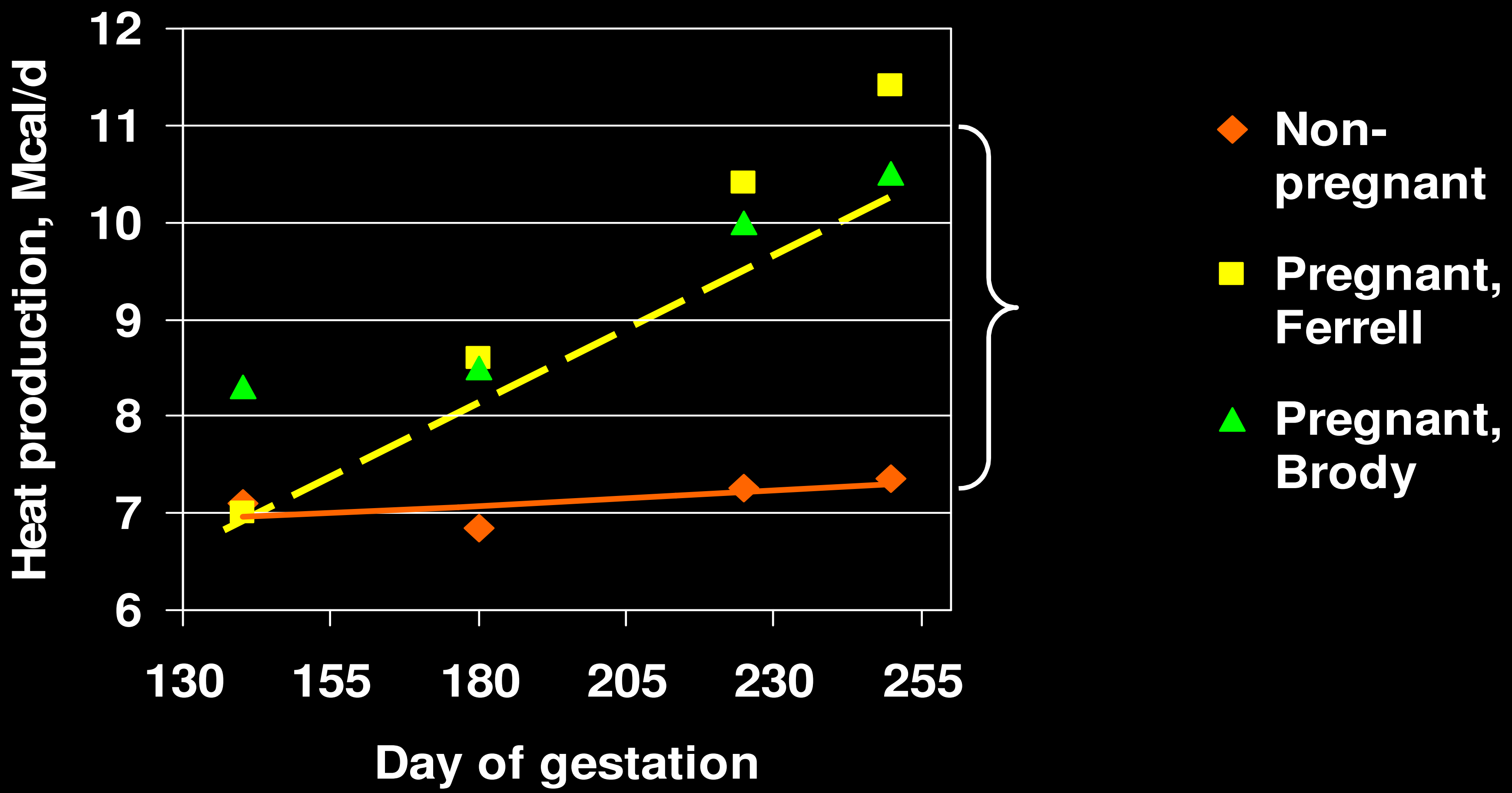
Maternal Nutritional Plane During Gestation

- Varies widely, especially in extensive production systems
- Importance to the livestock industry
  - Production system efficiency
  - Potential impacts on health, performance and product quality
  - Economic return
- Improved efficiency, profitability, and production of high quality healthy products.

Importance to Livestock Industry

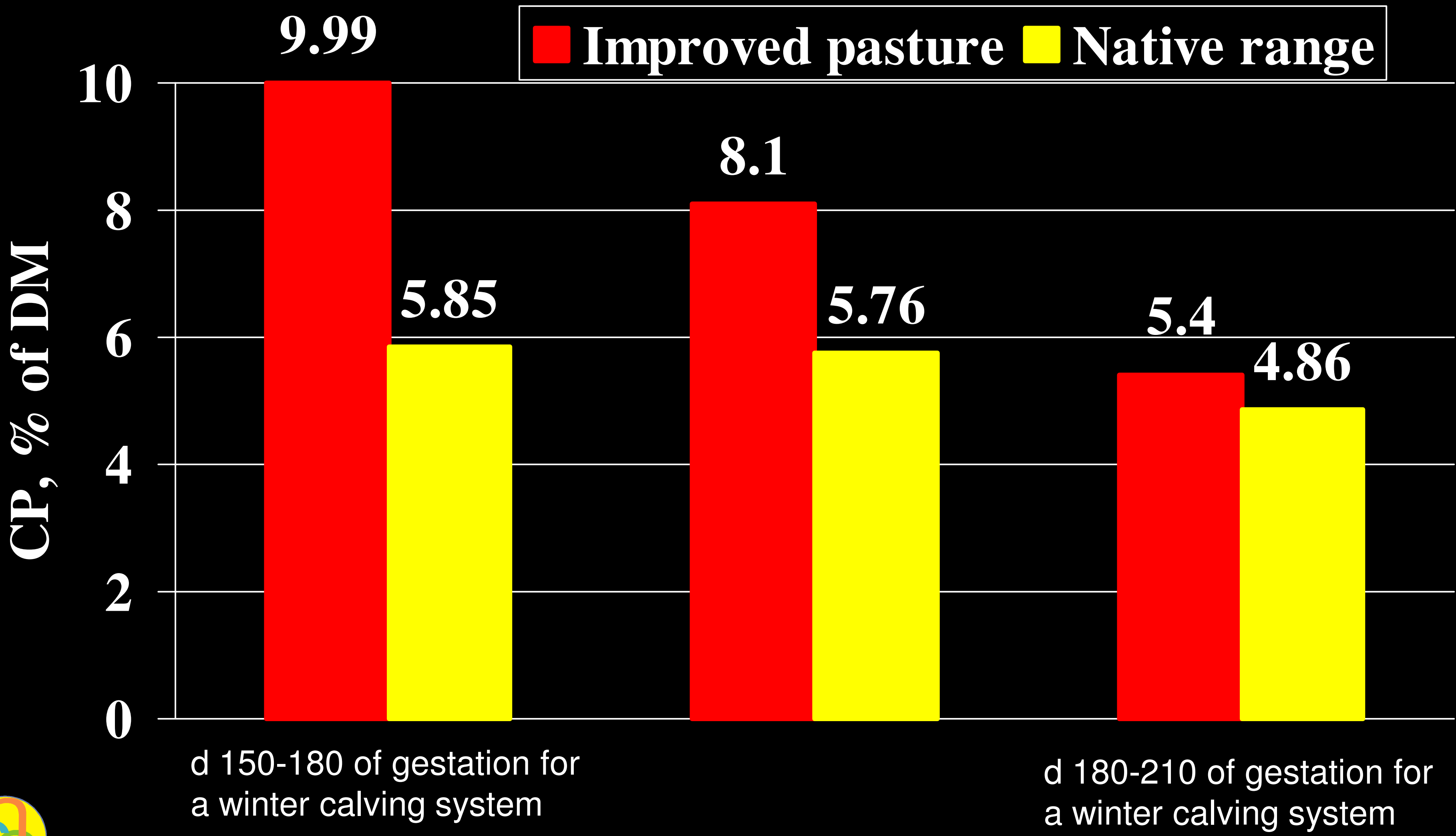
- 70 to 75 % of annual energy requirements for typical cow types are used for tissue maintenance functions.
- In ruminant livestock production systems, more energy is devoted to parent than slaughter populations.
- Feed costs represent over 60% of annual costs of production associated with cow herds.
- Most of the energy cows use and money we spend are for maintenance.

Pregnancy is Energetically Costly*

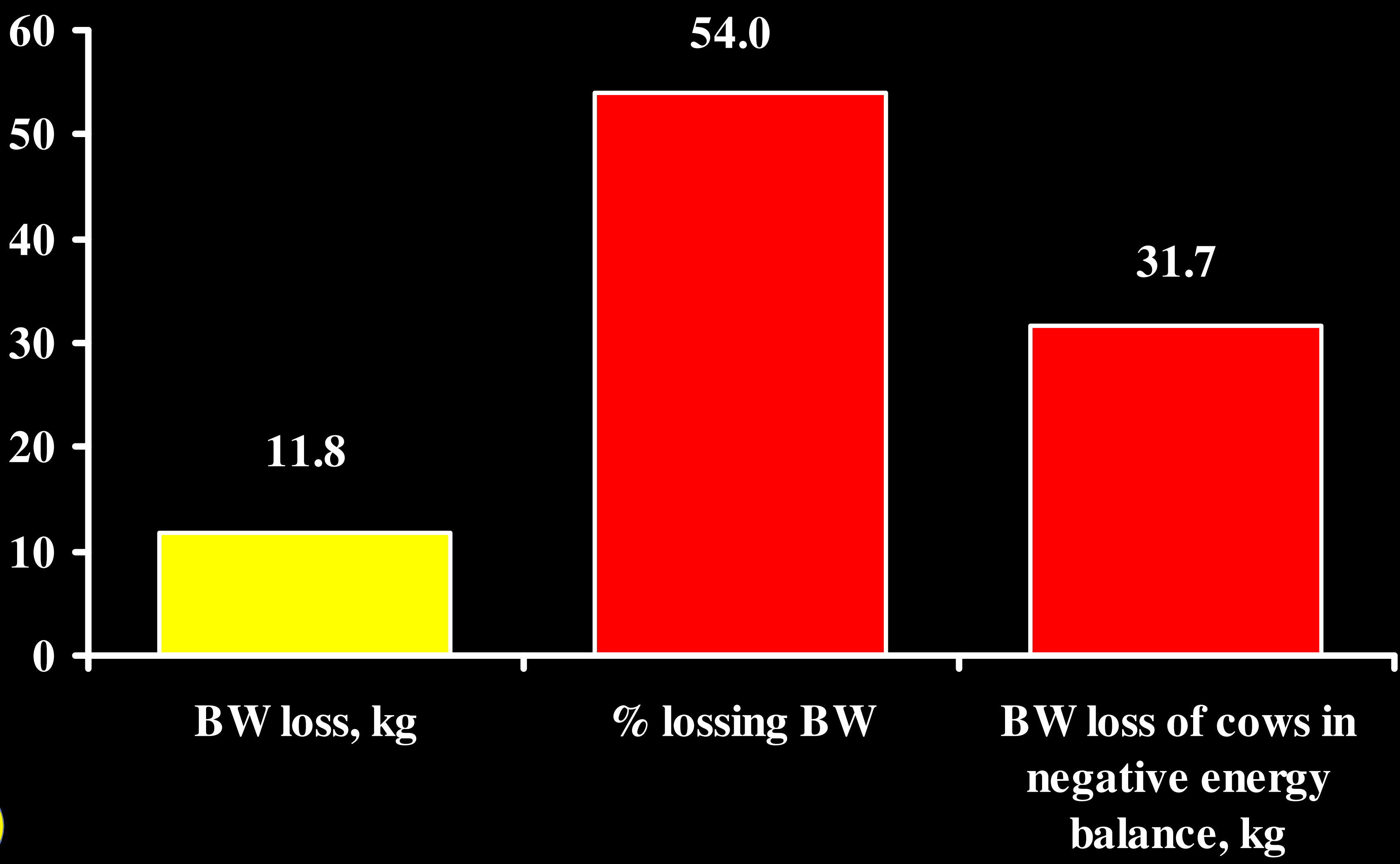


*Data of Brody (1938) and Ferrell et al. (1976) for cows – data are similar for other mammals.

Crude Protein Content of Improved Pasture and Native Range in Autumn



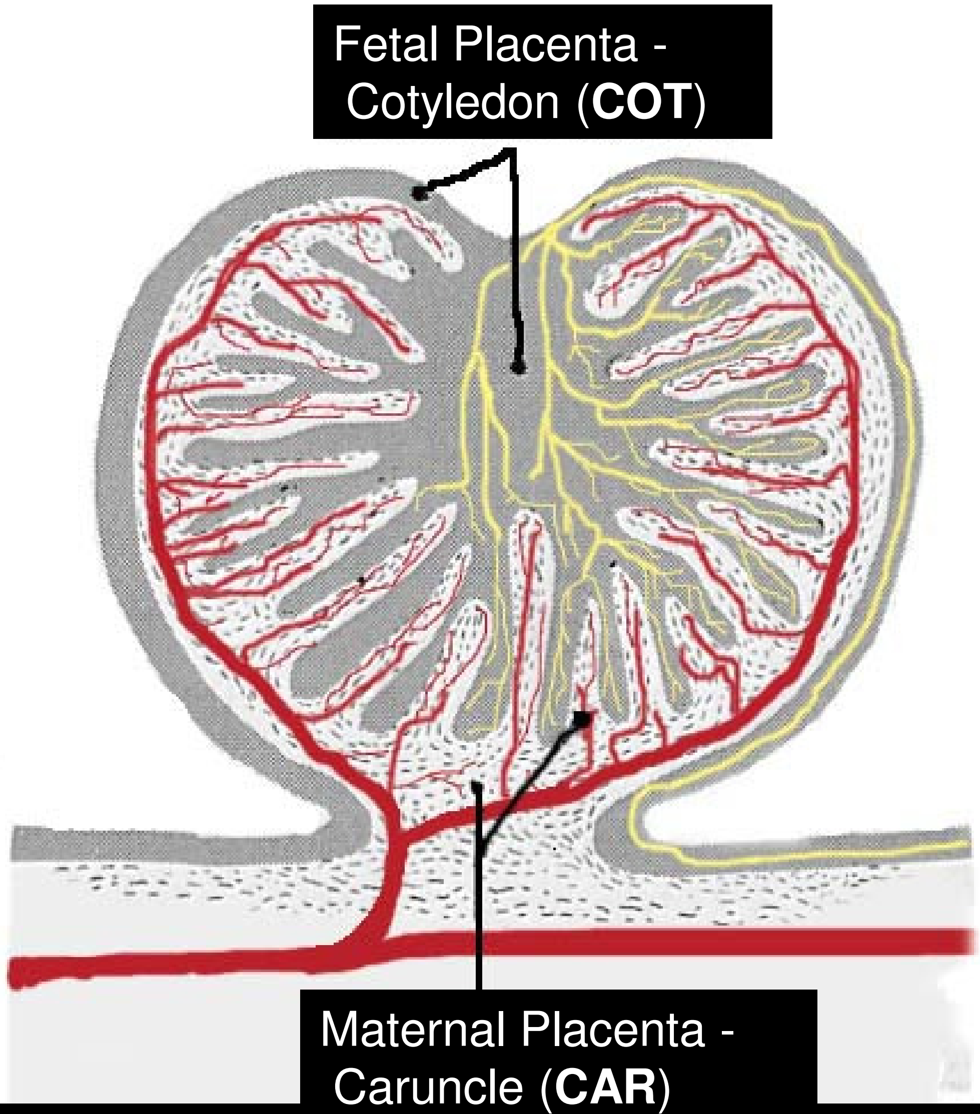
Body Weight Loss by Cows Grazing Summer Native Range



Fetal Nutrition

- Critical for normal healthy development and neonatal survival
- Placenta is one of the “Key Nutrient Transferring Tissues”
- Proper placental function is essential for adequate fetal nutrient supply
- Other key nutrient transferring tissues include maternal gut, fetal and perinatal gut, and mammary gland

Sheep Placentome

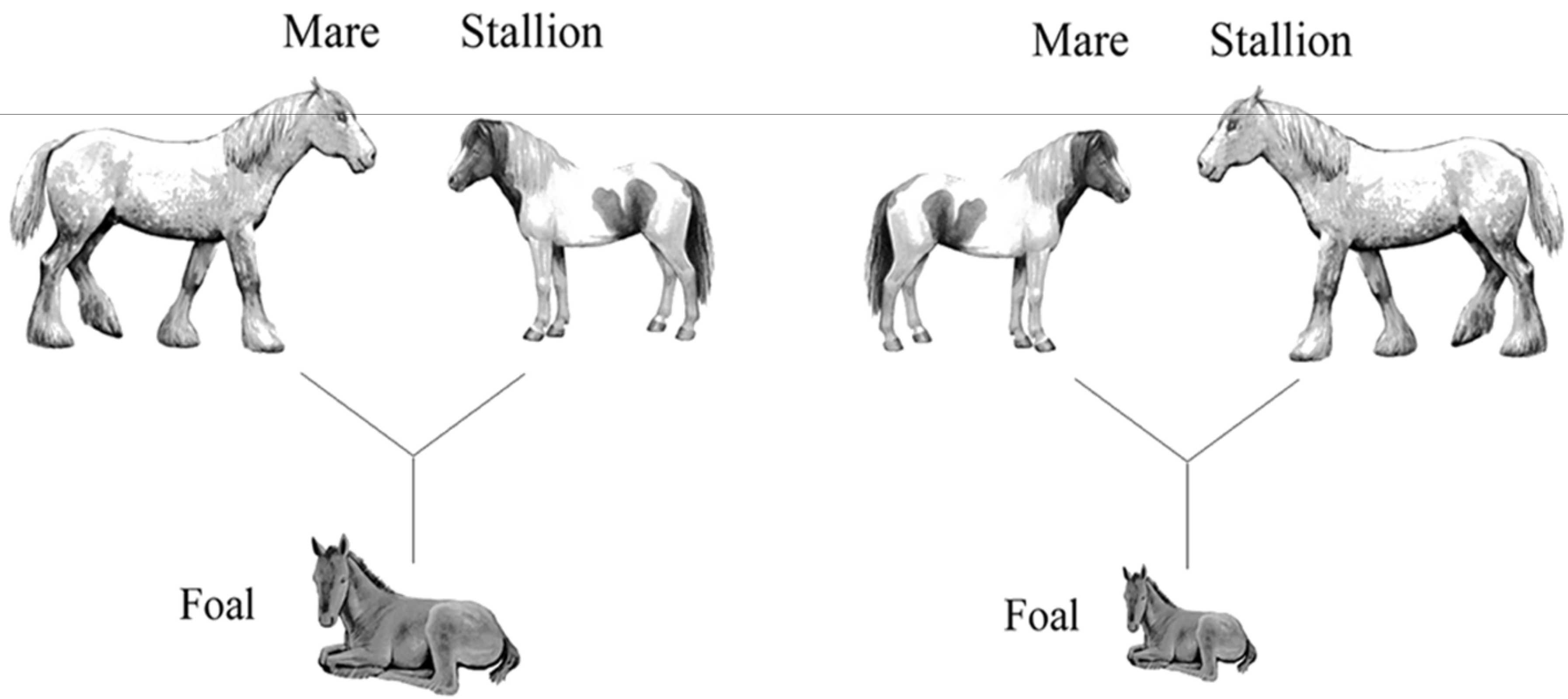


Fetal Nutrition and Development

- Adequate fetal nutrient supply is essential to proper development and a healthy start for offspring.
- Many factors can alter placental function and/or fetal nutrient supply, including:
  - Maternal nutrient restriction and/or excess
  - Placental insufficiency
  - Intrauterine growth restriction (IUGR)
  - Environmental stress
  - Number of fetuses
- Early work clearly demonstrated that intrauterine environment impacted birth weight and adult body size.

The Classical Study of Hammond and Wallace (1938)

"maternal constraint to fetal growth."



Developmental Programming and Livestock Production

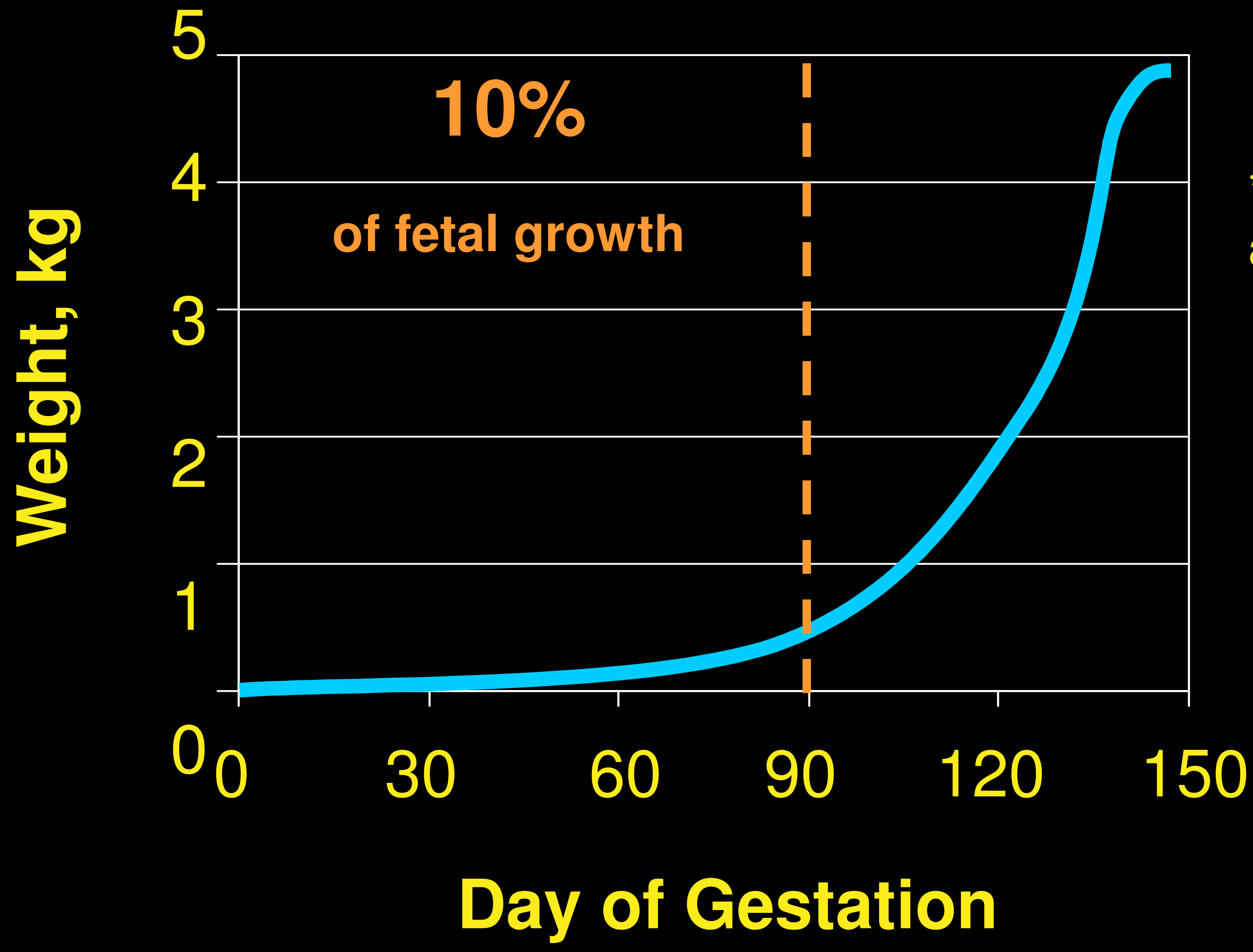
- "Developmental Programming" is also termed the "Barker Hypothesis," or, "Developmental Origins of Health and Disease"
- Developmental programming is the concept that perturbations during critical developmental periods may have long-term impacts on offspring outcomes.
- Epidemiological evidence in humans and controlled studies in animals, indicate that poor fetal growth and development can result in problems with both the neonate and during adult life (Barker, 1994; Wilson and Grundy, 2003).
  - Reduced birth weight
  - Metabolic syndrome
- Additional work with relevant livestock species has also provided evidence for developmental programming, which is often associated with IUGR (Wu, 1996).

Developmental Programming

- Intrauterine growth restriction (IUGR) can result from
  - External environment to dam
    - Temperature, hypoxia
  - Maternal environment
    - Gestational nutrition
    - Metabolic state
  - Intrauterine environment
    - Fetal number
- IUGR can result in impaired development and potential long-term consequences (Godfrey and Barker, 2000; Wu et al., 2006)
  - This can occur even when birth weight is unaffected (Ford et al., 2007; Martin et al., 2007; Larson et al., 2009)

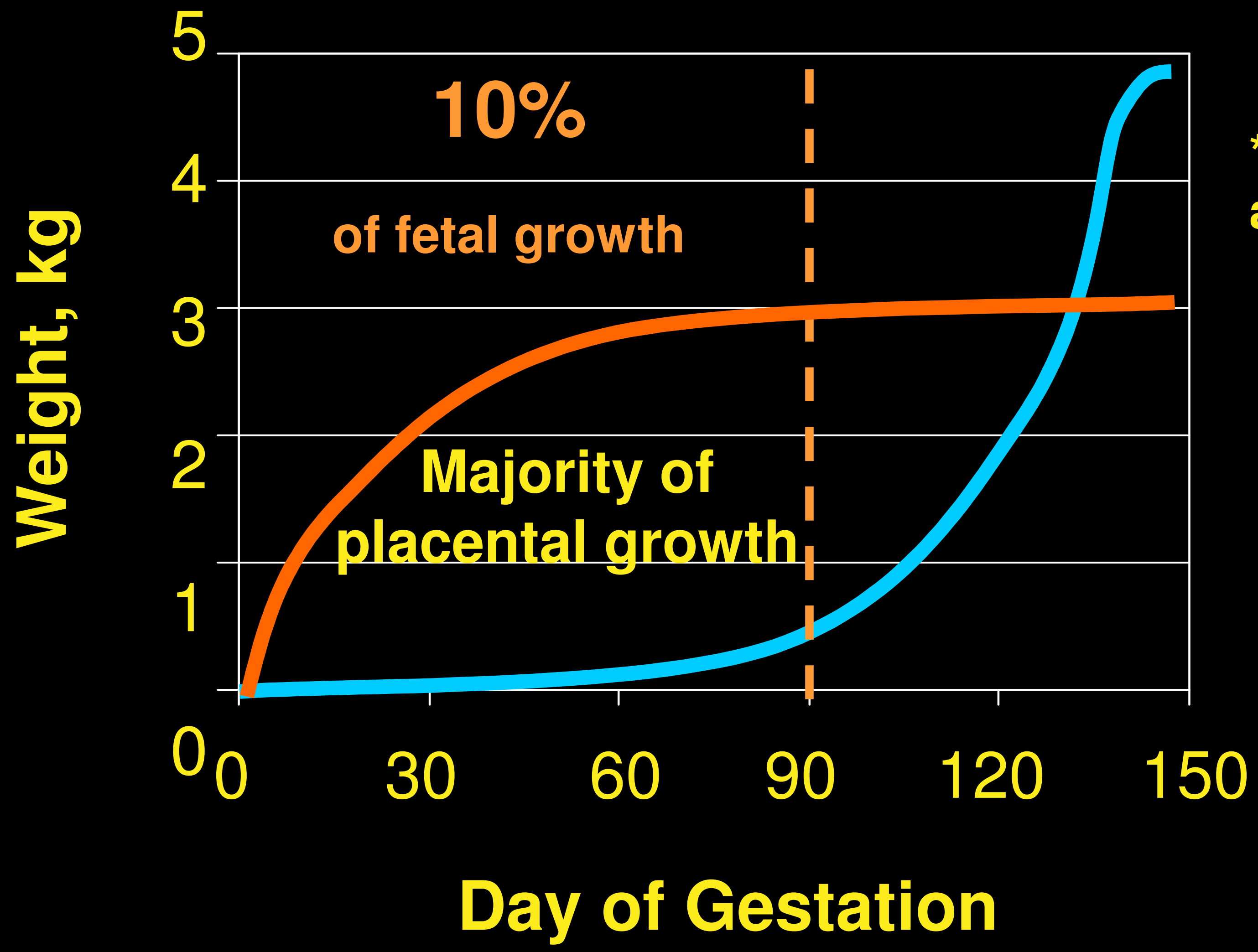
Fetal Growth and Critical Windows: Opportunities for Developmental Programming

Relationship of Fetal Weight to Stage of Gestation in Sheep*



*Ferrell et al., 1976

Fetal Growth; Relationship of Fetal and Placental Weight to Stage of Gestation in Sheep*



*Ferrell et al., 1976

Placental Development and Function

- A primary role of the placenta is to provide for physiological interface, including nutrient and waste exchange (Meschia, 1983; Reynolds and Redmer, 1995; Reynolds et al., 2010).

- Adequate placental circulation is imperative to successful pregnancy and is exemplified by observed close relationships among fetal weight, placental size, and uterine and umbilical blood flows during normal pregnancies (Reynolds et al., 2005a, 2005b, 2006; 2010).

- In the ewe, cotyledonary growth is exponential during the first 10 to 11 wk of pregnancy, with significant slowing until term (Stegeman, 1974: Ferrell et al., 1976).

- In the cow, the cotyledonary growth progressively increases throughout gestation (Reynolds et al., 1990; Vonnahme et al., 2007).

Placental Development and Function

- Uterine and umbilical blood flows, which represent the circulation to maternal and fetal portions of the placenta, respectively (Ramsey, 1982; Mossmann, 1987), increase exponentially throughout gestation, essentially keeping pace with fetal growth (Reynolds and Redmer, 1995; Magness, 1998).

- In sheep the absolute rate of uterine blood flow increases by approximately 3-fold throughout the last half of pregnancy (Meschia, 1983). Over a similar interval of gestation, uterine blood flow in cows increase by 4.5-fold (Reynolds et al., 1986).

- As summarized in the following slide, in sheep studied during late gestation, uterine or umbilical blood flows, or both, are reduced in every model of compromised pregnancy in which they have been evaluated.

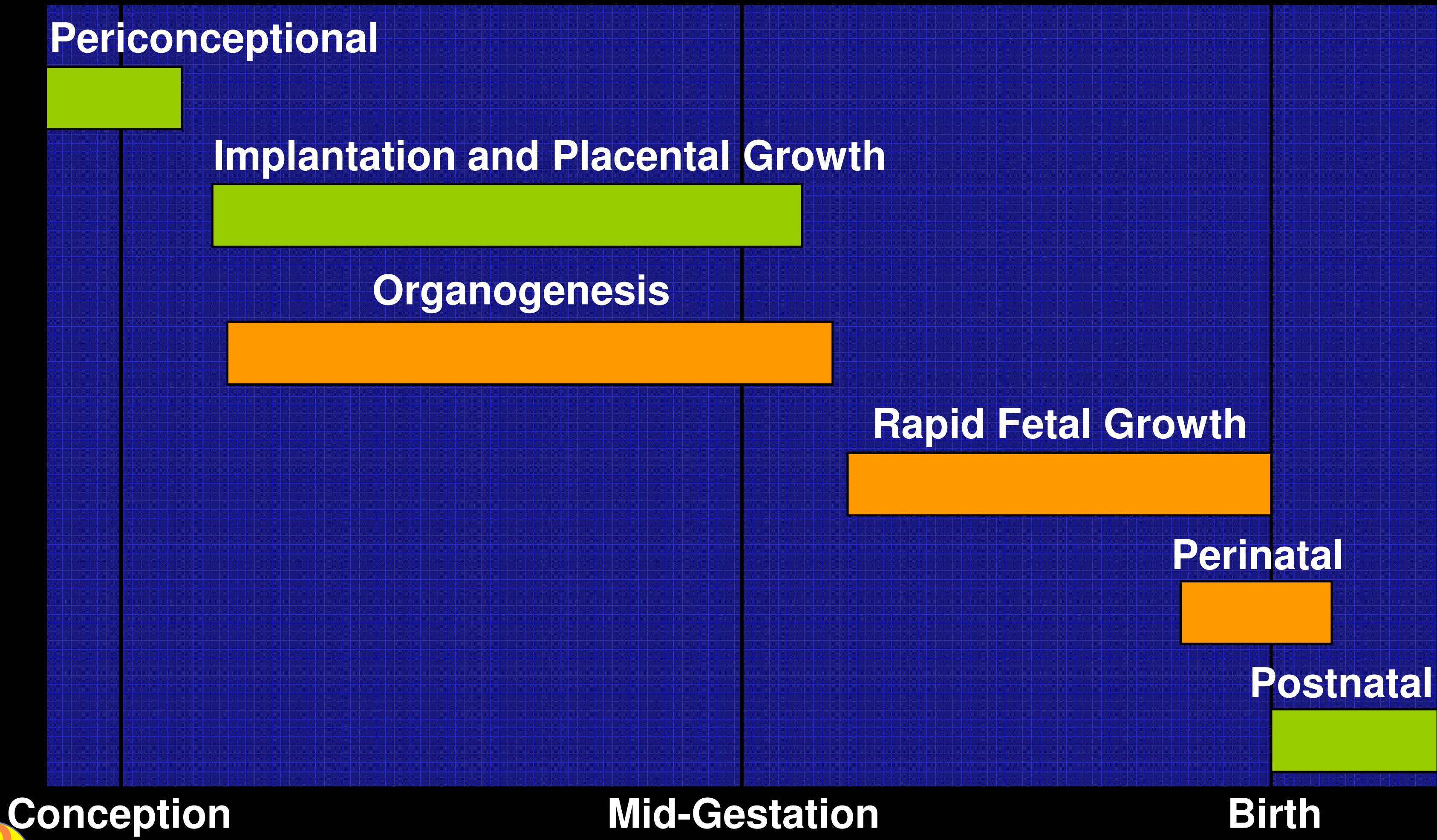
Changes in fetal and placental weights, uterine and umbilical blood flows, and placental vascularity in various models of compromised pregnancy in sheep[1]

Model	Day of Gestation[2]	Fetal Wt	Placental Wt	Uterine Blood Flow	Umbilical Blood Flow	Vascularity[3]
Overfed Adolescent	130-134	↓20-28%	↓45%	↓36%	↓37%	↓31%
Underfed Adolescent	130	↓17%	NSE[4]	----	----	↓20%
Underfed Adult	130-144	↓12%	---	↓17-32%	NSE	↓14%
Adolescent vs. Adult	135	↓11%	↓29%	----	----	----
Genotype	130	↓43%	↓47%	----	----	↑36%
Heat-stressed Adult	133-135	↓42%	↓51%	↓26%	↓60%	----
Multiple Pregnancy	140	↓30%	↓37%	↓23%	----	↓30%
High Dietary Se	135	NSE	↓24%	----	----	↑20%
Hypoxic Stress	140	NSE	----	↓35%	----	↑(cap. Area)

[1]Table adapted from Reynolds et al. (2006; 2010).
[2]Length of gestation = approximately 145 d.
[3]cap. = capillary; CAR = caruncle (maternal placenta); COT = cotyledon (fetal placenta/villus).
[4]NSE = no significant effect.

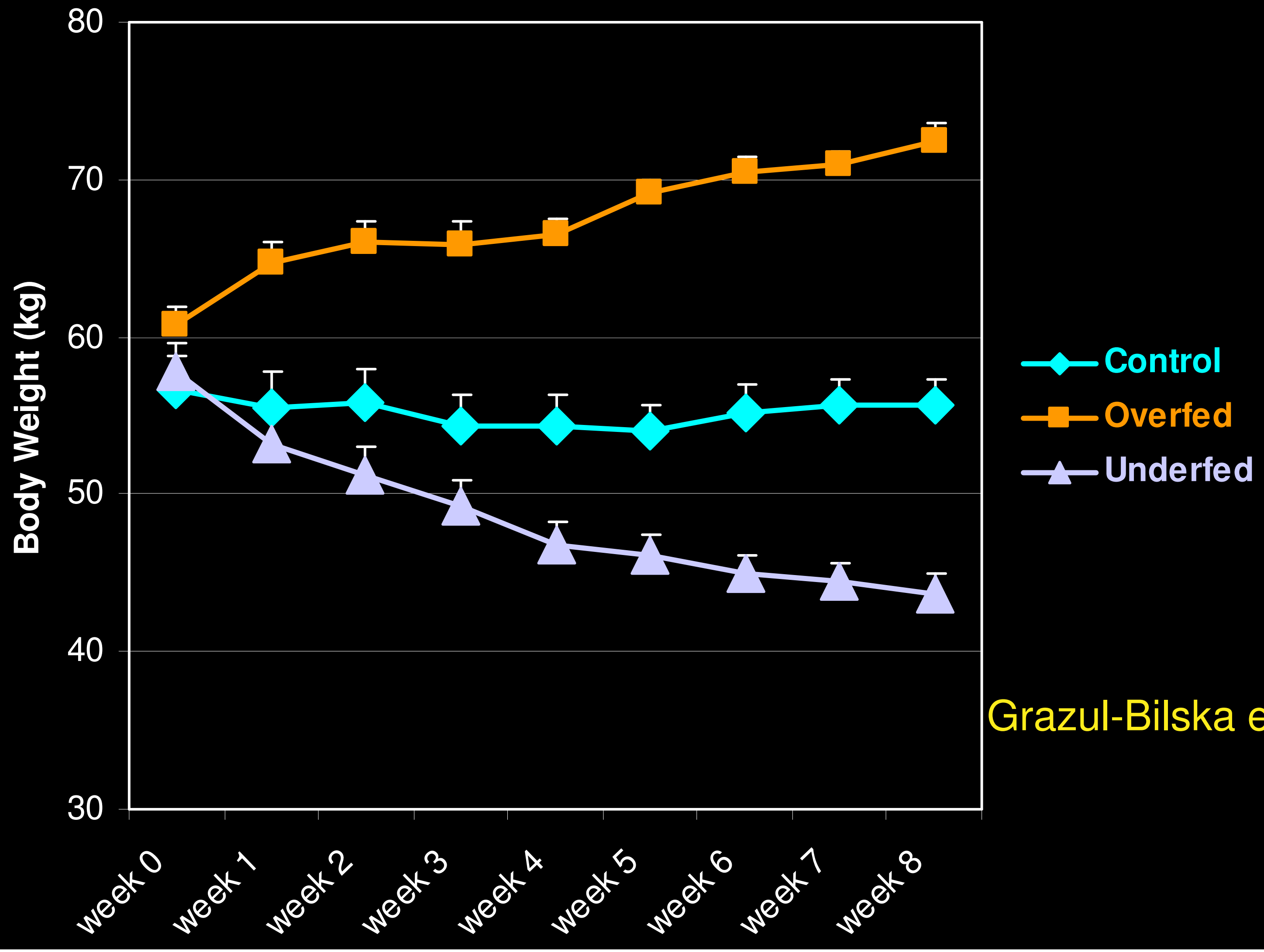
Perturbations of Fetal Development: Offspring Responses in Ruminant Livestock

Developmental Programming: Windows of Opportunity



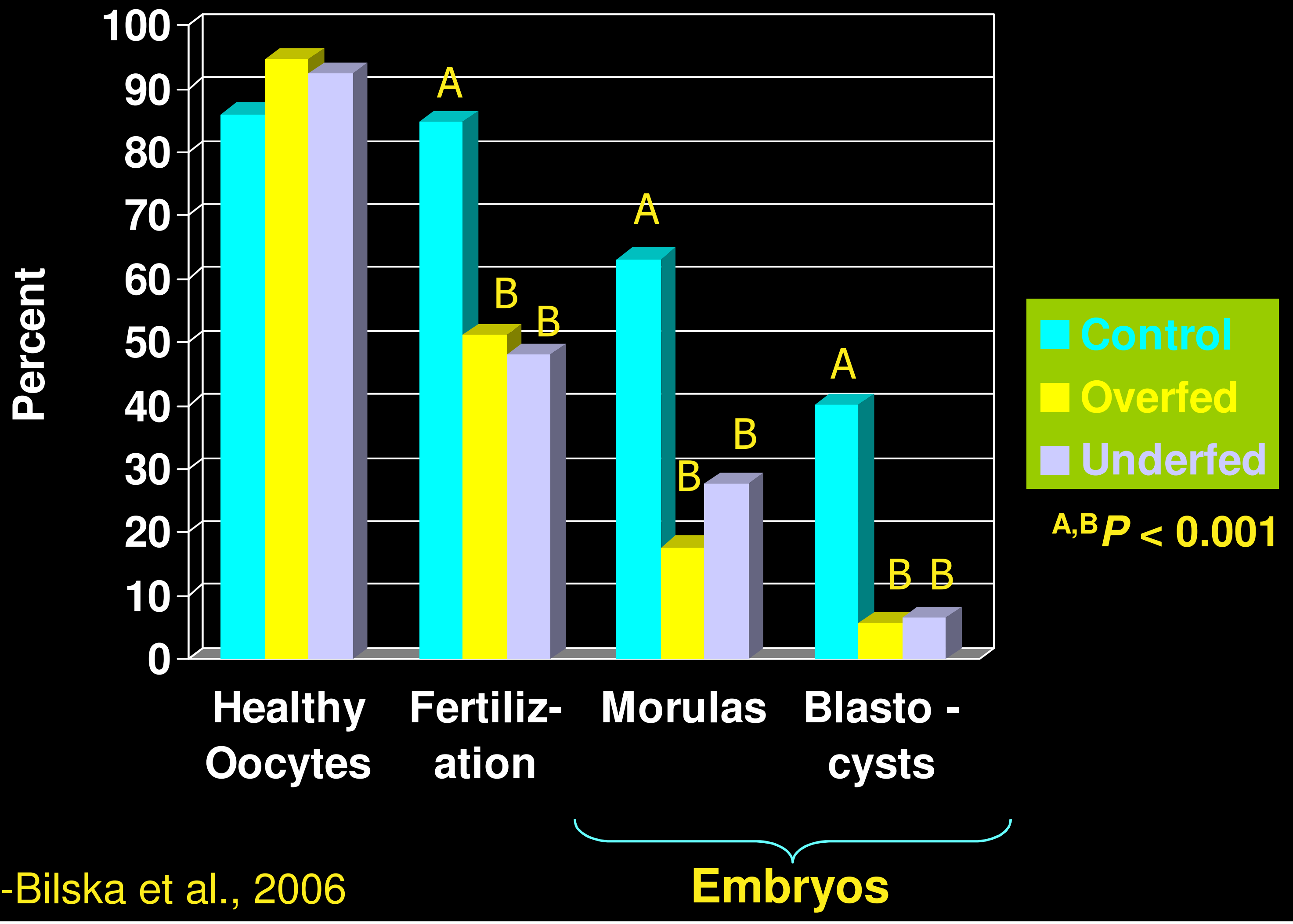
Adapted from Fowden et al., 2006

Maternal Nutrition Before Mating (Peri-Conceptional Period)



Grazul-Bilska et al., 2006

Effects of Maternal Nutrition Before Mating on Oocyte Quality



Grazul-Bilska et al., 2006

Bovine Fetal Growth

Day 0	Ovulation
Day 9-11	Hatching from the zona pellucida
Day 15-18	Critical period for maternal recognition of pregnancy
Day 18-22	Time of conceptus attachment to the uterine wall
Day 21-22	Heart beat apparent
Day 28	Gonadal ridge formed
Days 25-30	Limb development
Day 40-50	Differentiation of the rumen stomach; formation of the rumen, reticulum, and omasum Cellular differentiation and growth of the pancreas, liver, adrenals, lungs, thyroids, muscle and kidneys
Day 45	Testicular development
Day 50-60	Bone ossification begins Limbs are increasing in length Ovarian development
Day 70	Completion of rumen differentiation Orientation of stomach is complete
Day 80	First detection of adipose cells
Day 120	Marked increase in caruncular vascularization and blood flow
Day 150	Completion of caruncular arterial vascularization
Day 190	Brown fat is detectable
Last third of gestation	Further cellular differentiation and growth of all tissues

Courtesy of Dr. Kimberly Vonnahme

Fetal Organ Development and Postnatal Function

- Nutrient restriction to the developing conceptus, regardless of the reason often results in impaired fetal organogenesis and/or development.
- More severe with increasing extremes of nutrient restriction.
- Timing of nutrient deprivation can also result in differential effects on fetal organ systems because of differing growth trajectories and maturation time points.
- Data indicate that both low and high planes of maternal nutrition can impact growth of numerous fetal organs (Reed et al., 2007; Caton et al., 2009; Neville et al., 2010).

Inappropriate Maternal Nutrition Impacts Fetal Organogenesis

- Responsive tissues include:
  - Small intestine (Trahair and Sangild 2002; Greenwood and Bell, 2003; Reed et al., 2007; Neville et al., 2007, 2010)
  - Pancreas (Osgerby et al., 2002; Limesand et al., 2005, 2006; Moberg et al., 2006; Effertz et al., 2007)
  - Heart (Hawkins et al., 2000; Osgerby et al., 2002; Han et al., 2004: Gilbert et al., 2005; O'Rourke et al., 2007)
  - Lung (Gnanalingham et al 2005)
  - Kidney (Gilbert et al., 2007)
  - Others

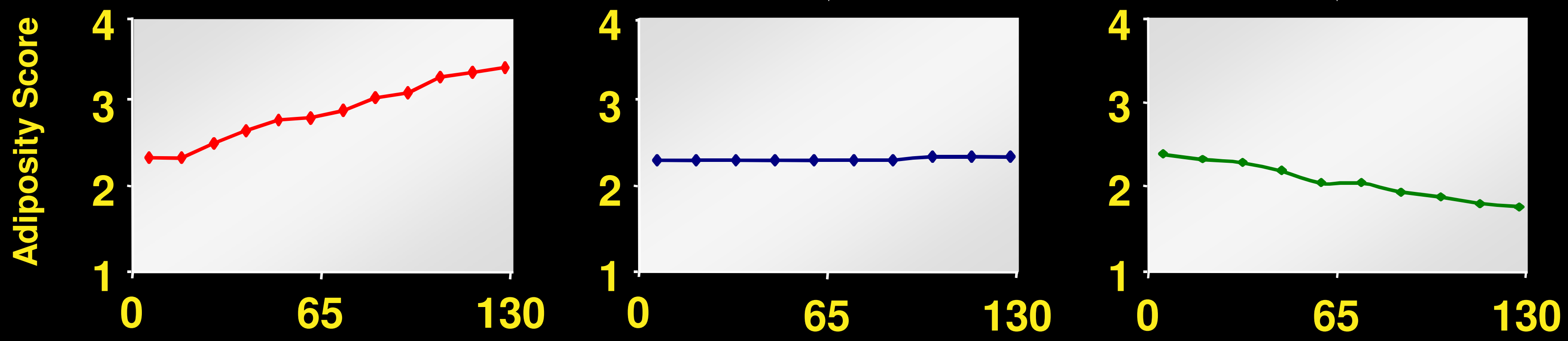
Inappropriate Maternal Nutrition Impacts Fetal Organogenesis

- Our laboratories have a particular interest in intestinal development, growth, and function (Reed et al., 2007; Carlson et al., 2008; Caton et al., 2009; Neville et al., 2010, and Meyer et al., 2010).
- Intestinal tissues are important to livestock production because of their role in nutrient uptake, immuno-competence, and their disproportional use of energy (and other nutrient resources) in relation to their contribution to overall body mass.
- A detailed discussion of fetal organ responses to perturbations during gestation are beyond the scope of this presentation.

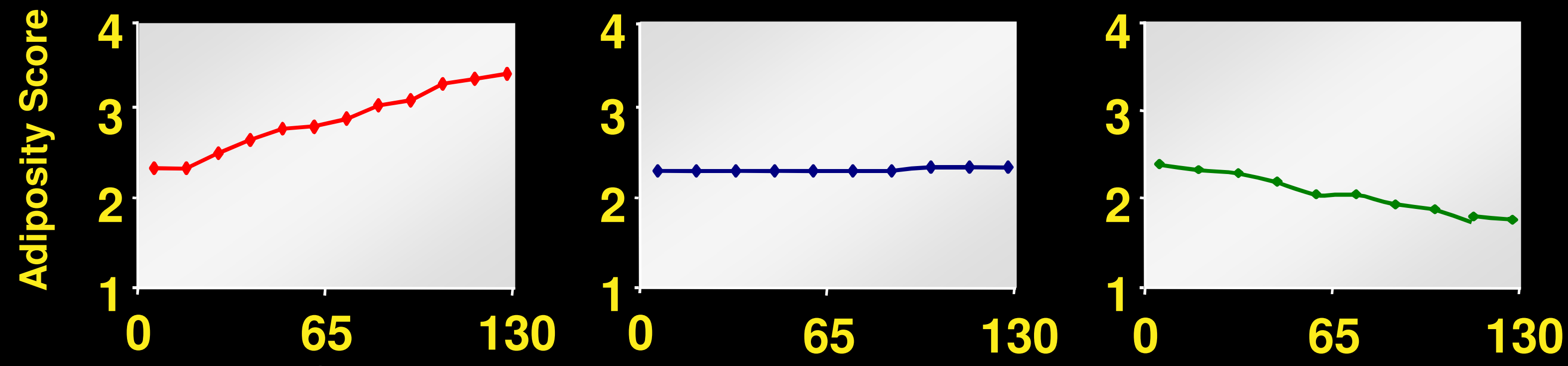
Nutrient Supply in First Parity Ewes: Maternal Responses and Birth Weight

Overnourished adolescent paradigm — Undernourished adolescent paradigm

High Intake (~2 X maintenance)	Moderate Intake (maintenance)	Low Intake
Rapid maternal growth and fat deposition	Maintains maternal adiposity = CONTROL	Prevents maternal growth and depletes nutrient reserves



Luther, Wallace, Redmer, Reynolds, et al., 2006



Increased insulin, IGF-I and glucose

↓

Impaired placental growth (47%↓)

↓

Growth restricted fetus (20%↓)

↓

Premature delivery (~143 days)

↓

Reduced colostrum yield (63%↓)

Normal insulin, IGF-I and glucose

↓

Normal placental growth

↓

Normally-grown fetus

↓

Normal gestation length (~147 days)

↓

Normal colostrum yield

Decreased insulin, IGF-I and glucose

↓

Normal placental growth

↓

Growth restricted fetus (17%↓)

↓

Normal gestation length (~147 days)

↓

Reduced colostrum yield (50%↓)

Low Birth Weight: Postnatal Implications in Livestock

- Low (2.3 kg) and normal birth weight (4.8 kg) lambs selected and reared separately from dams on milk replacer.
- Lambs were not allow to suckle dams and were individually housed and fed for either low or rapid growth rates.
- Data were collected until lambs were approximately 20 kg BW.
- Lambs were necropsied and tissues collected.

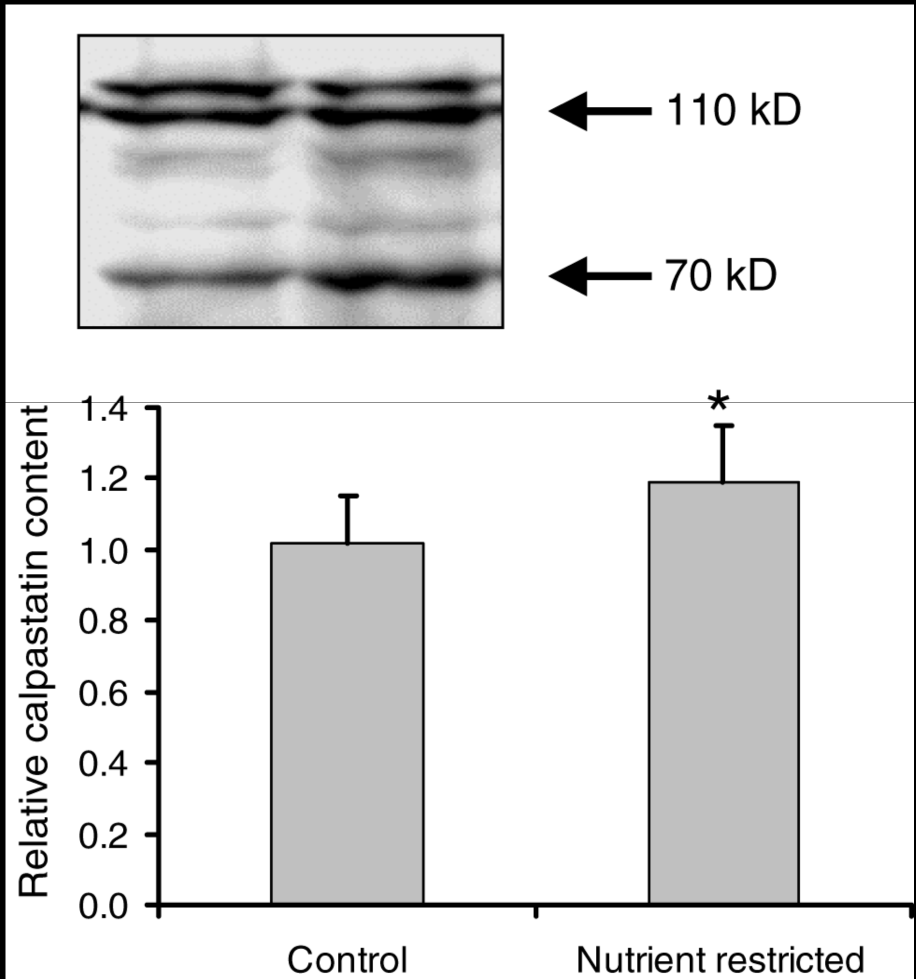
Greenwood et al., 1998; 2000, 2002, 2004

Low Birth Weight: Postnatal Implications in Livestock

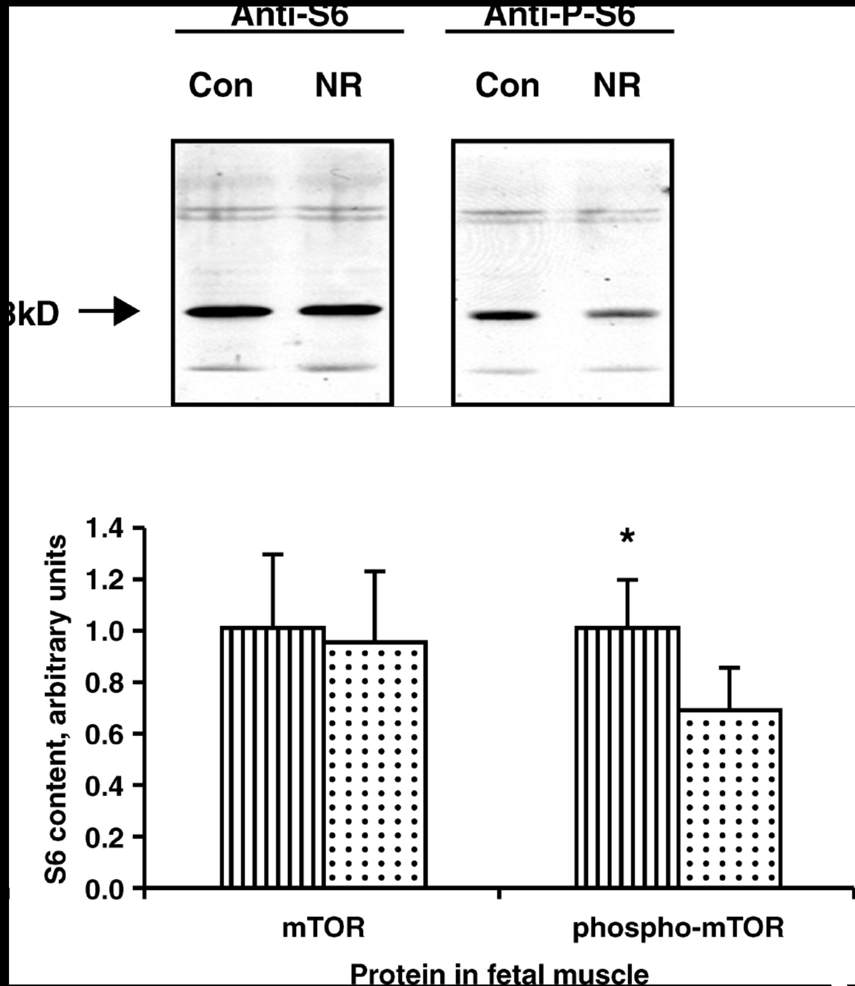
- Low birth weight lambs had less body N and more ash
- Low birth weight lambs had more fat and less lean at any give empty BW likely because maintenance energy requirements were 30% lower and intakes were relatively greater.
- Myonuclei proliferation may be influenced by fetal nutrition during late pregnancy
- Reduced myonuclei number in very low birth weight lambs may impact postnatal skeletal muscle growth capacity

Greenwood et al., 1998; 2000; 2002; 2004

Protein Turnover of Bovine Fetal Skeletal Muscle



Du et al., 2004



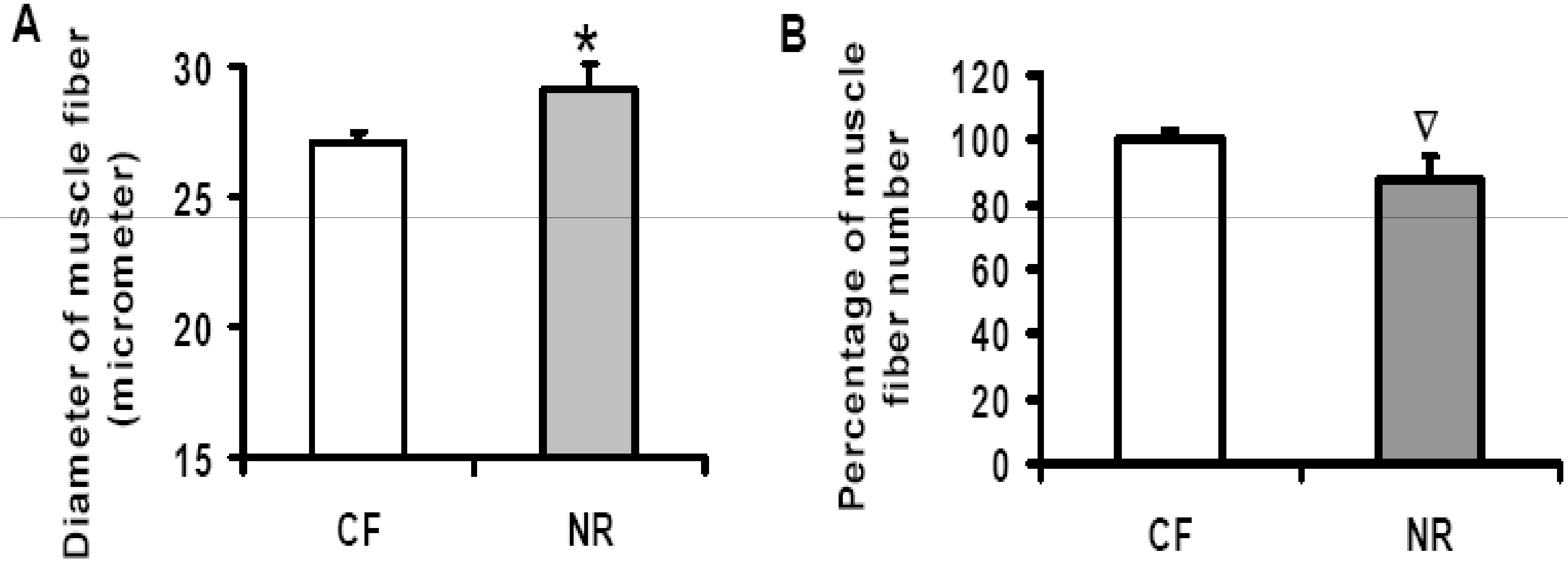
Du et al., 2005

Selected Fat and Muscle Weights of 8-Month Old Lambs

Zhu et al., 2006

Item	Control	Restricted	P-value
Live BW, kg	56.8	61.7	< 0.05
Carcass wt, kg	28.8	31.6	< 0.10
KPH, kg	0.46	0.68	< 0.05
KPH, % carcass	1.66	2.18	< 0.05
Left LD muscle, % carcass	2.71	2.46	< 0.10

Muscle Fiber Number and Diameter of 8-month old Offspring



Zhu et al., 2006

Influence of maternal dietary selenium and nutritional intake during pregnancy on offspring body weight from birth through weaning at 57 d of age (Adapted from Neville et al., 2010)

Item	Selenium Treatment[1]			Nutrition Treatment[2]				*P*-Values[3]		
	ASe	HSe	SEM	RES	CON	HIGH	SEM	Se	Nut	Se*Nut
BW, kg										
Birth										
Males	4.49	4.06	0.25	3.95[a]	4.78[b]	4.10[a]	0.29	0.18	0.06	0.96
Females	4.11	4.43	0.12	3.85[a]	4.50[b]	4.45[b]	0.15	0.05	0.002	0.71
Combined	4.25	4.37	0.10	4.02[a]	4.67[b]	4.25[a]	0.12	0.37	0.0007	0.66
Weaning, 57 d										
Males	19.52	19.45	0.95	18.10	20.35	20.01	1.27	0.96	0.28	0.75
Females	19.60	19.72	0.64	18.85	20.18	19.96	0.82	0.89	0.32	0.25
Combined	19.61	19.55	0.49	18.57[a]	20.33[b]	19.84[ab]	0.67	0.94	0.06	0.40
180 d										
Males	53.04	52.61	1.43	52.22[ab]	55.75[a]	50.51[b]	1.91	0.83	0.08	0.98
Females	49.41	51.47	1.73	50.59	50.80	49.94	2.15	0.35	0.95	0.85
Combined	51.23	51.98	1.11	51.31	53.27	50.24	1.48	0.61	0.26	0.80

[1]Selenium treatments were daily intake of organically bound Se, adequate Se (ASe; 9.5 µg/kg BW) vs. high Se (HSe; 81.8 µg/kg BW).

[2]Nutritional treatments were RES (fed at 60% of CON), CON (control; 100% requirements for gestating ewe lambs), and HIGH (fed at 140% of CON).

[3]Probability values for effects of selenium (Se), nutrition (Nut), and the interaction.

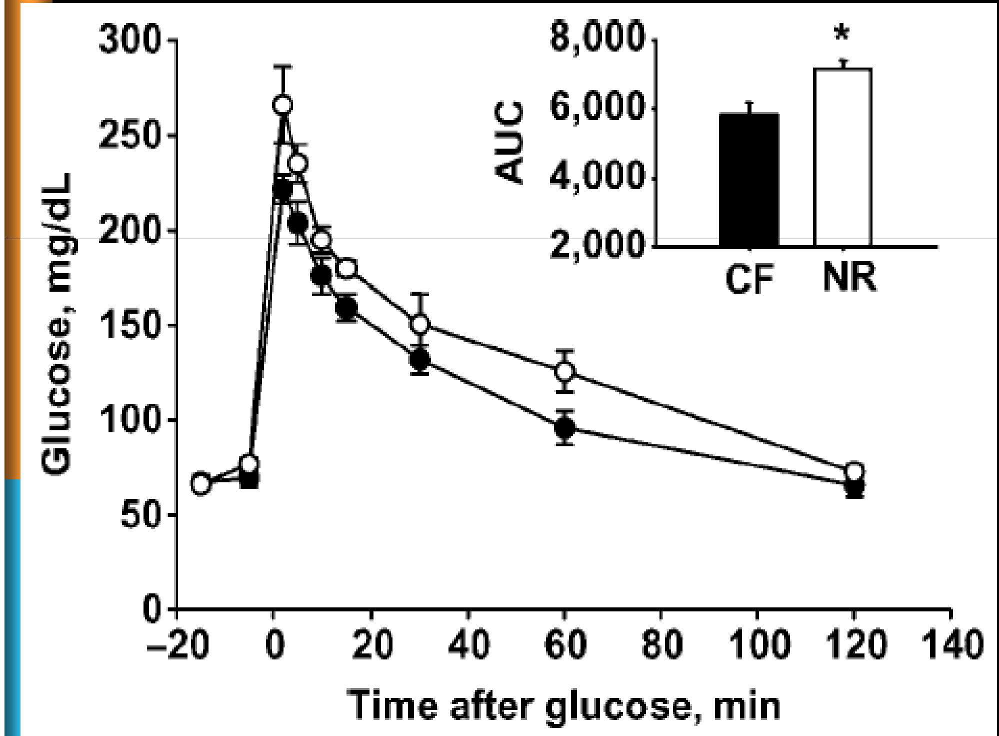
[ab]Means within a row having differing superscripts differ ($P < 0.10$).

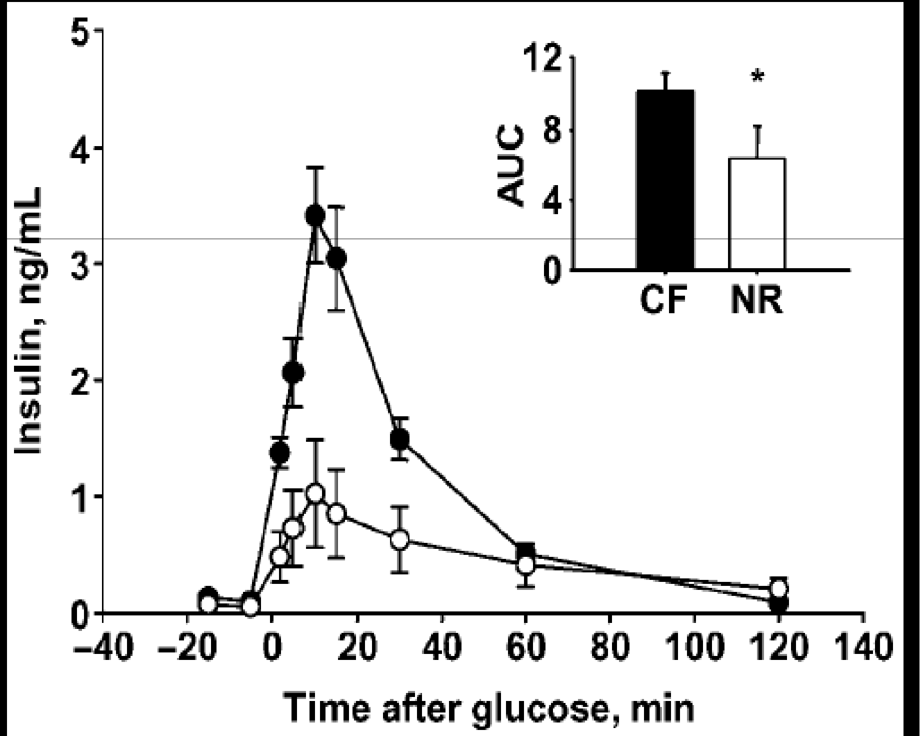
Low Birth Weight: Postnatal implications in Livestock

- Low birth weight lambs appear less mature in terms of metabolic and endocrine development.
- All new born lambs exhibited the fetal characteristic of high rates of amino acid oxidation during the early postnatal period.
- Low birth weight lambs had increased insulin when fed for moderate or high rates of growth
- Both low birth weight and postnatal nutrient supply altered internal organ growth.

Greenwood et al., 1998; 2000, 2002, 2004

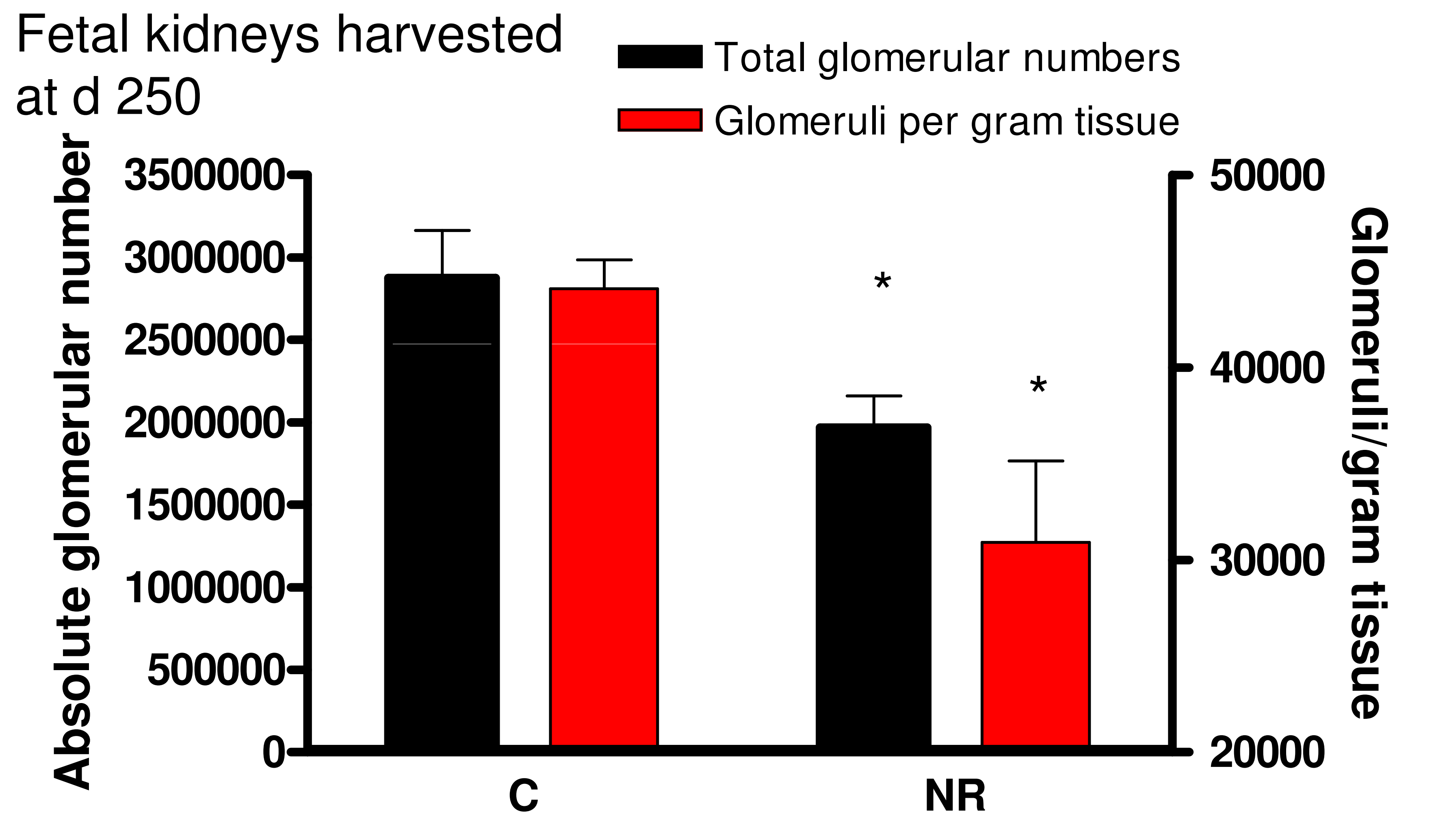
Effect of Ewe Plane of Nutrition on Lamb Response to Glucose Challenge at 250 Days of Age





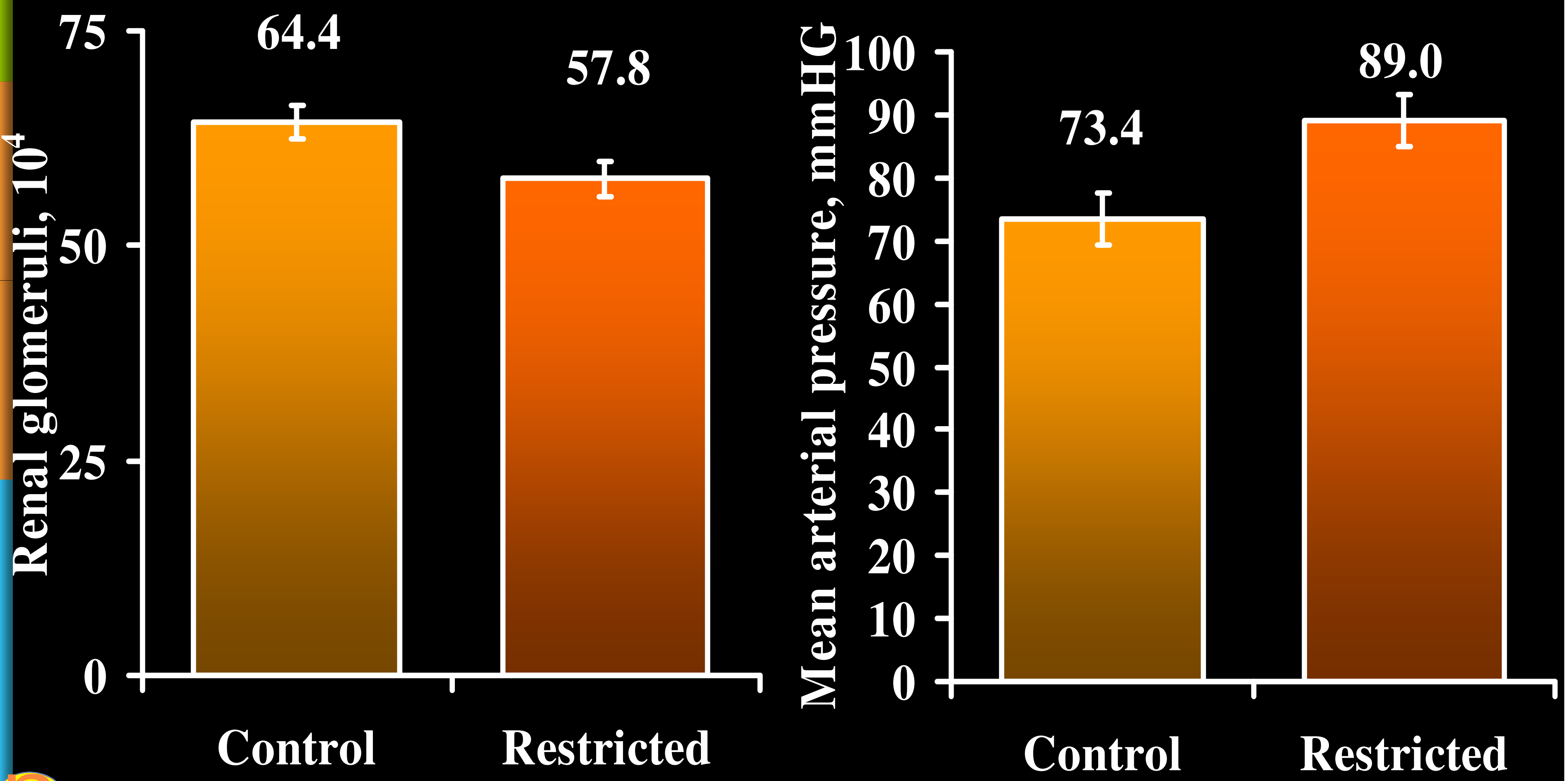
Ford et al., 2007

Effects of Cow Plane of Nutrition on Fetal Renal Characteristics



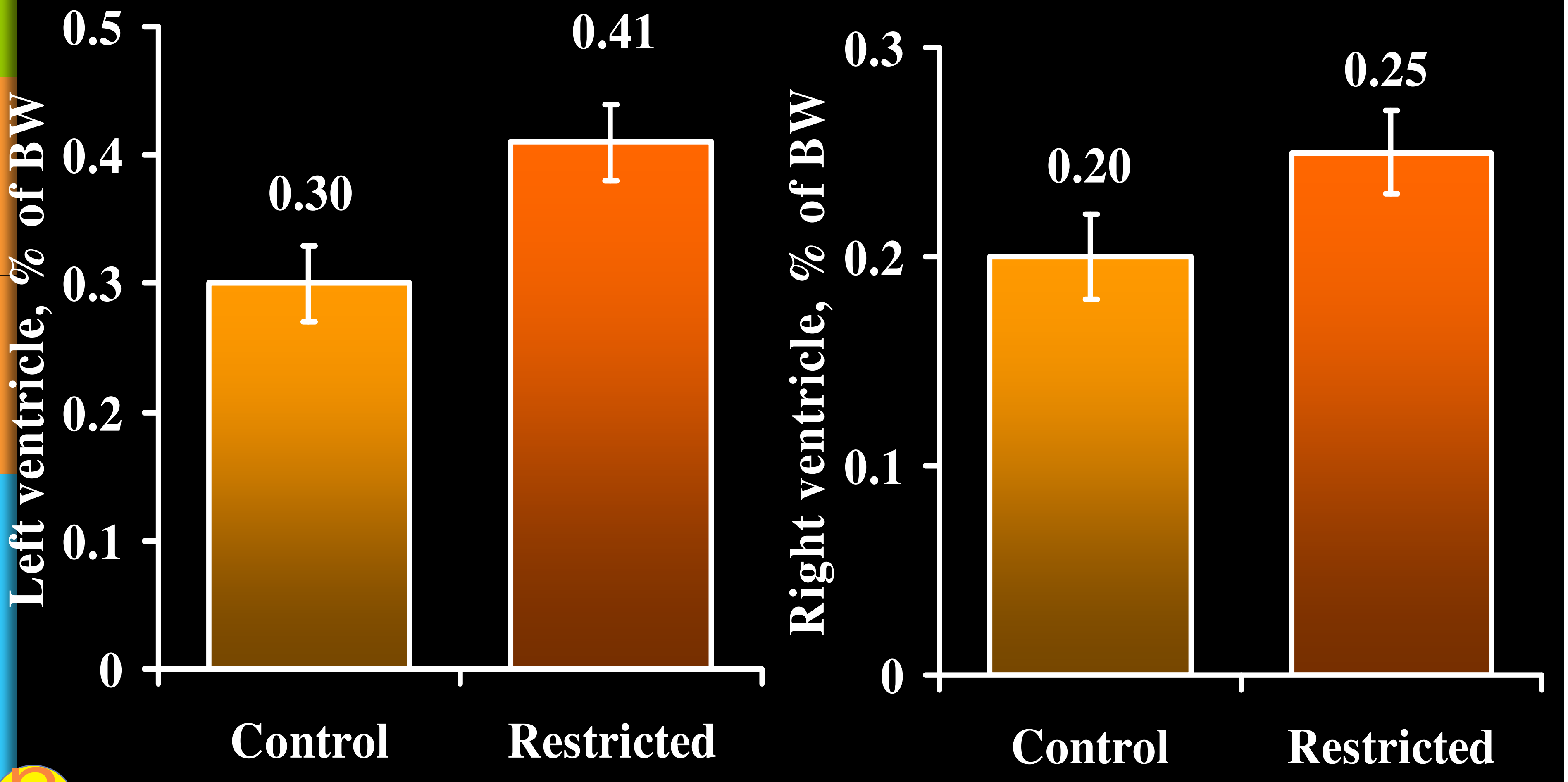
Ford et al., 2005

Postnatal Hypertension of Lambs at 245 Days of Age



Gilbert et al., 2005

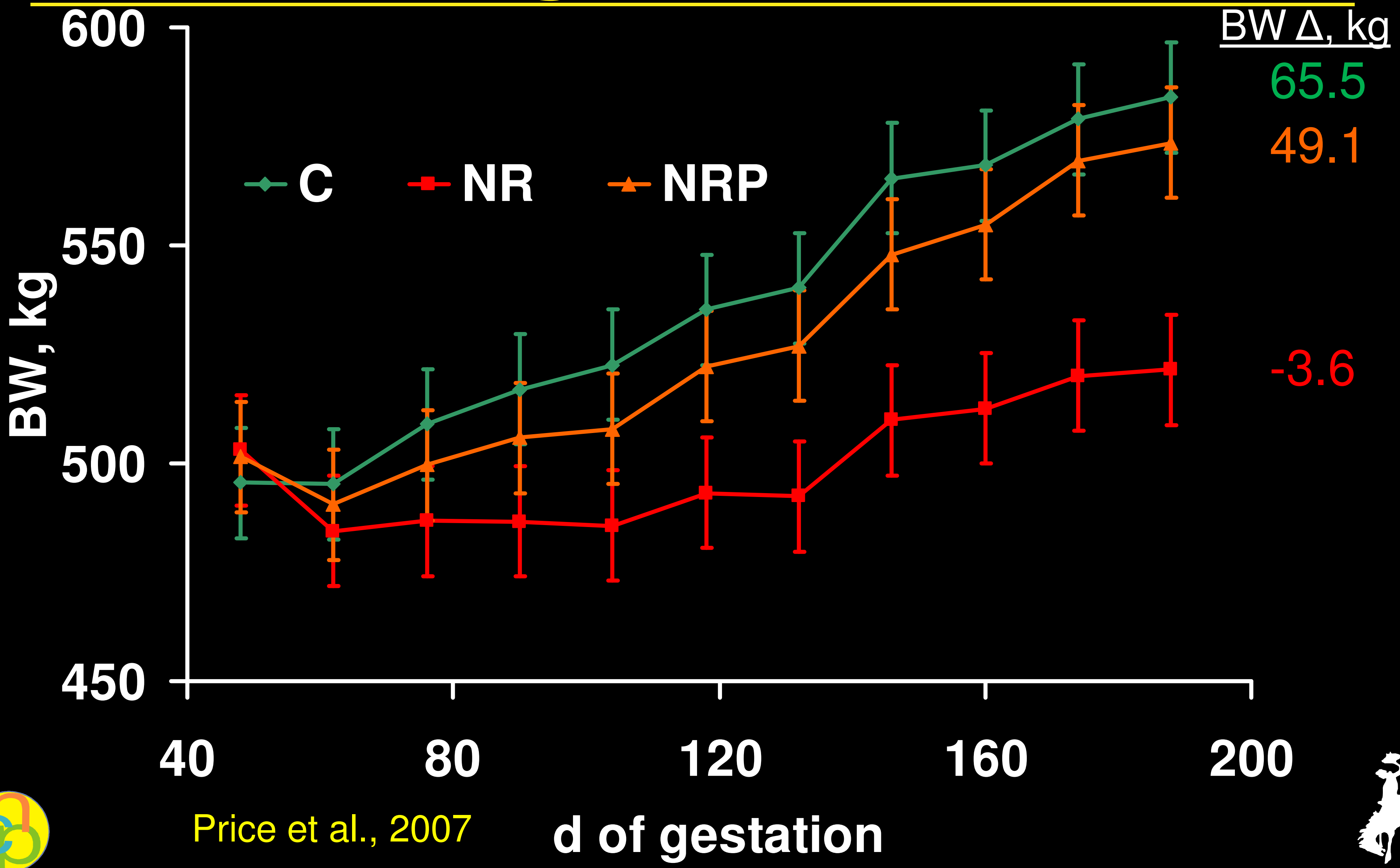
Fetal Cardiac Development of 78-day Lambs Fetuses



Vonnahme et al., 2003

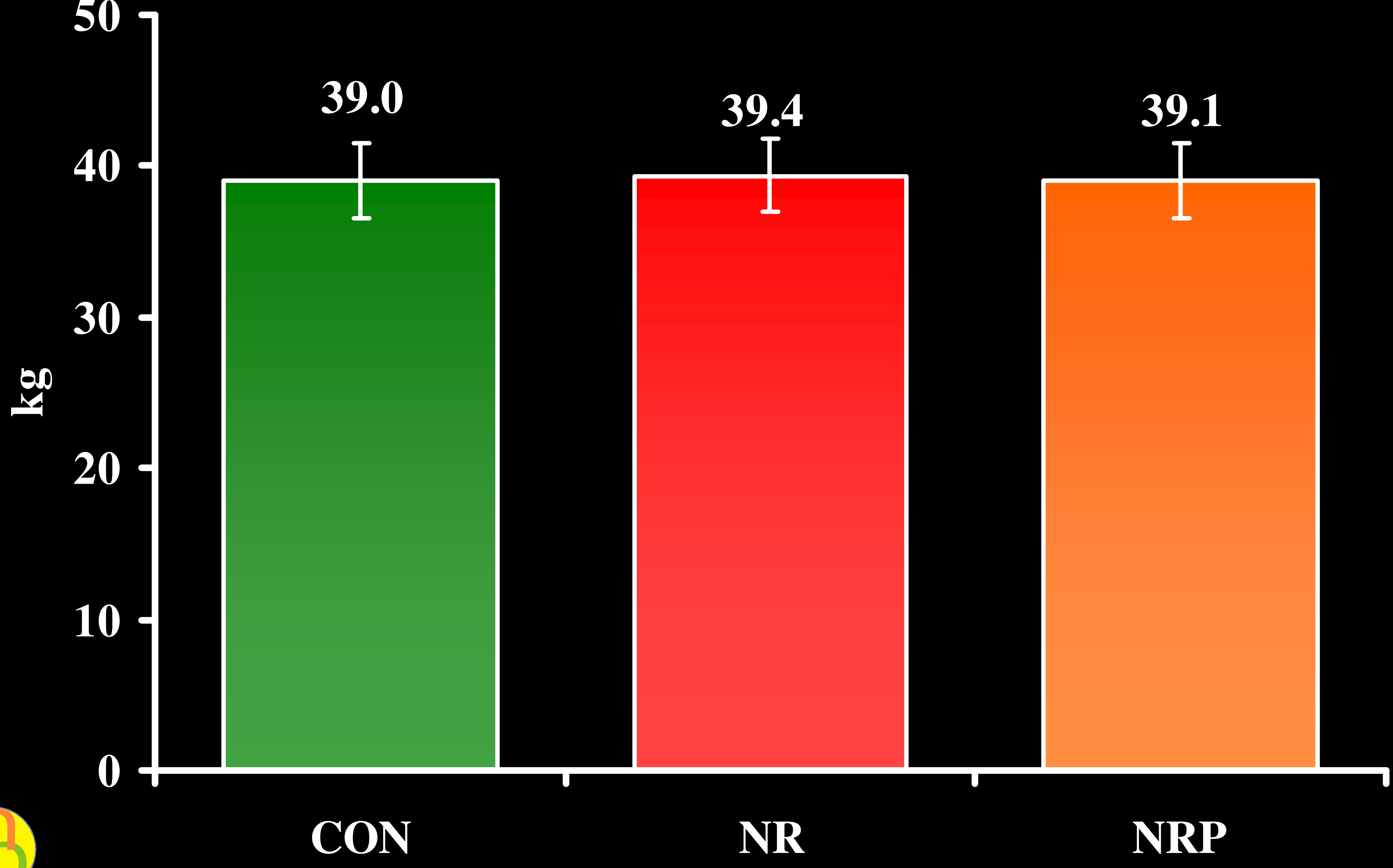
Protein Supplementation During Pregnancy

Effect of Gestational Plane of Nutrition and Supplemental RUP on Cow BW Change



Price et al., 2007

Calf Birth Weights



Postnatal Offspring Responses

Effects of Supplemental Protein During the Last Third of Gestation on Performance of Heifer Calves

Item	No Sup.	Sup.	*P*-value
Birth Weight, kg	35	36	0.25
Actual Weaning Wt, kg	207	212	0.14
Adjusted Weaning Wt, kg	218	226	0.02
Prebreeding BW, kg	266	276	0.04
Preg Check BW, kg	386	400	0.03
Calving in 21 d, %	49	77	0.01
Overall Pregnancy Rate, %	80	93	0.05

Martin et al., 2007

Effects of Supplemental Protein During the Last Third of Gestation on Steer Offspring Performance

Item	No Sup.	Sup.	*P*-value
Birth Weight, kg	36.6	38.0	NS
Actual Weaning Wt, kg	225	247	0.05
Adjusted Weaning Wt, kg	219	231	0.10
Initial Feedlot BW, kg	222	243	0.05
Reimplant BW, kg	422	456	0.05
Final BW, kg	591	622	0.05
ADG, %	166	171	0.09

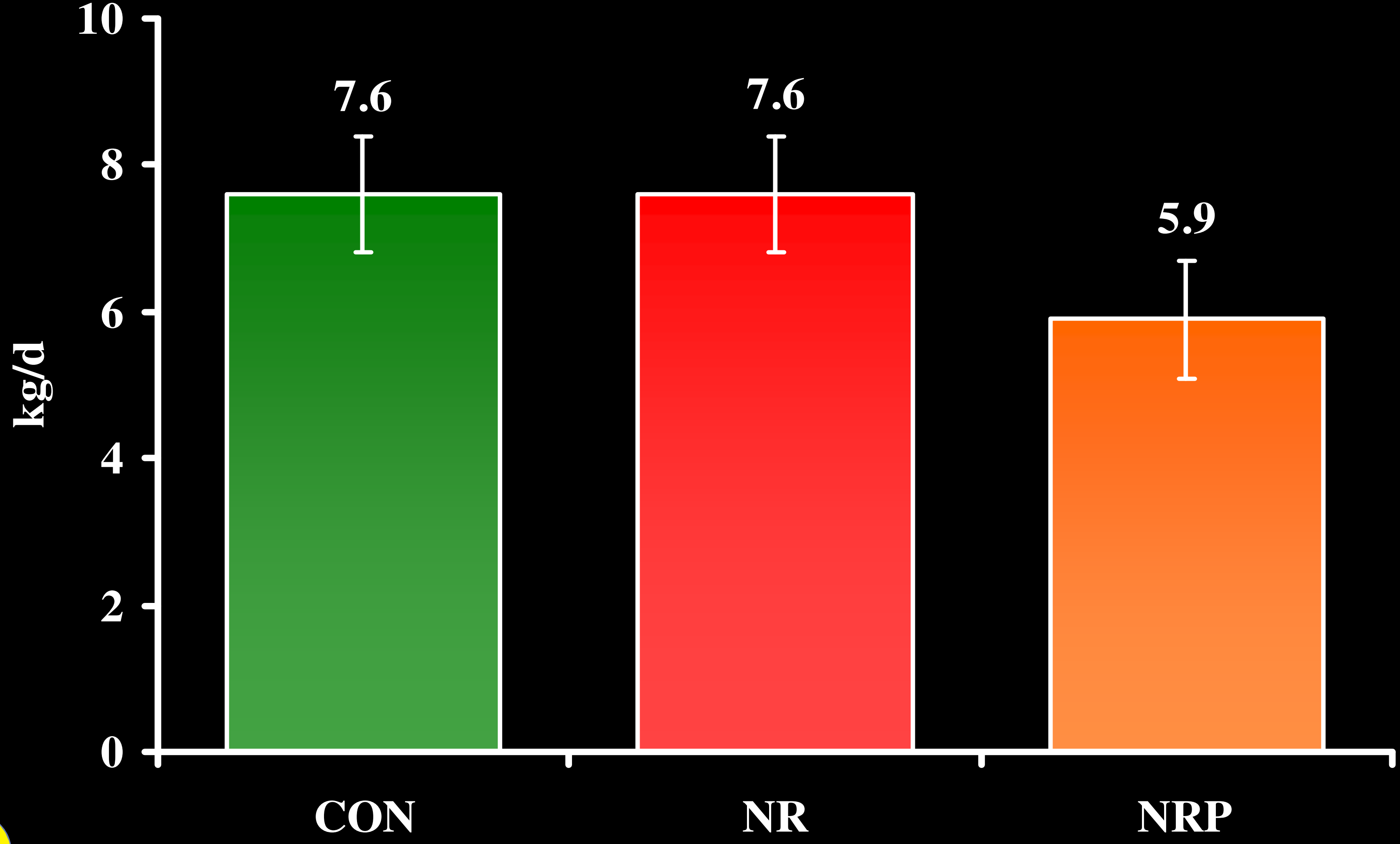
Larson et al., 2008

Effects of Supplemental Protein During the Last Third of Gestation on Steer Offspring Carcass Characteristics

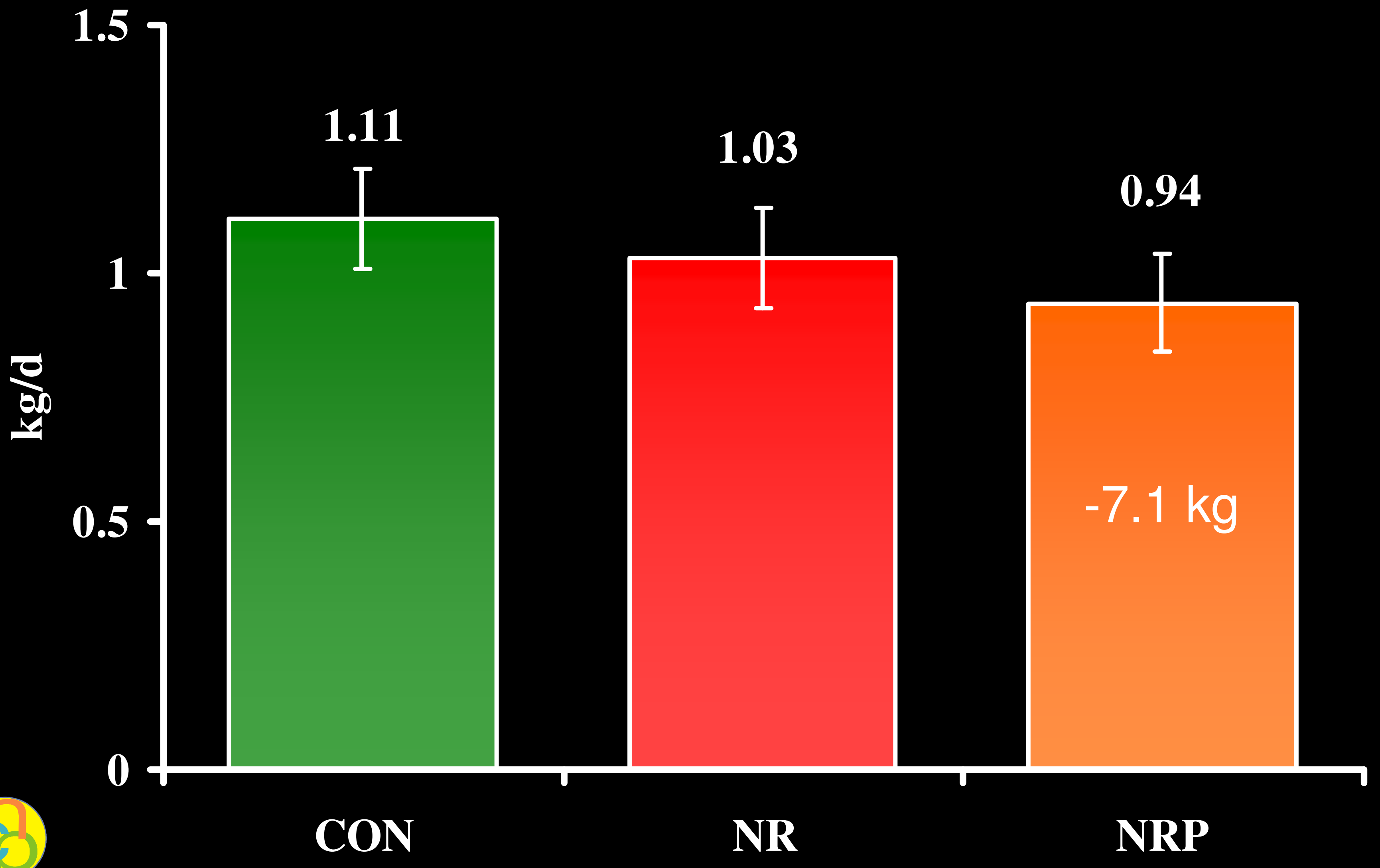
Item	No Sup.	Sup.	*P*-value
HCW, kg	357	376	0.05
Marbling Score	457	503	0.01
Empty Body Fat, %	28.7	29.9	0.06
LM area, cm^2	88.4	88.5	NS
Yield Grade	2.69	2.94	NS
Quality Grade, %Md >	26.6	43.2	0.03
12th Rib Fat, cm	1.16	1.71	NS

Larson et al., 2008

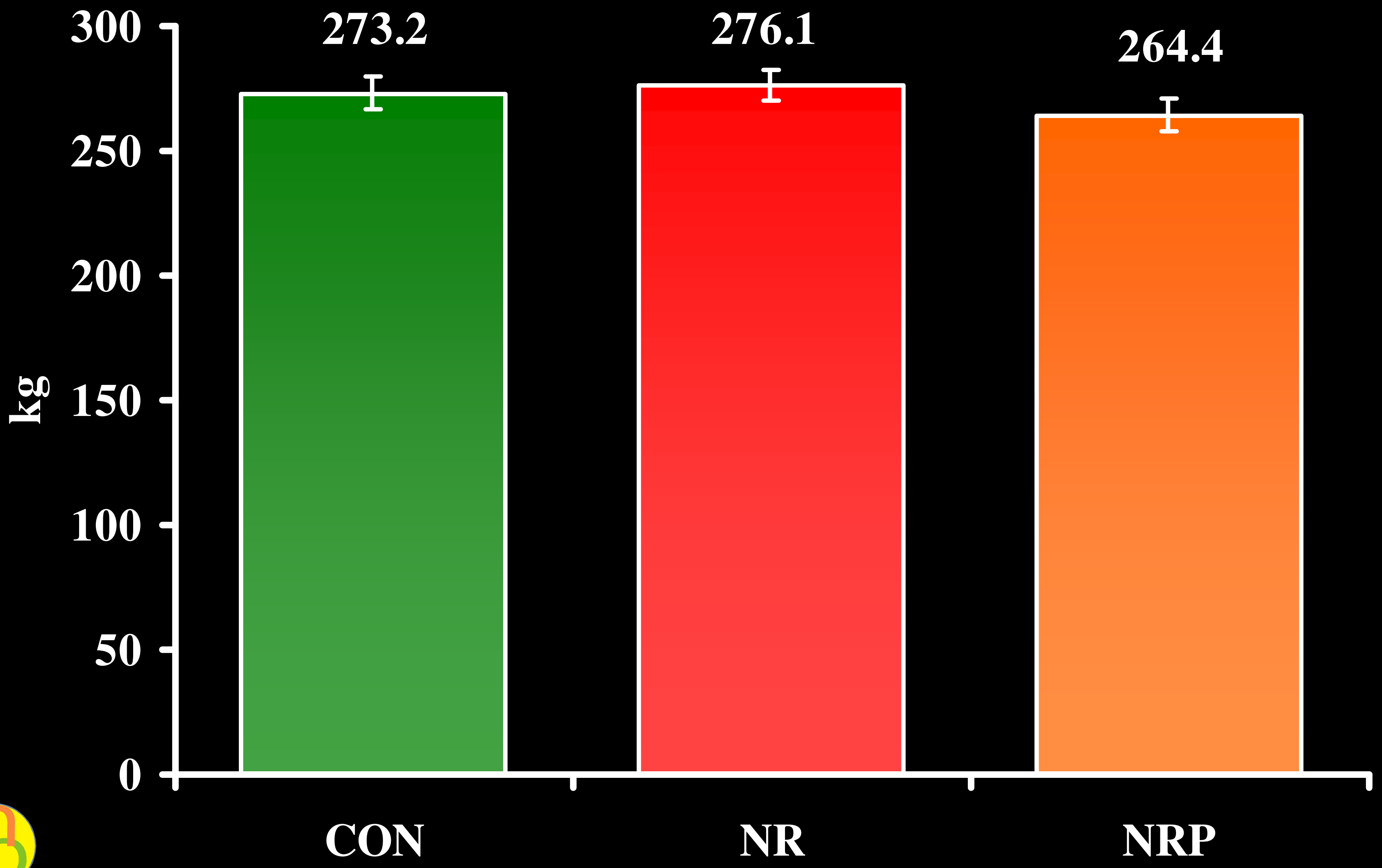
Effect of Gestational Plane of Nutrition and Supplemental RUP on Average Milk Production (d 50 & 70)



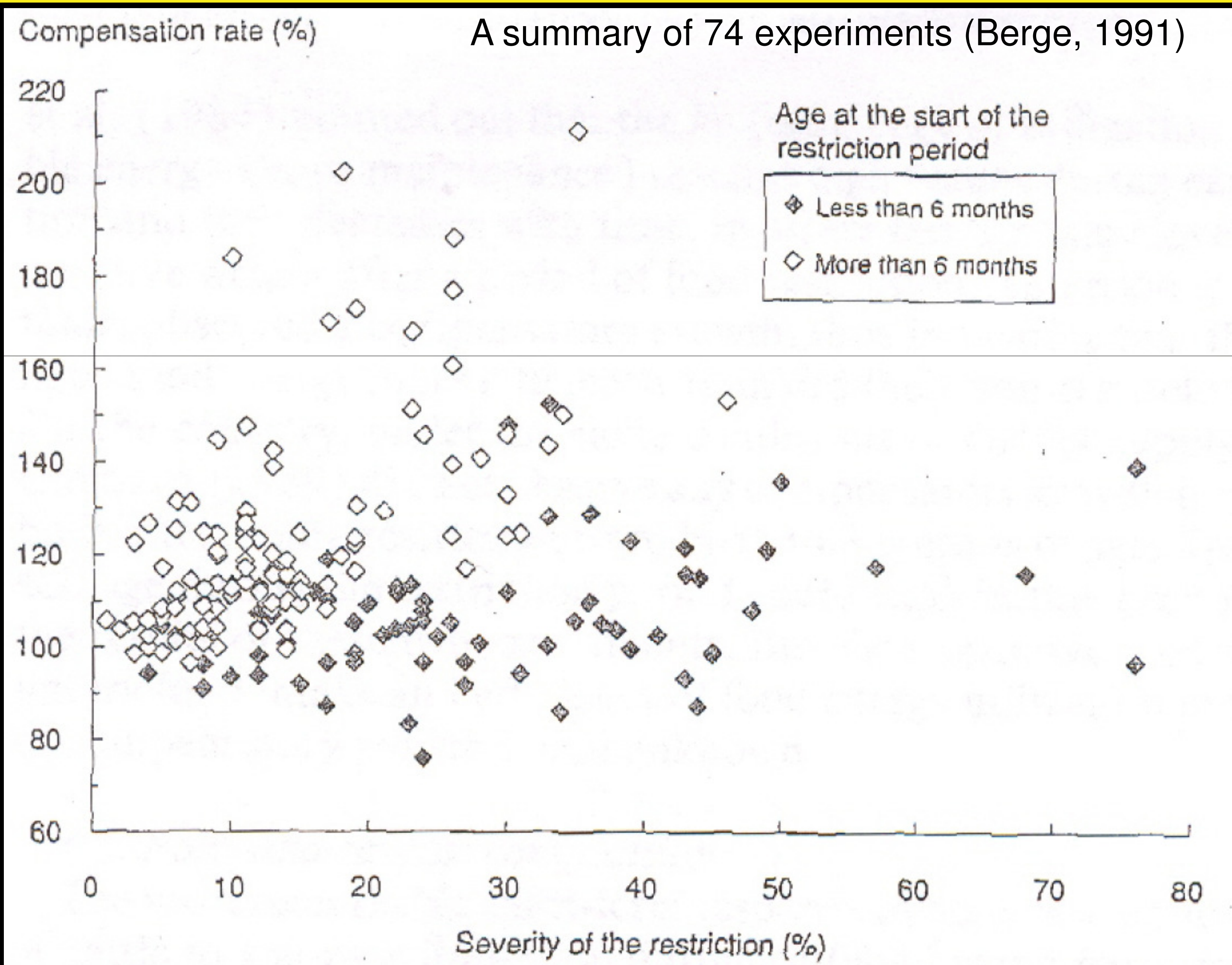
Effect of Gestational Plane of Nutrition and Supplemental RUP on Calf ADG from d 50 to 70



Calf Weights at Weaning



Interaction Between Severity of Restriction and Calf Age at the Start of the Restriction



Summary and Conclusions

- Maternal nutritional perturbations impact fetal nutrient supply and result in measurable impacts on fetal and postnatal outcomes.
- Developmental programming is real in relevant livestock species.
- This is an emerging area of research interest in animal agriculture that has potential to shape our understanding of the long term consequences of fetal nutrition on offspring performance.
- Degree of impact on livestock production responses, underlying mechanisms, and methods to mitigate potential negative consequences or capitalize on positive attributes remains to be determined.

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