IMPACT OF EARLY LIFE NUTRITION ON SURVIVAL AND PRODUCTION PERFORMANCE IN MULTIPLE-BORN LAMBS

Sue McCoard, Quentin Sciascia, Francisco Sales, Danitsja van der Linden
AgResearch Grasslands, Palmerston North, New Zealand

WHY IS EARLY LIFE NUTRITION IMPORTANT?

- Tissues and organ systems develop during the prenatal and neonatal periods - critical time window for interventions
- Strategic feeding systems may provide “tools” for farmers to manage animal performance in challenging environments
- Early life nutrition may provide the opportunity to “tailor” performance and increase productivity
- Lifetime growth performance impacts profitability for farmers and processors alike

agresearch

INTRODUCTION

Advances in genetic selection, breeding and nutritional management have led to increased lambing percentage

Figure 1 Effect of scanning % on number of ewes carrying singles, twins, triplets or quads.

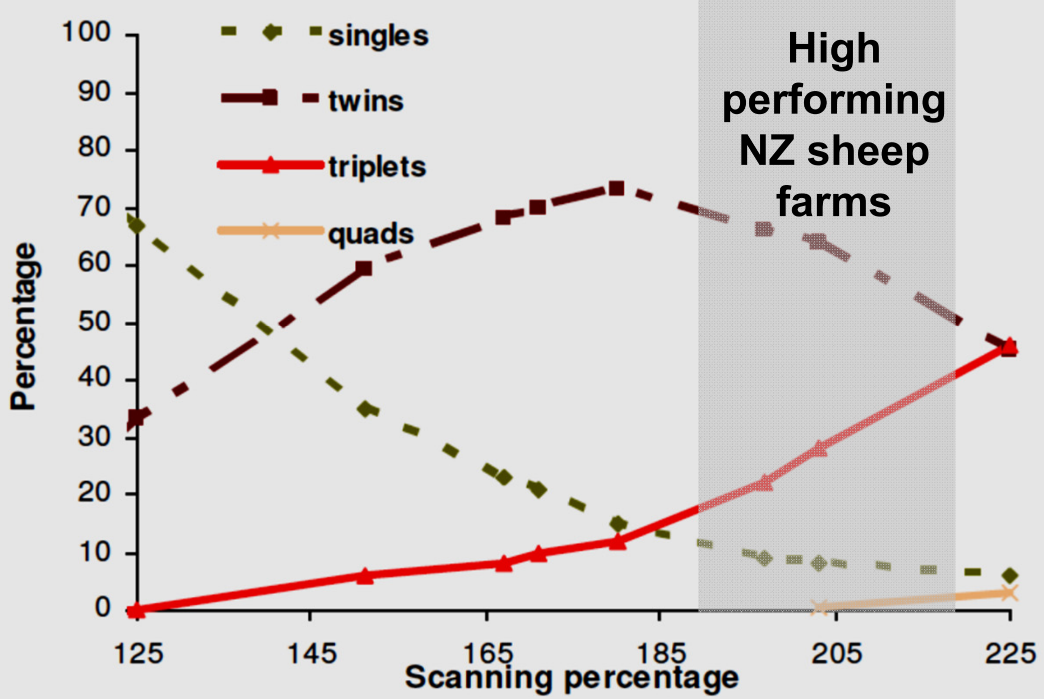


Figure 1 is sourced from Muir and Thomson (2009) Survival and performance of multiple lambs MWNZ Report 030FR01

agresearch

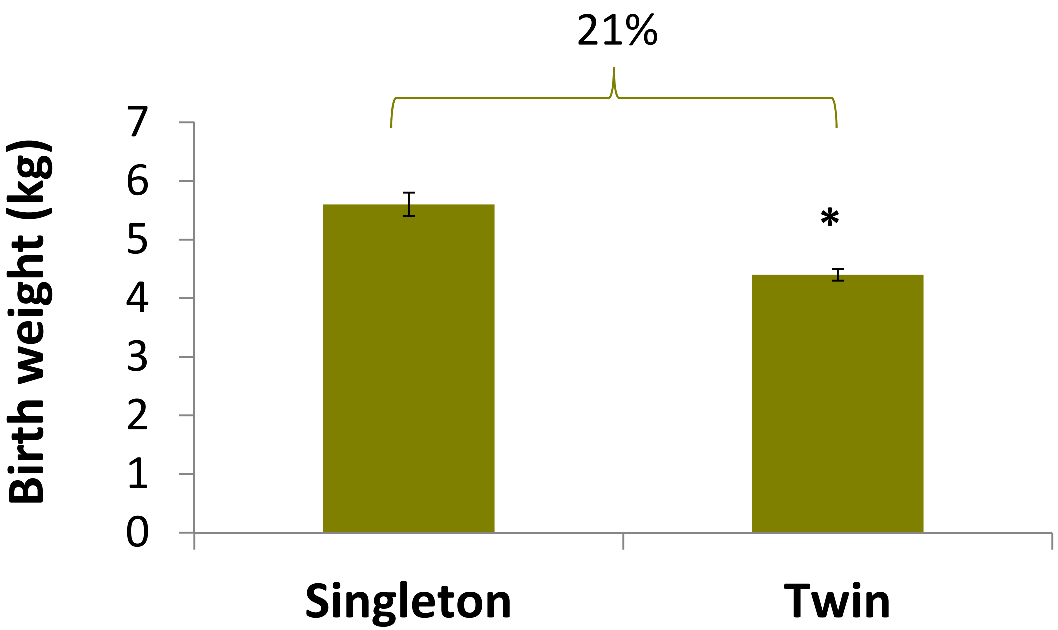
LAMB PRODUCTION – ECONOMICS AND WELFARE

- Improved genetic selection and breeding ↑ lambing %
- Multiples have higher rates of mortality
  - *Lost production opportunity (2% ↓ mortality = $53M)*
  - *Risk of negative consumer perception*
- Slow growth of multiples
  - *↑ post-weaning feed costs*
  - *↓ capacity to finish lambs on hill country*
  - *Impact on other stock classes, e.g. breeding ewes*
  - *Impacts consistency of supply*

agresearch

JUST FEED THE EWES BETTER?........NO

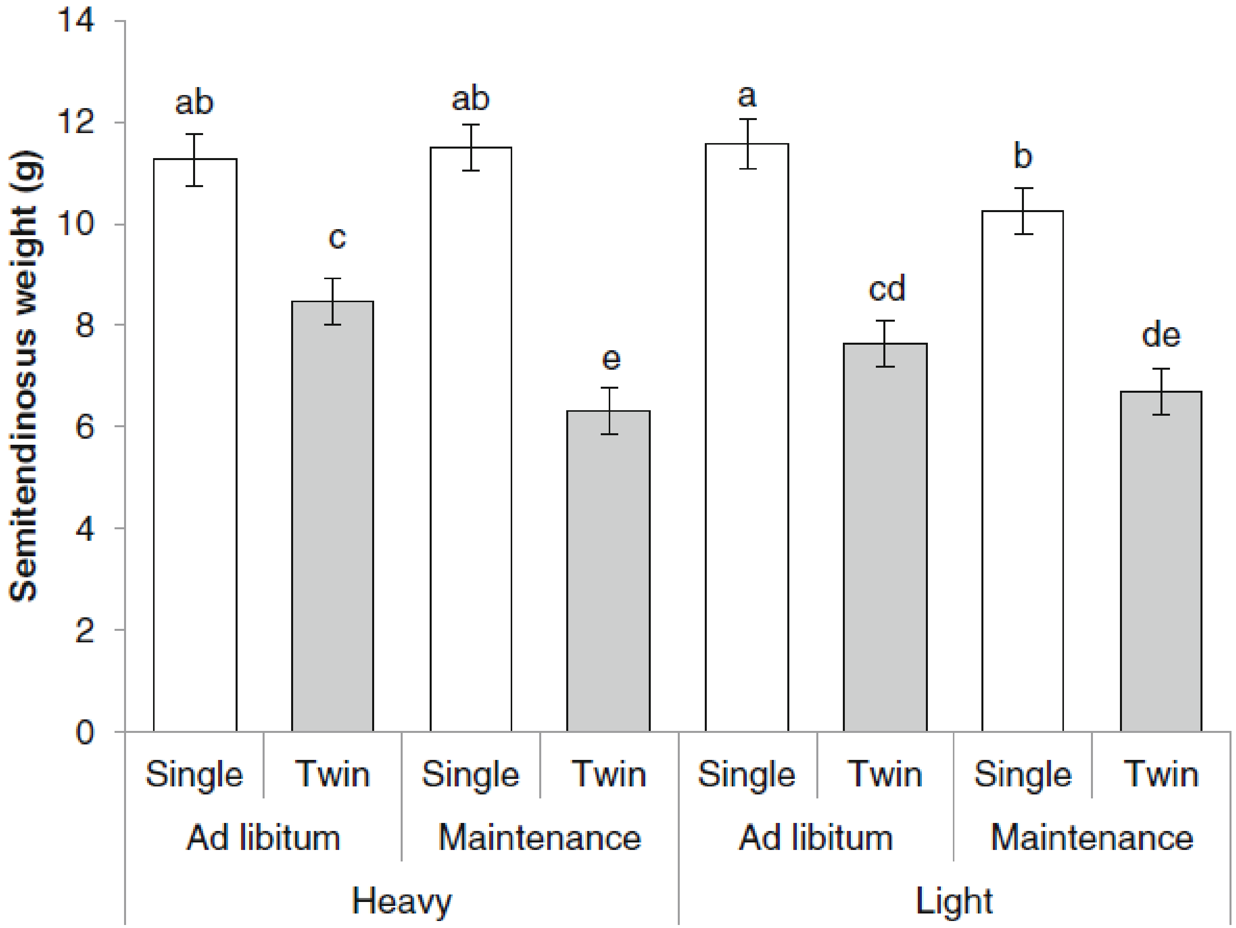
Ewes offered 2200-2500 kg DM/ha pasture, i.e. ad libitum – intake above 1400 kg DM/ha is not limited *Morris and Kenyon, 2004*



agresearch

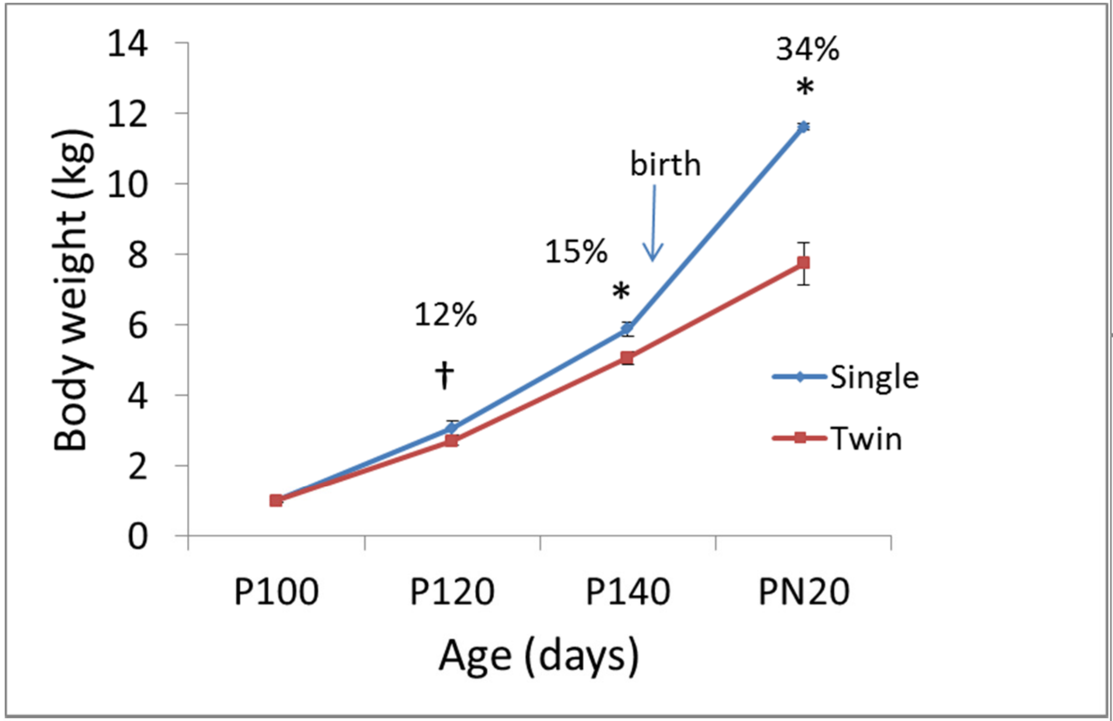
Sales, Pacheco, Blair, Kenyon, Nicholas, Senna Salerno, McCoard (2014) J. Anim. Sci. (accepted)

MUSCLE WEIGHT NEAR TERM IS ALSO REDUCED

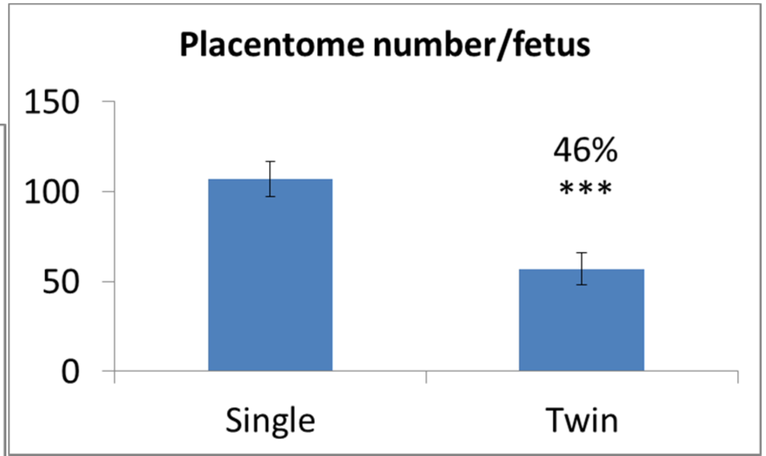


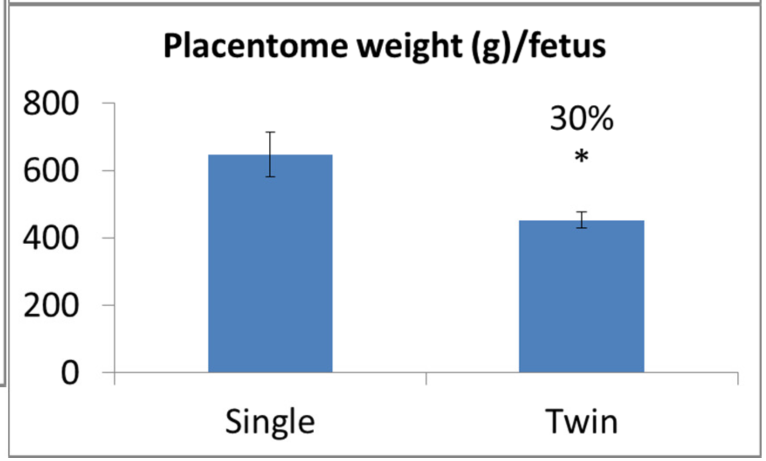
agresearch

Sales, Pacheco, Blair, Kenyon, McCoard (2013) SpringerPlus 2:483



Body weight diverges between twins and singles after 100 days gestation





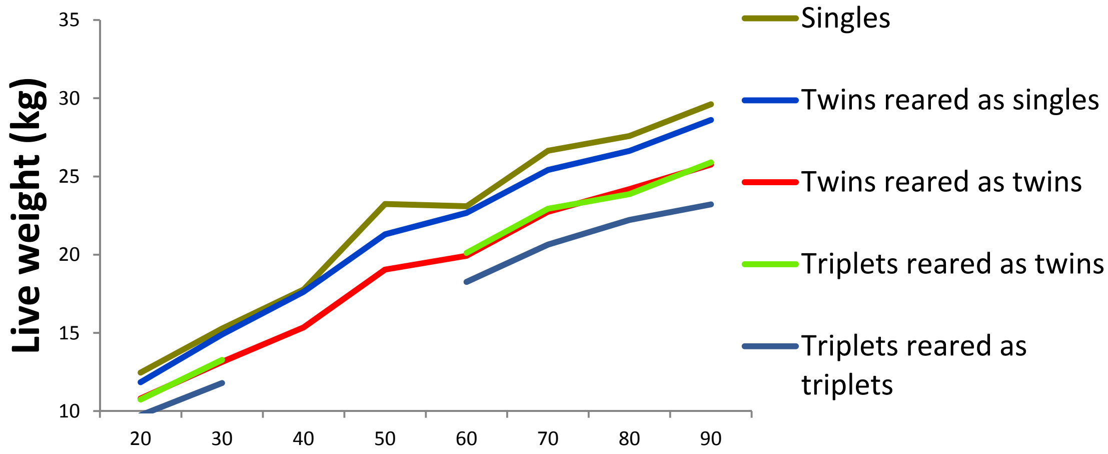
Smaller placenta per fetus in twins

agresearch

Adapted from McCoard et al. (2001) Cells, Tissues & Organs 169:21-23

EFFECT OF LITTER SIZE ON LAMB GROWTH

Effect of birth and rearing rank on live weight from birth to weaning (n=3188 lambs)



The proportion of rearing ranks reaching 30kg live weight by weaning

	Overall %
Overall	16
Singles	53
Twins	
Reared as twin	8
Reared as single	28
Triplets	
Reared as triplet	0
Reared as twin	2
Reared as single	21

Capacity for muscle growth is reduced in multiples

Feed and feeding systems

The most profitable lamb is finished at weaning

McCoard, unpublished

agresearch

EFFECT OF SEX & TWINNING ON CARCASS TRAITS

Using a dataset from 11,072 lambs (2003-2007):

- Carcass weight: Twins 10% (1.7 kg) < singles
- Carcass fatness:
  - Twins < Singles – dependent on carcass weight
  - Single females 64% > single males
  - Twin females 26% > twin males
- Sex and birth rank remain major determinants of carcass weight and fatness in lambs under current NZ grazing and management systems

➡ Incentives for lamb producers to gain better control over animal growth performance

agresearch

McCoard, Koolaard, Charteris, Luo (2010) Proc. NZ Soc. Anim. Prod.

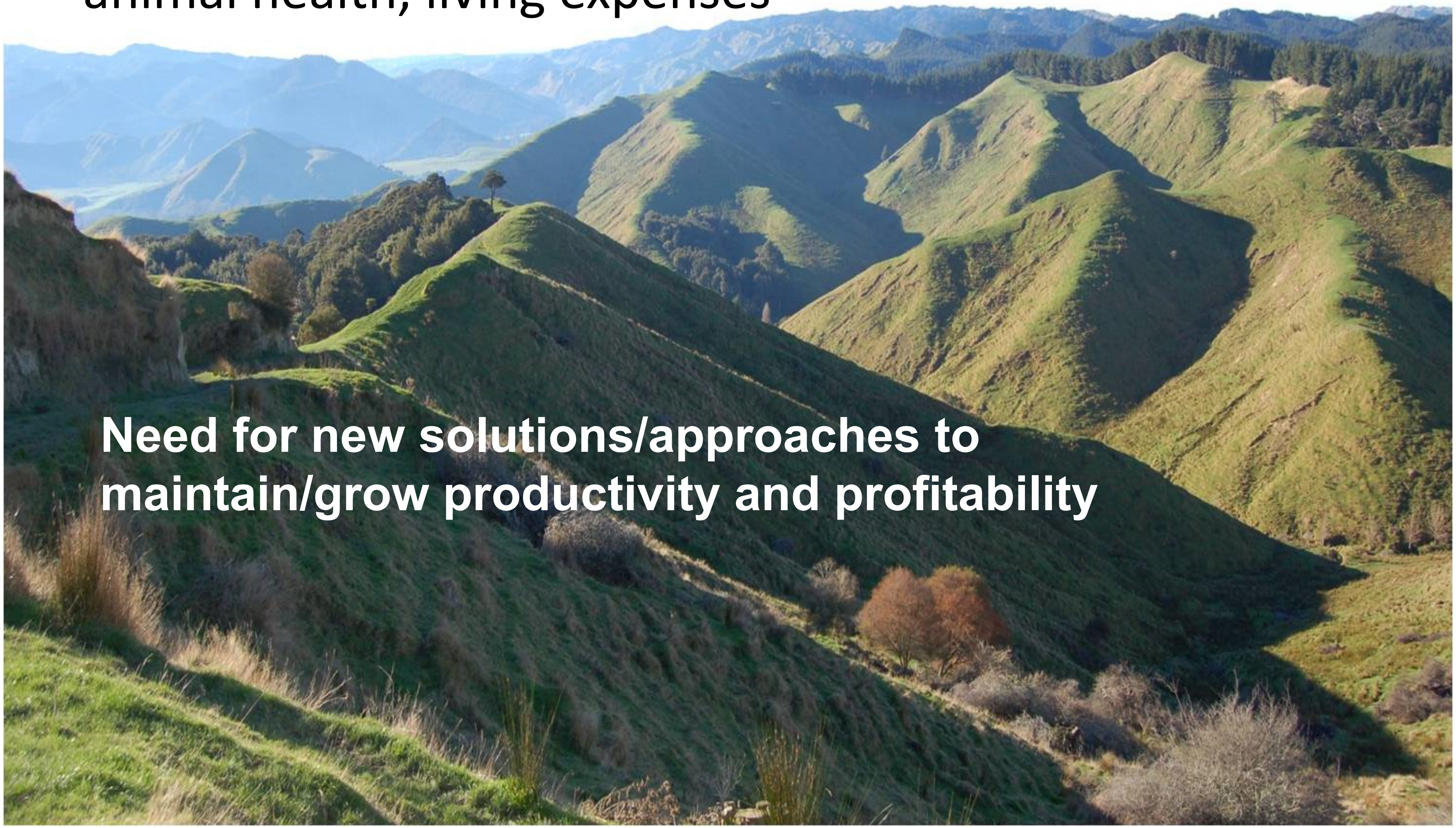
RISSINGTON BREEDLINE [bring your future into focus]

No intervention strategies are currently available to ameliorate growth restriction in twins on-farm

The ability to improve the growth performance of twin lambs would have significant implications for the profitability of the lamb production enterprise

agresearch

- More diverse, challenging landscapes and climates
- Competition for land-use with dairying
- Rising operating costs, e.g. labour, energy, fertiliser, animal health, living expenses



Need for new solutions/approaches to maintain/grow productivity and profitability

NUTRITIONAL INTERVENTIONS TO MODIFY PHENOTYPE

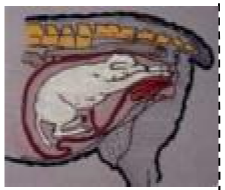
Goal: To understand how targeted nutrition (e.g. specific nutrients/supplements/diets) can be used to modify tissue growth and development to enhance livestock productivity and the biological mechanisms underpinning these phenotypic shifts.

Nutritional programming of production phenotypes

Nutrient-gene interactions

Nutrients as signalling molecules to influence phenotypic variance

Nutritional intervention strategies for application on farm to improve productivity



agresearch

AMINO ACIDS AS SIGNALLING MOLECULES…

- Amino acids are not just building blocks for protein formation, but they can also act as signals, modulating the activation of specific pathways which regulate protein formation, metabolism etc. *Wu 2009*
- Changes in the concentration of specific FAA in the cell alter these signalling pathways, e.g. those protein accretion
- Maternal nutrition influences the pattern of FAA in maternal and fetal plasma *Kwon et al. 2004*

ROLE OF AMINO ACID SIGNALLING IN THE REGULATION OF OVINE PLACENTAL NUTRIENT TRANSPORT

Better understanding of placental nutrient transport to ameliorate fetal growth restriction in sheep

Morphology

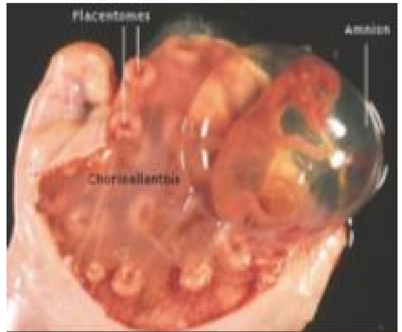
Nutrient transport

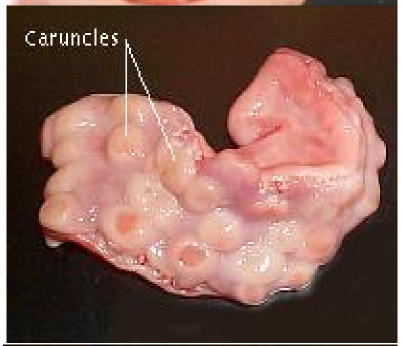
Functionality

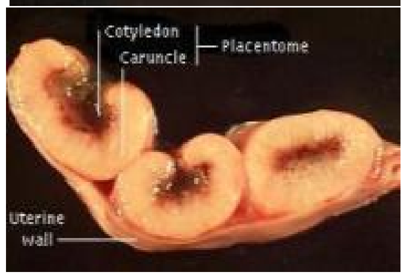
agresearch

IS PLACENTAL NUTRIENT TRANSPORT AFFECTED BY PREGNANCY RANK IN SHEEP?

- Placenta is the main regulator of fetal growth
- Insulin and IGF-I
  - Fetal/placental growth factor
  - Regulate amino acid (AA) transport across the placenta
    - Human; in vitro *Karl et al., 1992; Karl 1995; Fang et al., 2006*
    - Sheep; in vivo *Jensen et al, 2000; Harding et al., 1994*



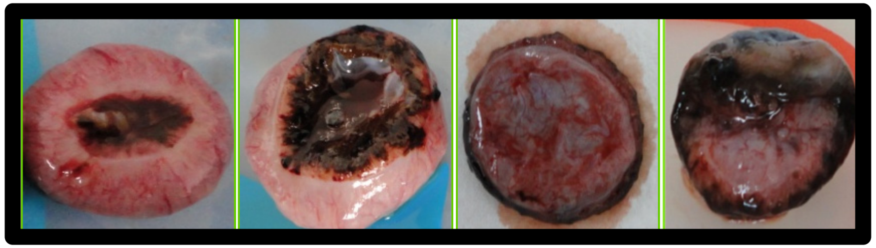




agresearch

➢4 types of placentomes

A B C D



- Adverse intra-uterine conditions leads to more type C and D placentomes
- Placentome size rather than type is related to vascularity

Is placentome size or type more important for growth of twin fetuses?

Placentas from 10 singleton vs 5 twin-bearing ewes at 140 days gestation were compared

agresearch

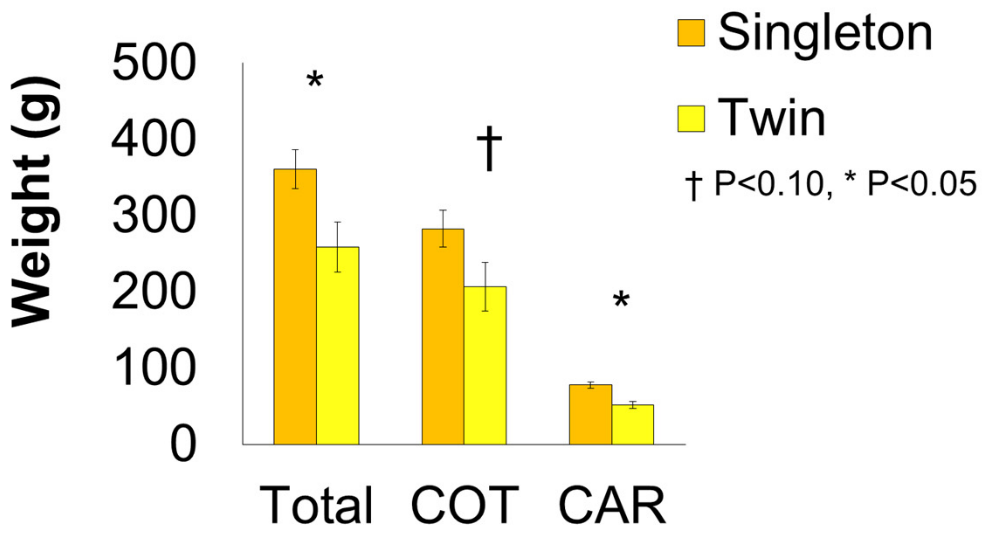


Figure 1. Total placentome (Total), cotyledon (COT) and caruncle (CAR) weight of singleton and twin placentae

Compared to singletons, twins had:

- Reduced total placentome weight by 28% (P=0.001)
- Reduced COT weight by 27% (P=0.08)
- Reduced CAR weight by 33% (P=0.002)
- Reduced fetal weight by 16% (P=0.006)
- Reduced placentome numbers by 35% (P=0.001)

agresearch

Adapted from van der Linden, Sciascia, Sales & McCoard (2012) J. Anim. Sci.

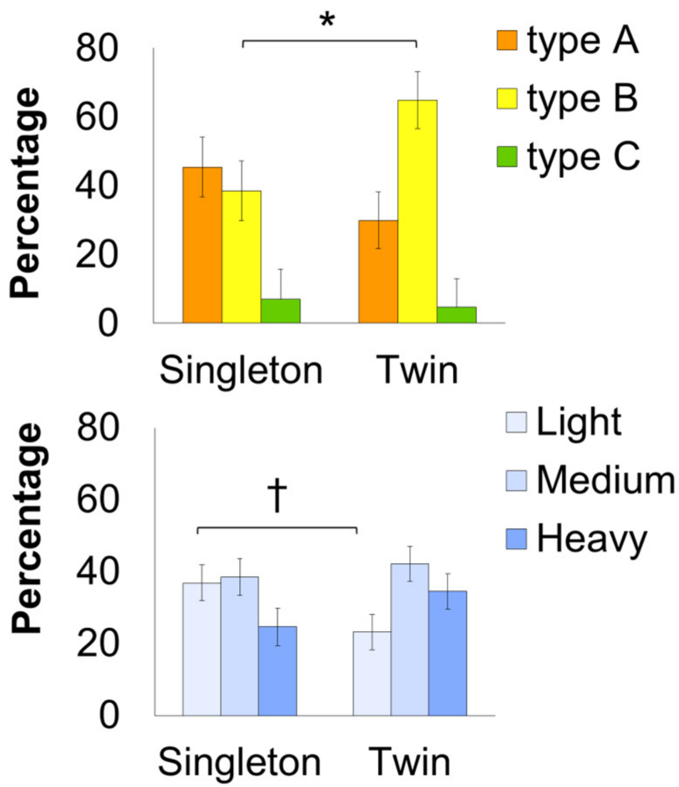


Figure 2. Placentome type (A, B, C) or size (light, medium, heavy) distribution of singleton and twin placentae

Compared to singletons, twins had:

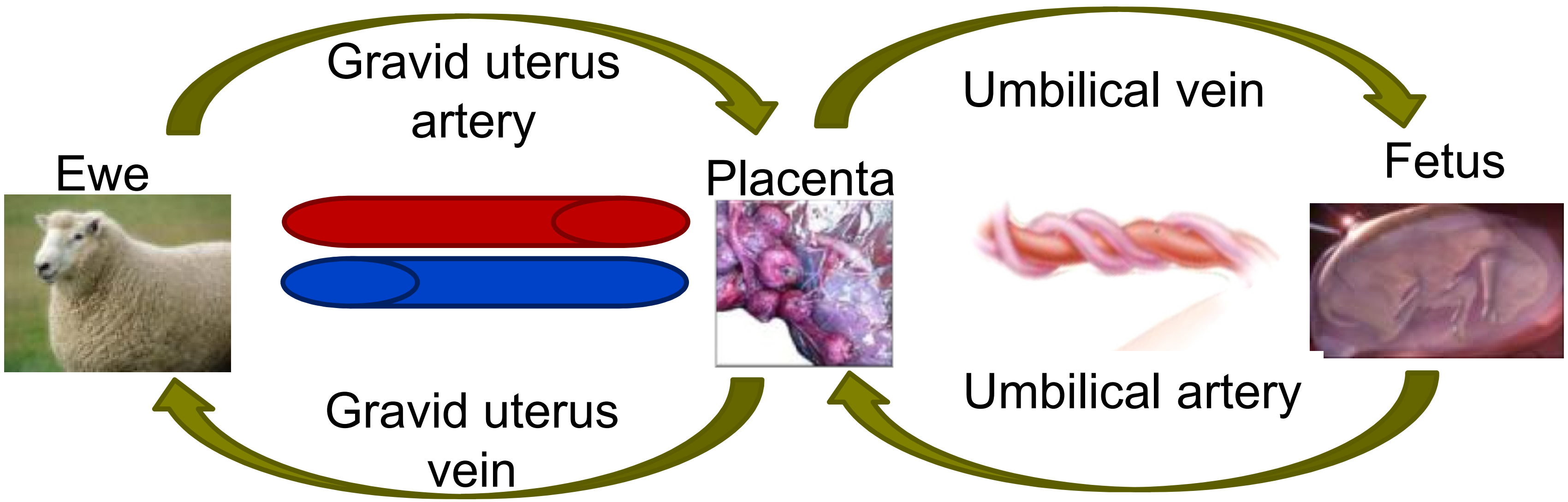
- Greater proportion of type B placentomes by 65% (P= 0.03)
- Smaller proportion of light placentomes by 38% (P= 0.07)
- Different distribution of placentome type and size

agresearch

Adapted from van der Linden, Sciascia, Sales & McCoard (2012) J. Anim. Sci.

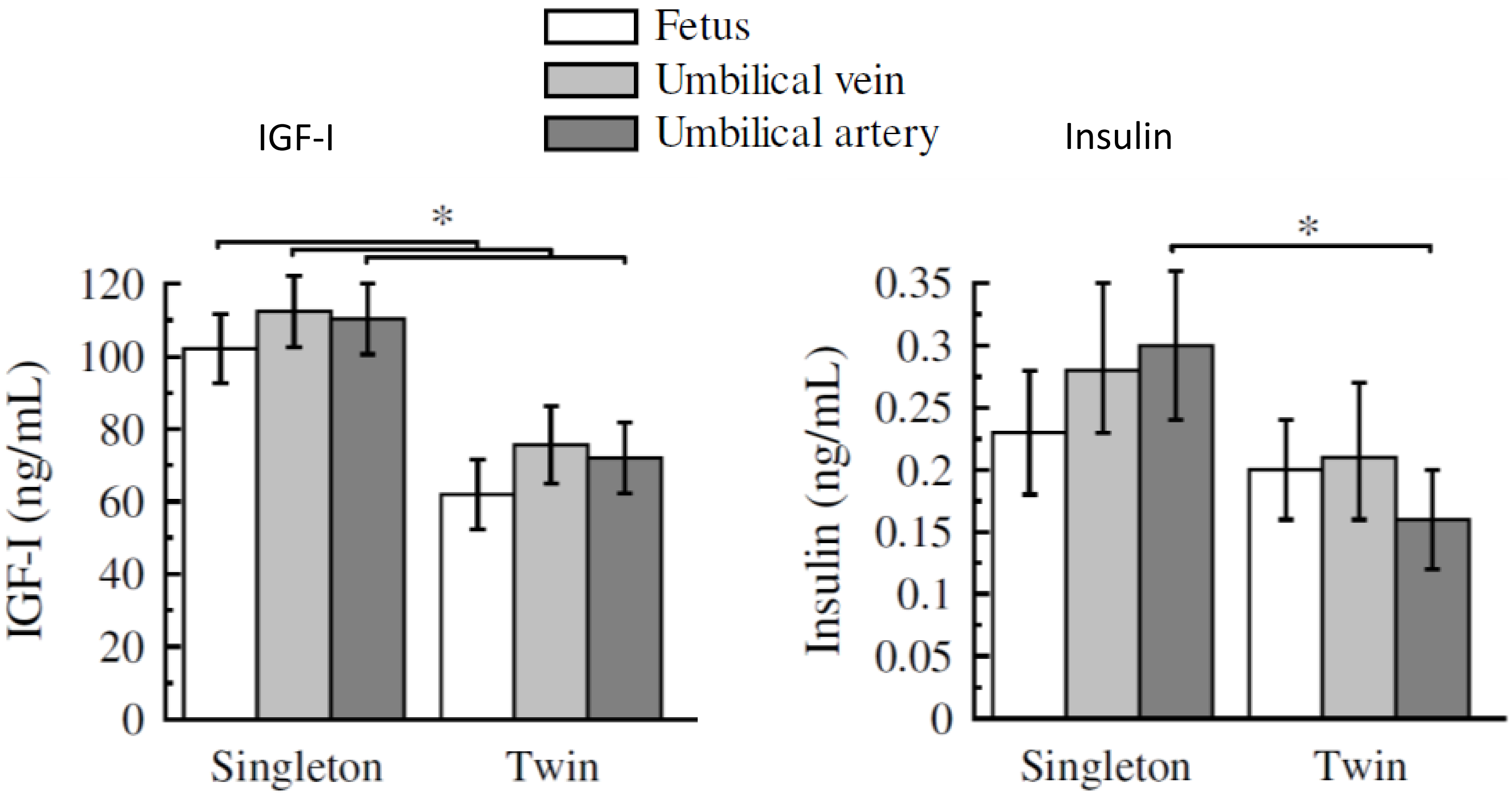
BLOOD PROFILES (AMINO ACIDS, INSULIN, IGF-I)

Placental nutrient transport



agresearch

HORMONES – IGF-I, INSULIN

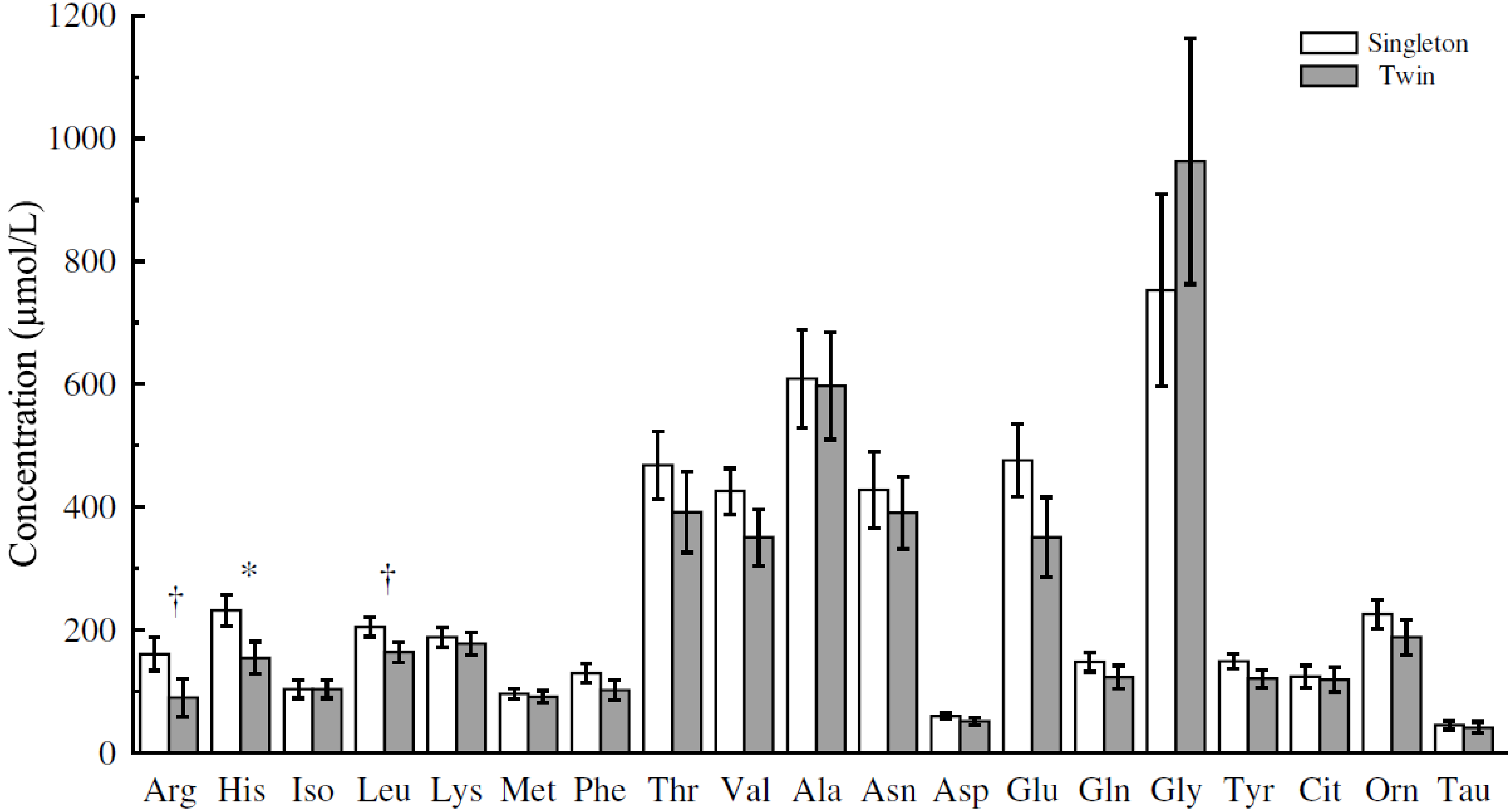


* P<0.05

agresearch

van der Linden, Sciascia, Sales & McCoard (2012) J. Anim. Sci.

AA IN FETAL PLASMA



No differences between singletons and twins in umbilical artery or vein plasma

agresearch

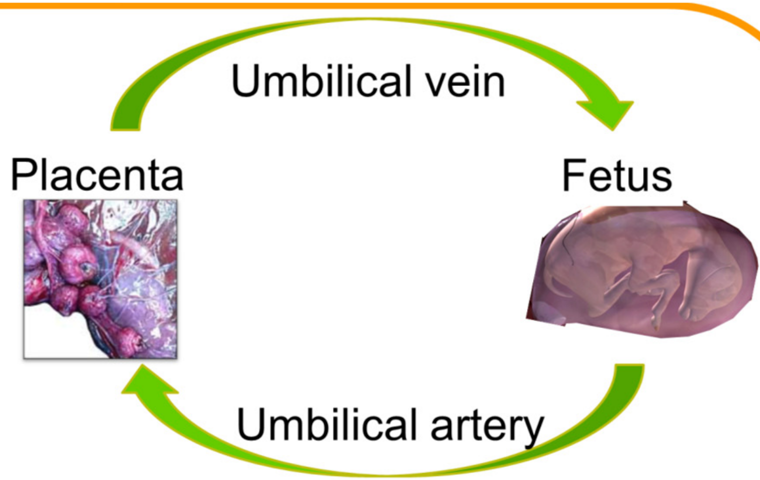
van der Linden, Sciascia, Sales & McCoard (2012) J. Anim. Sci.

AMINO ACID (AA) PROFILES

AA concentrations in fetal plasma

Compared to singletons, twins had:

- Histidine (His) by 33% (P=0.03)
- Arginine (Arg) by 44% (P=0.07)
- Leucine (Leu) by 20% (P=0.06)



In TWINS only:

Umbilical artery plasma had:

- Greater Glutamate (Glu) by 28% (P=0.09)
- Reduced Asparagine (Asn) by 53% (P=0.02)

compared to umbilical vein plasma

Umbilical artery plasma had:

- Greater Glutamate by 45% (P=0.006)
- Reduced Asparagine by 55% (P=0.004)

compared to fetal plasma

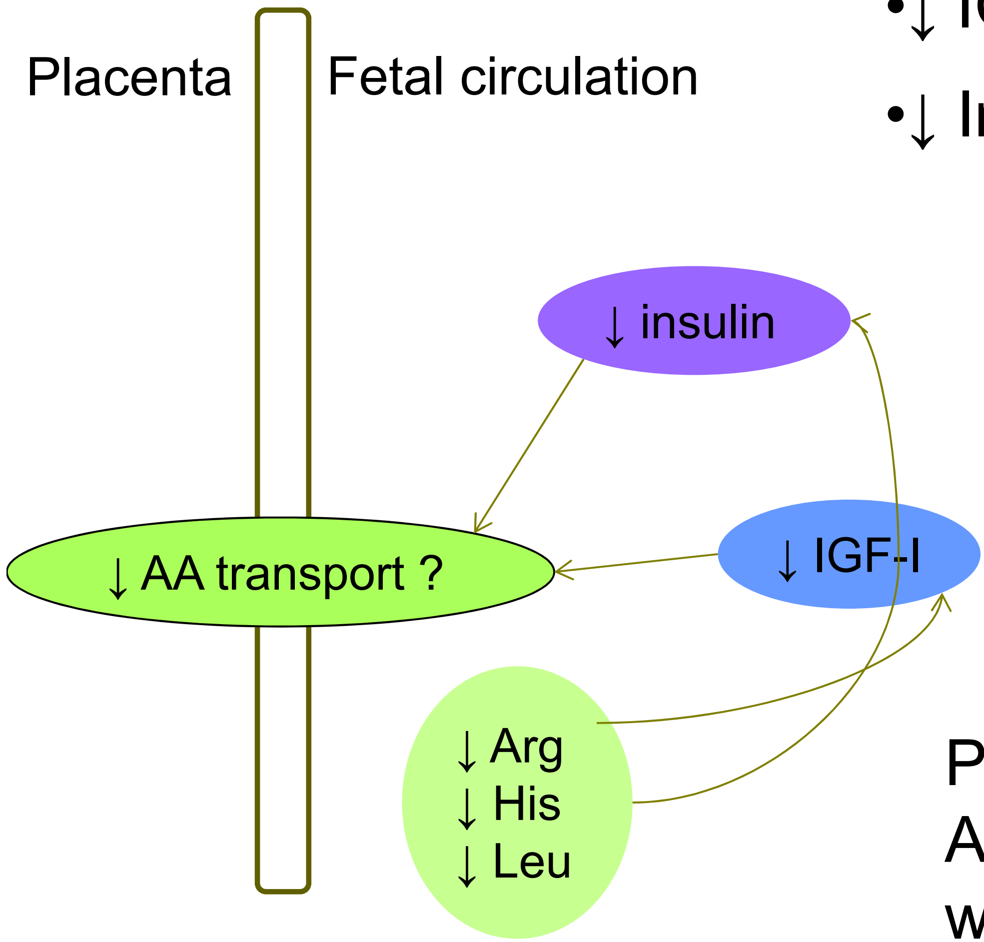
- Indicates the feto-placental unit functions differently between singletons and twins
- Is arginine limiting fetal growth?

agresearch

van der Linden, Sciascia, Sales & McCoard (2012) J. Anim. Sci.

Twin vs. Singleton

- ↓ Arg, His and Leu in fetal plasma
- ↓ IGF-I all 3 plasma pools
- ↓ Insulin in umbilical artery



Low birth weight
↓16%
twins vs. singleton

Placenta a likely link between AA, insulin-IGF axis and low birth weight in sheep as observed in humans and rodents

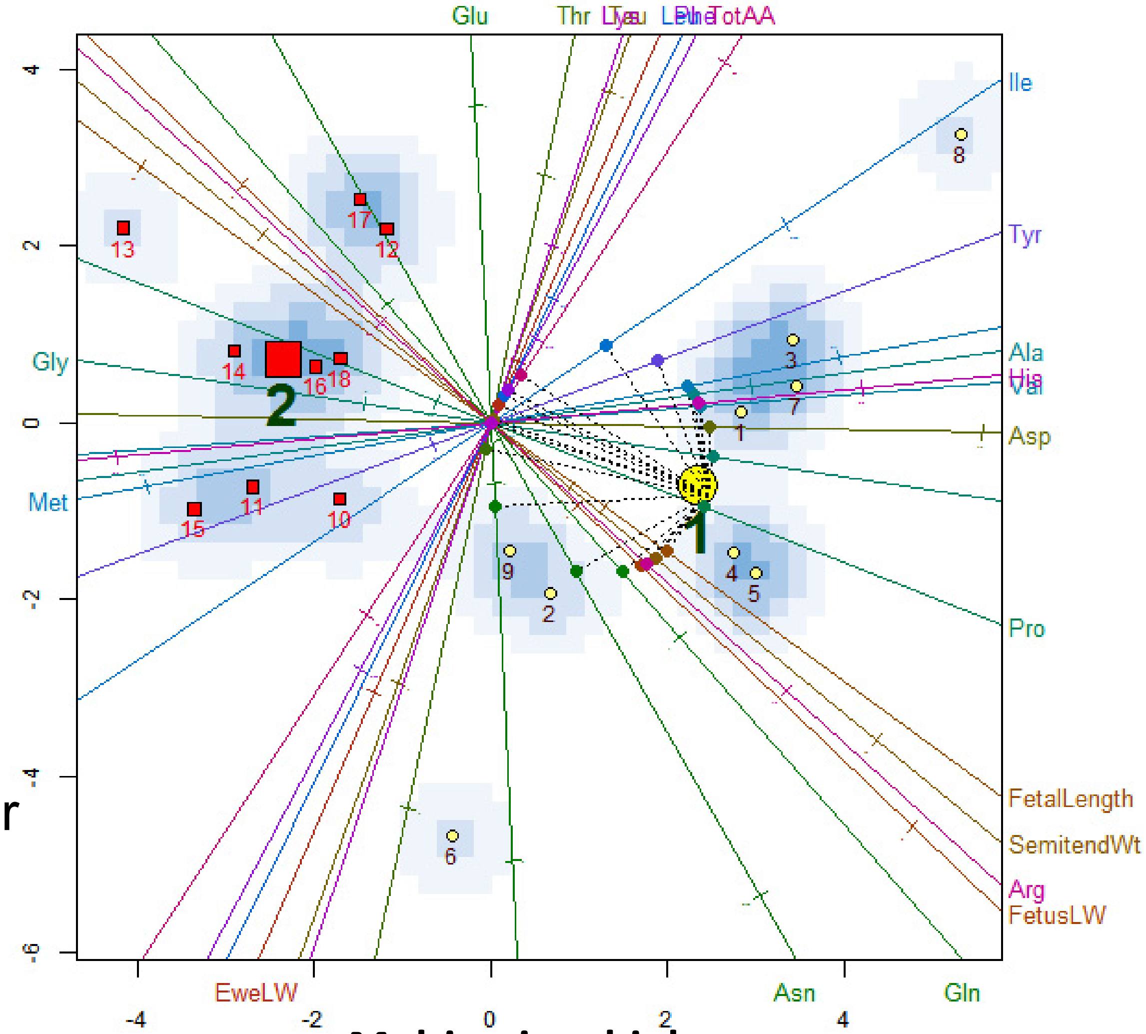
reviewed by Cleal et al 2008

agresearch

FREE AMINO ACID PROFILES IN MUSCLE OF SINGLE AND TWIN FETUSES AT 140 DAYS GESTATION

- Fetal weight twins<singles
- Arg, Gln, His, Val, Ala, Pro, Tyr, Val greater in singletons
- Arg closely related to fetal size

Changes in specific AA, rather than [Total AA] appears to be associated with lower muscle masses in twins



Multivariate biplot

agresearch

Pacheco, Treloar, Kenyon, Blair, McCoard (2010) Proc. NZ Soc. Anim. Prod.

Sales *et al. SpringerPlus* 2013, **2**:483
http://www.springerplus.com/content/2/1/483

SpringerPlus
a SpringerOpen Journal

RESEARCH Open Access

Muscle free amino acid profiles are related to differences in skeletal muscle growth between single and twin ovine fetuses near term

Francisco Sales[1,2,4], David Pacheco[1], Hugh Blair[2,3], Paul Kenyon[2,3] and Sue McCoard[1,2*]

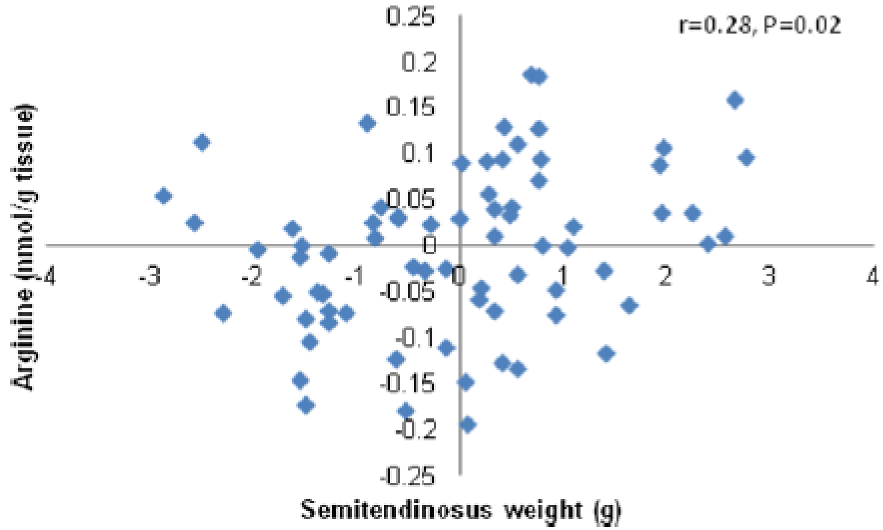


Figure 2 Partial correlation plot for ST muscle weight with arginine concentration. The plot graphic shows the partial correlation analysis for ST muscle weight (g) with arginine concentration (nmol/g wet tissue). The analysis considered pooled data of all fetuses and was performed after accounting for the effects of pregnancy rank, maternal size and nutrition.

agresearch

Partial correlations were estimated on the residual the AA concentration and muscle mass, after accounting for the effects of pregnancy rank, maternal size and nutritional treatments and results consider all animals.

ARGININE AS A SIGNALLING MOLECULE

Amino acids are natural therefore acceptable for NZ production systems. Arginine has many functions including:

- Direct activation of mTOR signalling (cell nutrient sensor)
- Antioxidant
- Regulation of hormone secretion
- Ammonia detoxification
- Regulation of gene expression
- Immune function
- Nitrogen reservoir
- Regulation of nutrient metabolism
- Angiogenesis
- Mitochondrial biogenesis & function

ARGININE SUPPLEMENTATION….

Research shows that maternal L-arginine supplementation in mid-gestation ewes can:

- Increase birth weight of single & twin lambs from under-fed ewes *Lassala et al 2010*
- Increase the birth weight of quadruplet lambs, but not triplets, twins and singles from well-fed ewes supplemented from 100-121 days gestation
  Lassala et al 2011
  – Fetal growth restriction in twin sheep is not observed until ~115-120 days gestation *McCoard et al. 2001*
  – Was L-arginine administration stopped too early?

agresearch

OBJECTIVE

To evaluate the effects of parenteral administration of L-arginine to well-fed twin-bearing ewes from day 100 of gestation to birth on fetal growth, body composition

Hypothesis: *that maternal parenteral administration of Arg to well-fed twin-bearing ewes from d 100 of gestation to birth would increase offspring birth weight*.

McCoard *et al. SpringerPlus* 2013, 2:684
http://www.springerplus.com/content/2/1/684

SpringerPlus
a SpringerOpen Journal

RESEARCH Open Access

Parenteral administration of twin-bearing ewes with L-arginine enhances the birth weight and brown fat stores in sheep

Sue McCoard[1*], Francisco Sales[1], Nina Wards[1], Quentin Sciascia[1], Mark Oliver[2], John Koolaard[1] and Danitsja van der Linden[1]

MATERIALS AND METHODS

Animal Trial

- Synchronized ewes naturally mated
- Indoor housing and feeding at P80
- 3X daily *iv.* bolus of L-arginine (345 μmol/kg BW) or saline (control) from P100 to birth

Data collection:

Day 140 gestation (P140; n=9 L-arginine, n=11 control ewes):

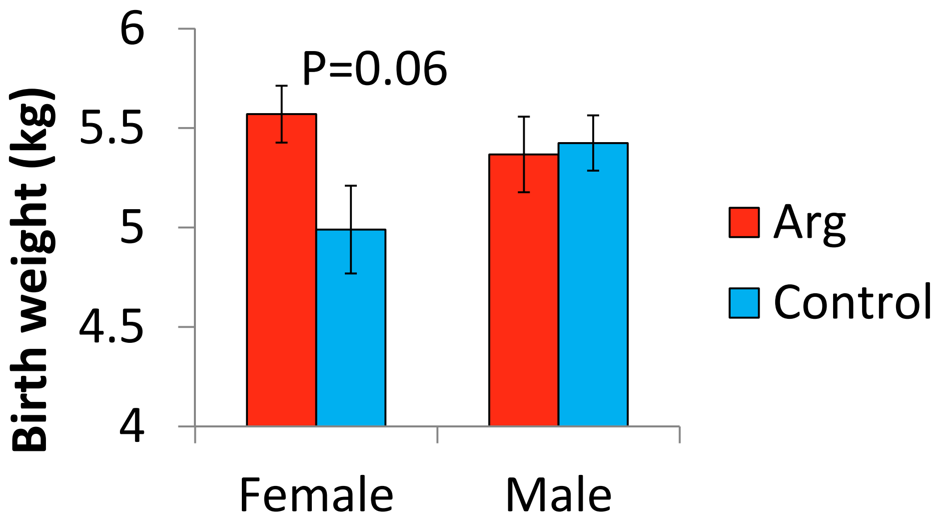
- Fetal weight, organ mass
- Blood samples (1 hr post bolus)

Birth (n=13 L-arginine, n=11 control ewes):

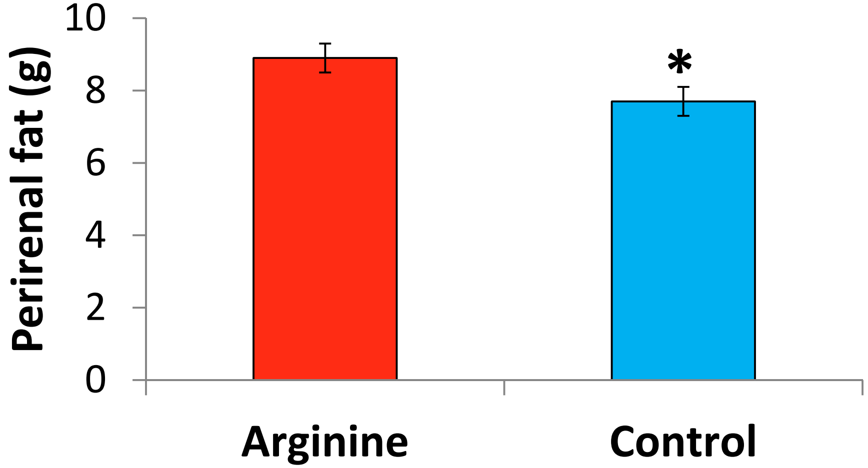
- Birth weight
- Blood samples (2 hours post-partum)

Amino acid profiles determined by ion-exchange chromatography

van der Linden et al 2012



12% ↑ in birth weight of female twin lambs without increasing ewe intake

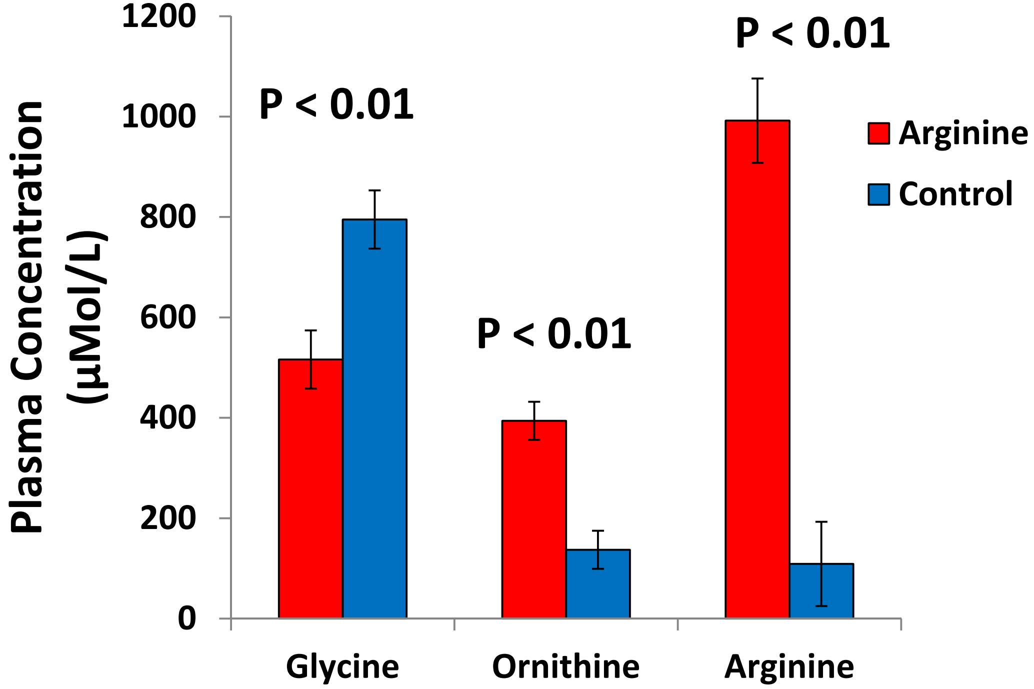


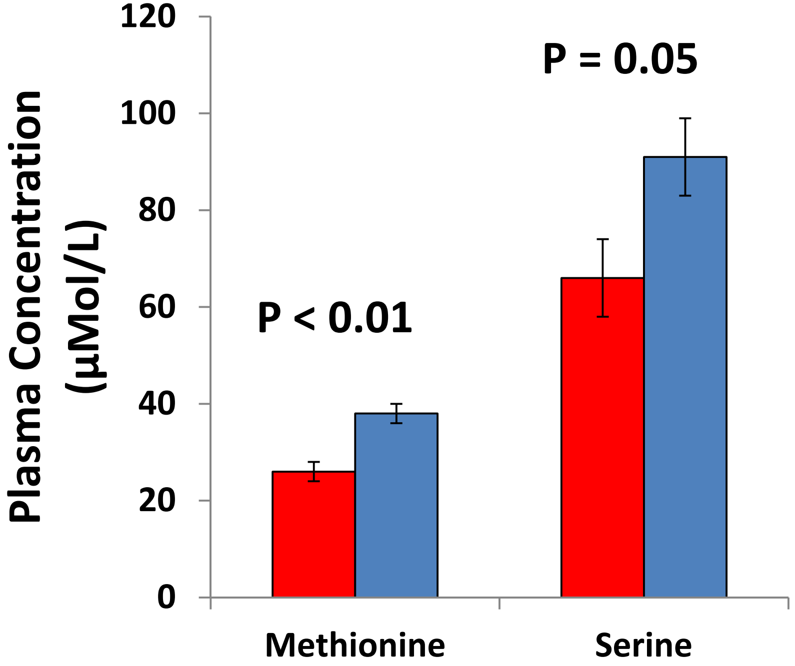
16% ↑ peri-renal fat – rectal temperatures increased 2 hrs post-birth by 0.6°C

No effect on any other organ weights

agresearch

EWE PLASMA AMINO ACIDS P140

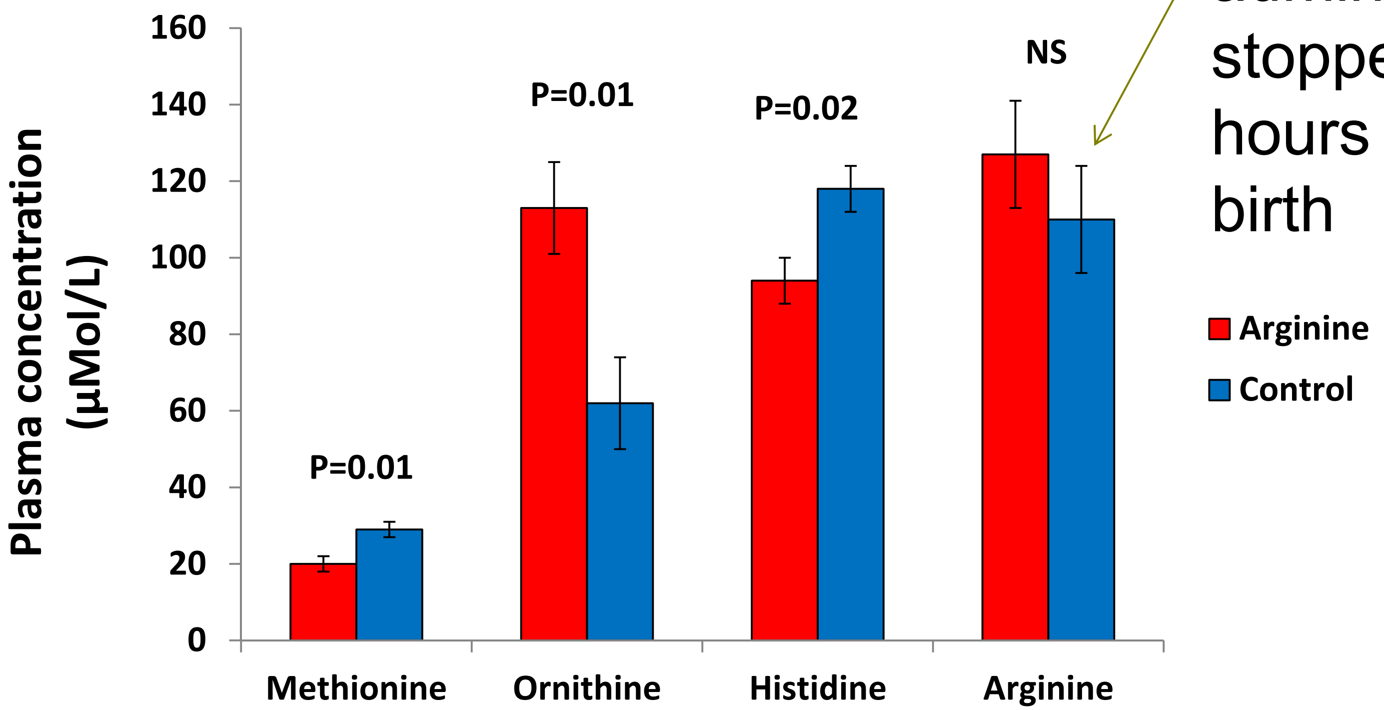




↑ concentrations of arginine and ornithine

↓ concentrations of glycine, methionine and serine

EWE PLASMA AMINO ACIDS - BIRTH



Arginine administration stopped 2-12 hours prior to birth

↑ concentrations of ornithine

↓ concentrations of methionine and histidine

HORMONE AND METABOLITE PROFILES

Arg vs Control ewes at day 140 gestation:

- ↑ insulin (0.33 vs 0.05 ng/mL; P=0.002)
- ↑glucose (3.74 vs 2.92 mmol/L; P=0.01)

No change in IGF-1, NEFA, glycerol, triglycerides

No change in any hormones or metabolites 2 hours post-birth (Arg supplementation ended 2-12 hours pre-birth)

agresearch

KEY FINDINGS

Maternal arginine administration to ewes from 100 days gestation to birth:

↑ birth weight of female lambs (12%)
↑ peri-renal fat stores in all lambs (16%)

agresearch

McCoard et al. 2013

BIRTH WEIGHT EFFECT

Birth weight effect contrasts Lassala et al. 2011

Timing of arginine administration (100-121 d vs. 100 – birth)?
Animal numbers (3-7 per group vs. 11-12 per group)?

Sex-specific effect of L-arginine on lamb birth weight intriguing

-Sex-specific effect of periconception nutrition on fetal development (Jaquiery et al. 2012)

-Potentially important implications for meat production, breeding replacements & hogget mating

THERMOREGULATION

- Effect on peri-renal fat stores is consistent with Satterfield et al. 2012

    -under-nourished & diet-induced obese sheep model –
    -observations at d125 of gestation

- Essential for neonatal thermogenesis and survival – effective adaptation to the cold challenge of the extra-uterine environment

- Constitutes 2% of body weight but accounts for 50% of the heat generated in the newborn (via non-shivering thermogenesis)

agresearch

THERMOREGULATION CONT…

- Increased peri-renal fat stores was associated with the up-regulation of UCP-1 (30%) and PRDM16 (17%)
    - *UCP-1 – marker for BAT thermogenesis and involved in the regulation of energy balance*
    - *PRDM16 – co-activator responsible for BAT lineage determination*

      Kajimura et al. 2010

- Increased UCP-1 was associated with a 68% increase in cortisol levels in the fetuses - known to regulate UCP-1

- Associated with increased rectal temperatures (0.6^{o}C) of the lambs 2 hours post-birth in the Arginine group

agresearch

McCoard, Wards, Senna Salerno (2014) Anim. Prod. Sci. (in press)

THERMOREGULATION

- Maternal arginine supplementation in mid-late gestation improves brown adipose tissue development in the twin sheep fetus which may increase lamb survival through enhanced thermoregulatory capacity

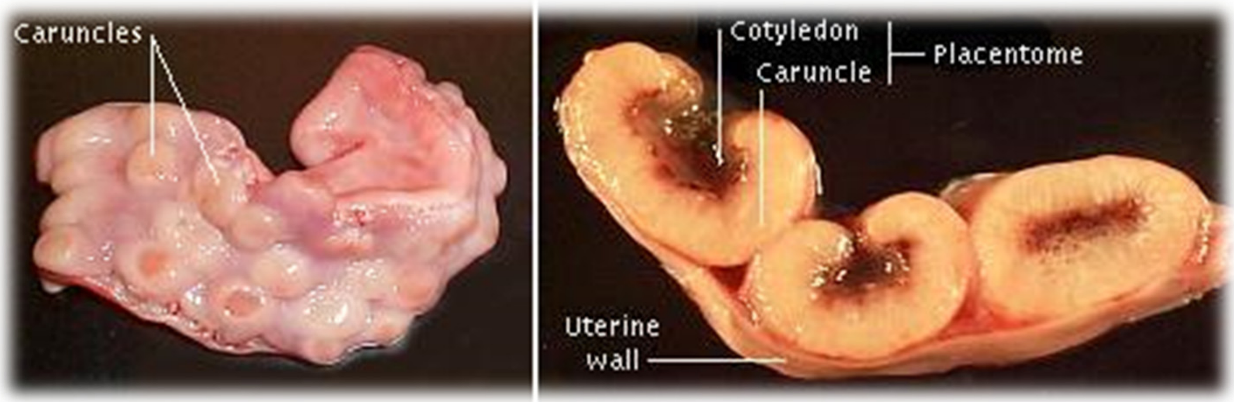
agresearch

DISCUSSION – PLACENTA

- Arginine – important for synthesis of nitric oxide (NO) and polyamines which play a key role in placental angiogenesis and growth in mammals

  Wu & Morris 1998, Sheppard et al. 2001, Wu et al. 2007, Ishikawa et al. 2007

  - Placentas from arginine-treated ewes were heavier than controls
  - Currently studying the impact on placental development and nutrient transfer



agresearch

SUMMARY

- The ability of maternal arginine supplementation to increase birth weight in females and brown fat stores in all lambs may have important implications for new-born survival and postnatal production performance
- Validation is required with larger numbers of animals and direct evaluation of impacts on survival
- Such knowledge is of importance to agriculture and medicine

agresearch

ACKNOWLEDGMENTS

Ngapouri Research Farm Staff

- *Mark Oliver*
- *Maggie Honeyfield-Ross*
- *Basil Koberstein*
- *Travis Gunn*
- *Ana-Mishel Sproski*
- *Anita Wylie*
- *Keith McCallum*
- *Anne Jaquiery*

Ulyatt-Reid Animal Facility Staff

- *Greg Skelton*
- *Hailey Gillespie*
- *Trevor Holloway*

AgResearch Staff

- *David Pacheco*
- *Bryan Treloar*
- *John Koolaard*
- *Nina Wards*

Funding

- *Ballance Agri-Nutrients*
- *AgResearch Capability Fund*
- Programa Formación de Capital Humano Avanzado, Becas Chile, CONICYT doctoral scholarship
- *Landcorp Farming Limited*

Students

- *Nick Palevich*
- *April Adiletta*
- *Amy Patten*


Thank you