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Does maternal size, nutrition and metabolic status affect offspring production traits in domestic species?

Morgane Robles, Pascale Chavatte-Palmer[1]

UMR BDR, INRA, ENVA, Université Paris Saclay, 78350, Jouy en Josas, France.

Abstract

The Developmental Origins of health and Disease state that environmental conditions during pregnancy affect long term outcomes in offspring. In the present paper, effects of maternal size and breed as well as maternal nutrition on offspring size, growth and production traits are described. Although birthweight is mostly not affected, metabolic perturbations are often observed in adult offspring. In animal production, however, the relation between developmental conditions and long-term offspring outcome may remain unnoticed. Nevertheless, improving dams' health and nutrition before and during pregnancy may help improving production traits in domestic animals.

Keywords: DOHaD, embryo transfer, fetal programming, nutrition, pregnancy.

Introduction

In mammals, developmental conditions at the time of conception, during pregnancy and the neonatal period are known to affect long-term post-natal health, as known under the term “Developmental Origins of Health and Disease” (DOHaD). This phenomenon, is associated with modifications in gene expression due to environmentally induced epigenetic mechanisms. Maternal environment, such as maternal metabolism and nutrition, or the use of reproductive biotechnologies, may have an effect on feto-placental development, growth and subsequent adult health, thus affecting offspring performance and longevity.

This article aims to summarize existing knowledge on long term effects of maternal phenotype in domestic species and their potential impact on animal health, fertility and welfare. Future directions both in research and for improvement of field management are discussed.

The other side of genetics: effect of maternal phenotype/genotype

Genetic selection for production traits is the basis of animal breeding. Taking into consideration maternal genetic value and production, the sire is selected based on his genetic indices and heritability, in order to improve desired production traits. Maternal genotype and phenotype are also seminal in determining the environment in which the embryo and fetus will develop, regardless of production traits. This can be studied by comparing cross-bred offspring born to dams of different genotypes, or by studying phenotypic variation in genetically identical animals (Fig. 1).

In pigs, the cross-breeding between Meishan sows (200 kg adult weight) and Yorkshire males (300 kg adult weight) yields lighter piglets than the opposite crossing (Meishan males and Yorkshire sows; Biensen *et al.*, 1999). Similarly, in cattle, calves born to South Devon cows (790 kg adult weight) and Dexter bulls (340 kg adult weight) were approximately 6 kg heavier than crossbred calves born to a Dexter cow (Joubert and Hamond, 1958). Moreover, Charolais breed embryos transferred into Brahman cows are lighter at birth (mean 29 kg) compared to Charolais embryos transferred into Charolais recipients (mean 63 kg). Inversely, Brahman embryos transferred into Charolais recipients result in calves with heavier birthweight (mean 41 kg) than those produced by the transfer of Brahman embryos into Brahman cows (mean 19 kg; Ferrell, 1991). These results indicate that maternal breed and consequently maternal size and environment will affect offspring weight and size at birth, regardless of genetic potential.

Further consequences on postnatal development have been explored in horses. In the first half of the 20th century, Walton and Hammond elegantly demonstrated, using cross-breeding between large Shire horses and small Shetland ponies, that crossbred offspring whose dam was a Shetland pony were smaller at birth and remained smaller as adults than those whose dam was a Shire mare (Walton and Hammond, 1938). Almost 50 years later, Tischner *et al.* showed that Polish pony embryos transferred into draft mares produced foals that were larger at birth and remained larger as adults, compared to those that had been transferred into mares of their own breed (Tischner *et al.*, 2000). More recently, the transfer of pony embryos into mares of larger breeds was shown to consistently increase fetal and postnatal growth until adulthood. Conversely, foals from a larger breed born to pony mares were small at birth and only partially caught-up to controls of the same breed (Allen *et al.*, 2004; Peugnet *et al.*, 2014). Moreover, both excess and reduced fetal growth were associated with osteoarticular lesions and metabolic perturbations, some of which still present at 2 years of age (Peugnet *et al.*, 2014, 2016).

Effect of maternal nutrition

Procedures in terms of maternal nutrition in domestic animals vary greatly depending on breed, location, availability of feedstuff and season, amongst other factors. The choice of dietary treatments in

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[1] Corresponding author: pascale.chavatte-palmer@inra.fr
Phone: +33(1)3465-2558

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experimental protocols is also very diverse, rendering it difficult to draw clear conclusions. In general, the effects of maternal nutrition on offspring phenotype are marginal, except when dietary treatments are severe and prolonged as reviewed recently (Funston *et al.*, 2012; Chavatte-Palmer *et al.*, 2015, 2016; Sinclair *et al.*, 2016; Opsomer *et al.*, 2017). The list of studies presented here does not claim to be exhaustive as the authors have selected key examples to illustrate each nutritional condition.

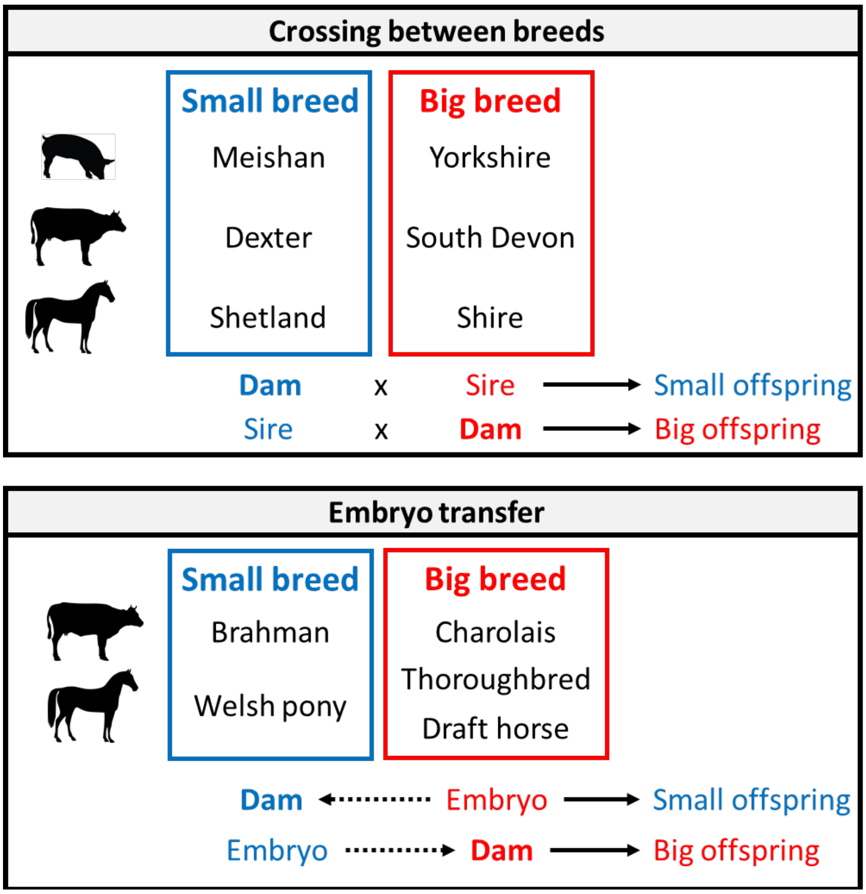

Figure 1. Effect of maternal and partenal size on offspring size after artificial insemination or embryo transfer. After Walton and Hamon (1938); Joubert and Hamon (1958); Ferrel. (1991); Biensen *et al.* (1999); Tischner *et al.* (2000); Allen *et al.* (2004); Peugnet *et al.* (2014).

Excess nutrition and obesity

In many studies, excess nutritional intake during pregnancy is confounded with maternal obesity. Obesity can be defined as excess adiposity above a certain level as defined by the authors depending on studies, before breeding and during pregnancy. Here we tried to discriminate studies with maternal gestational overfeeding from studies with maternal obesity prior to breeding.

Effects of excess maternal nutrition have been mainly studied in sheep (Table 1) with little observed effects on lamb birthweight and postnatal growth (Hoffman *et al.*, 2014; Khanal *et al.*, 2014; Kleemann *et al.*, 2015; Sen *et al.*, 2016). Nevertheless, expression of Insulin Growth Factor 1 (IGF1) is increased in the lamb liver (Hoffman *et al.*, 2014) resulting in increased plasma IGF1 concentrations (Hoffman *et al.*, 2016) and lipid accumulation is also observed in the lambs' muscle (Hoffman *et al.*, 2014; Reed *et al.*, 2014), together with increased insulin resistance (Hoffman *et al.*, 2016), increased adiposity (Khanal *et al.*, 2014), hyperglycemia and alteration of hepatic signaling pathways (Philp *et al.*, 2008). Finally, increased ovarian size and reduced ovarian follicular numbers have also been observed (Da Silva *et al.*, 2003; Kleemann *et al.*, 2015). *Ad libitum* access to feedstuff at adulthood (19-22 months) increased food intake, weight gain, visceral and subcutaneous fat, basal glycemia and insulinemia in all animals but offspring born to obese dams were less affected than offspring born to control dams (Long *et al.*, 2010, 2015).

When maternal obesity was induced by overfeeding dams starting 2 months before breeding and until lambing, offspring birthweight was not affected but glucose metabolism was consistently and durably altered. The number of pancreatic β-cells was reduced in fetal life, resulting in hyperglycemia, un hypoinsulinemia and reduced pancreatic weight at birth and increased insulin resistance and altered glycemic regulation in adults. Moreover, muscular fibrosis and hyperleptinemia were observed (Long *et al.*, 2010, 2015; Huang *et al.*, 2012; Zhang *et al.*, 2012).

Table 1. Summary of studies performed on the effects of overnutrition in pregnant ewes on the post-natal development of the offspring. The level of excess nutrition is expressed as a percentage of the energy content ingested by the control group.

Level of overnutrition	Period of overnutrition	Function	Age	Phenotype	Source
Periconceptioal overnutrition					
150%	From 17 days before insemination to 6 days after	Growth	Birth	= Live weight	Kleeman *et al*., 2015
			5 days	↗ Ovary weight	
Overnutrition in the begining of gestation					
Ad libitum	The 100 first days of gestation (2 first third)	Endocrinology	103 days of gestation	↘ Progesterone concentration	Da Silva *et al*., 2003
		Ovary function		↘ Number of primordial follicles ↘ Number of total follicles	
175%	From 30 to 80 days of gestation	Growth	From birth to 5 months	= Live weight	Sen *et al*., 2016
		Muscle function	5 months	↗ Fibres density	
Overnutrition in the end of gestation					
126%	From 116 days of gestation	Growth	1 day	= Live weight ↗ Heart weight	Hoffman *et al*., 2014
			3 months	↘ Live weight	
		Endocrinology	From 1 day to 3 months	↘ IGFBP3 Concentration ↗ Leptin Concentration	
		Gene expression	1 day	↗ Liver *IGF1* expression ↗ Muscle *β-catenin* expression (stimulate the differentiation of stem cells into muscle cells)	
155%	From 115 days of gestation	Carbohydrate metabolism	From 1 to 30 days	↗ Fasting glycaemia ↘ % of phosphorylated AMPK in the liver (can contribute to ↗ the production of glucose by the liver)	Philp *et al*., 2008
150%	From 105 days of gestation	Growth	From birth to 2 months	= Live weight	Khanal *et al*., 2014
			From 2 to 6 months	↘ Live weight	
		Body condition	6 months	↘ % subcutaneous adipose tissue ↘ Subcutaneous adipose tissue / Visceral adipose tissue	

Level of overnutrition	Period of overnutrition	Function	Age	Phenotype	Source
Overnutrition during the most of gestation					
140%	From 31 days of gestation	Growth	From 1 day to 3 months	↗ Live weight, thoracic perimeter	Reed *et al*., 2014 Hoffman *et al*., 2016 Pillai *et al*., 2017
			1 day	↗ Length	
		Endocrinology	3 months	↗ IGF1 Concentration ↗ IGFBP2 Concentration ↗ Leptin concentration	
		Carbohydrate metabolism	3 months	↗ Insulin/basal glucose ratio ↗ Insulin resistance	
		Muscle function	1 day	↗ Fibres area (cross section) ↗ *Myostatin* expression	
			3 months	↘ Fibres area (cross section)	
			From 1 day to 3 months	↗ Lipid accumulation in muscle	
Modelling of obesity – Overnutrition throughout gestation					
150%	From 60 days before insemination	Gestation	Gestation length	↘ Gestation length	Long *et al*., 2010 Huang *et al*., 2012 Zhang et al., 2012 Long et al., 2015
		Growth	From birth to 19 months	= Live weight	
		Carbohydrate metabolism	135 days of gestation	↘ β pancreatic cells ↗ Production of insulin by remaining β cells	
			Birth	↗ Basale glycaemia ↘ Basale insulinemia ↘Pancreas weight	
			19 months	↗ Insulin resistance ↘ Glucose disposition by insulin independent glucose transporters	
		Muscle function	2.5 years (males)	↗ Collagen concentration (=↗ fibrosis) ↘ Metalloproteases expression ↗ Metalloproteases inhibitor expression	
		Endocrinology	2-3 years (males)	↗ Leptin concentration	

IGF1: Insulin Growth Factor 1; IGFBP3: Insulin growth Factor Binding Protein 3; AMPK: AMP-activiated protein kinase; IGFBP2: Insulin growth Factor Binding Protein 2.

In order to understand the importance of preconceptional obesity, embryos produced in adult obese or control ewes were transferred in adolescent control or obese ewes (Wallace *et al.*, 2017). Pregnancy length was shorter in obese recipients and resulted in reduced lamb birthweight compared to controls, regardless of donor group. The colostrum quality was also affected by obesity (Wallace *et al.*, 2017).

Finally, in cattle, feeding with 125% requirements from 3 months of gestation increases calf birthweight but weaning weight and carcass quality at 5 months of age were not different between groups (Wilson *et al.*, 2016). Thus, excess maternal nutrition and maternal obesity both affect lipid and glucose metabolism in offspring and may also alter body composition and muscle quality.

Undernutrition

As for excess nutrition, maternal undernutrition has been extensively studied in the ewe (Table 2). Only severe maternal undernutrition reduces birthweight whereas moderate undernutrition appears un-noticed in terms of offspring birthweight (Bispham *et al.*, 2003; Gardner *et al.*, 2005; Ford *et al.*, 2007; Hoffman *et al.*, 2014, 2016; Field *et al.*, 2015; Kleemann *et al.*, 2015; Sen *et al.*, 2016; Whorwood *et al.*, 2016). Nevertheless, lambs born to undernourished ewes have reduced plasma IGF1 and T3 (triiodothyronin) concentrations (Hoffman *et al.*, 2014; Field *et al.*, 2015) and physiological pathways involving corticosteroid hormones are disturbed (Whorwood *et al.*, 2016). Maternal undernutrition has also been associated with alterations in glucose metabolism, including hyperglycemia or hyperinsulinemia, increased insulin secretion by β-cells and reduced glucose tolerance (Gardner *et al.*, 2005; Ford *et al.*, 2007; Hoffman *et al.*, 2016). Intra-muscular lipid depositions are also increased in these lambs together with modifications in muscular fiber development (Ford *et al.*, 2007; Reed *et al.*, 2014) and increased perirenal fat mass was observed with or without reduction of subcutaneous fat (Gardner *et al.*, 2005; Ford *et al.*, 2007; Hoffman *et al.*, 2014, 2016).

In goats, a progressive maternal undernutrition (goats were fed 50 to 80% of the spontaneous intake of controls) in the last third of gestation reduced birthweight in male kids only although Non-esterified fatty Acid concentrations (NEFA) were increased in all kids (Laporte-Broux *et al.*, 2011). Subsequently at 1 and 2 years of age, restricted female offspring ate more than controls but no difference in energy metabolism was evidenced between groups (Laporte-Broux *et al.*, 2012).

In beef cattle, feeding cows at 80% requirements between 3 and 6 months of gestation reduced subcutaneous rib fat thickness and increased the intra- to inter-muscular fat ratio in 7 months old calves (Mohrhauser *et al.*, 2015). The birthweight of calves born to Angus cross-bred cows fed 60% of their requirements between 30 and 85 days or between 30 and 140 days of gestation was the same as offspring born to cows fed 100% of requirements but their liver was heavier (Prezotto *et al.*, 2016). Moreover, nutritional supplementation of restricted beef heifers during pregnancy did not increase offspring birthweight nor subsequent performance (Summers *et al.*, 2015) but increased feedlot efficiency and altered carcass characteristics with a tendency for high fat concentrations in the meat of animal born to restricted, non-supplemented heifers (Summers *et al.*, 2015).

In rabbits, a 50% maternal undernutrition from 7 to 19 days or from 20 to 27 days of gestation (31 days pregnancy) reduced pups' birthweight but post-natal growth, feeding behavior and body composition were not altered until 2,5 months of age (Lopez-Tello *et al.*, 2017).

Thus, whatever the species, although maternal undernutrition may not alter birthweight, offspring lipid and glucose metabolism are usually disturbed, affecting body composition and muscular development.

Effect of maternal metabolism

Independently from nutrition, maternal metabolism can be affected by many factors. Insulinoresistance is usually linked to obesity but can also be associated to production. Indeed, high yielding dairy cattle are prone to insulinoresistance because of their high energy requirements for milk production inducing a negative energy balance and this lactational insulinoresistance can persist for subsequent pregnancies (Bossaert *et al.*, 2008; De Koster and Opsomer, 2013; Zachut *et al.*, 2013; Opsomer *et al.*, 2017). Dairy cows insulinoresistant in late gestation produce lighter calves with reduced IGF1 plasma concentrations and increased insulinemia at birth (Kawashima *et al.*, 2016). Effects on subsequent offspring production have not been studied but epidemiological data indicate a slightly reduced milk yield if offspring from dams inseminated at peak lactation (González-Recio *et al.*, 2012).

Effect of maternal parity

The study of maternal age and parity on offspring development is difficult in production animals as age and parity are usually linked. Heifers are also non-lactating at breeding in contrast to cows.

In the horse, primiparous mares produce smaller and lighter foals at birth than multiparous mares (Fig. 2; Doreau *et al.*, 1991; Lawrence *et al.*, 1992; Pool-Anderson *et al.*, 1994; Cymbaluk and Laarveld, 1996; Wilsher and Allen, 2003; Elliott *et al.*, 2009; Klewitz *et al.*, 2015; Vazquez *et al.*, 2015; Meirelles *et al.*, 2017). Moreover, it has been shown that foals born to primiparous mares remain smaller until 1 year of age and lighter until 4 months of age compared with foals born to multiparous mares (Pool-Anderson *et al.*, 1994; Cymbaluk and Laarveld, 1996; Zoch *et al.*, 2016; Meirelles *et al.*, 2017). This difference of growth seems to be linked with decreased IGF-1 serum concentration in primiparous foals (Cymbaluk and Laarveld, 1996).

Table 2. Summary of studies performed on the effects of undernutrition in pregnant ewes on the post-natal development of the offspring. The level of undernutrition is expressed as a percentage of the energy content ingested by the control group.

Undernutrition	Undernutrition period	Function	Age	Phenotype	Source
Periconceptional undernutrition					
70%	From 17 days before insemination to 6 days after	Growth	Birth	= Live weight	Kleeman *et al*., 2015
			5 days	↗ Liver weight	
Undernutrition in early gestation					
50%	28 to 79 days of gestation	Growth	135 days of gestation	= Live weight	Field *et al*., 2015
50%	28 to 78 days of gestation	Growth	Birth	↘ Live weight	Ford *et al*., 2007
			From 4 to 8 months	↗ Live weight	
		Body condition	8 months	↗ Perirenal and muscle adipose tissue	
		Carbohydrate metabolism	2 months	↗ Basal glycaemia ↗ Pancreatic β cell response	
			8 months	↘ Pancreatic β cell response	
50%	28 to 77 days of gestation	Growth	Birth	= live weight, ↗ total length, ↗ kidneys weight	Whorwood *et al*., 2016
		Gene expression		↗ G*lucocorticoid receptor* expression (adrenal, liver, lung, perirenal adipose tissue, kidneys) ↘ *11- βHSD2* expression (adrenals, kidneys)	
40%	28 to 80 days of gestation	Growth	Birth	↗ Live weight	Bispham *et al*., 2003
50%	30 to 80 days of gestation	Growth	Birth	= Live weight	Sen *et al*., 2016
			5 months	↘ Live weight	

Undernutrition	Undernutrition period	Function	Age	Phenotype	Source
Undernutrition in late gestation					
60%	From 116 days of gestation	Growth	1 day	↘ Live weight, ↘ thoracic perimeter	Hoffman *et al.,* 2014
			3 months	↘ Back subcutaneous adipose tissue thickness	
		Endocrinology	1 day	↘ T3 concentration	
			From 1 day to 3 months	↘ IGF1 concentration ↘ IGFBP3 concentration	
50%	From 110 days of gestation	Growth	From birth to 1 year	= Live weight	Gardner *et al*., 2005
		Carbohydrate metabolism	1 year	↘ Glucose tolerance ↘ GLUT4 expression in the perirenal adipose tissue	
		Body condition	1 year	↗ Fat mass	
50%	From 105 days of gestation	Growth	From birth to 6 months	↘ Live weight	Khanal et al., 2014
			6 months	↘ Subcutaneous adipose tissue / visceral adipose tissue ratio	
Undernutrition throughout gestation					
50%	From 28 days of gestation	Growth	135 days of gestation	= Live weight, ↗ liver weight	Field *et al*., 2015
		Carbohydrate metabolism		↗ Umbilical insulinemia	
		Endocrinology		↗ Umbilical IGF1 concentration	
60%	From 31 days of gestation	Growth	From 1 day to 3 months	= Live weight, total length	Reed *et al*., 2014 Hoffman *et al*., 2016
			3 months	↗ Heart weight	
		Body condition	3 months	↘ Back subcutaneous adipose tissue thickness	
		Carbohydrate metabolism	3 months	↗ Basal insulinemia ↗ Basal insulin/glucose ratio	
		Muscle function	1 day	↗ Fibres area (cross section)	
			3 months	↘ Fibres area (cross section)	
			From 1 day to 3 months	↗ Lipid accumulation in muscle	

11-βHSD: 11β-hydroxusteroid dehydrogenase : converts cortison into cortisone; T3: Triiodothyronine; IGF1: Insulin Growth Factor 1; IGFBP3: Insulin growth Factor Binding Protein 3; GLUT4: Glucose transporter 4.

In dairy cattle, heifers have a shorter gestation length and produce smaller (-9%) and lighter calves compared to cows (Kertz *et al.*, 1997; Kamal *et al.*, 2014, 2015) with a reduced body mass index (weight/withers' heigth * crown-rump length) at birth (Kamal *et al.*, 2014, 2015). Nevertheless, alterations of the glucose metabolism were not observed at birth in these calves (Kamal *et al.*, 2015). Finally, heifers' colostrum contains less calcium, phosphorus and magnesium than multiparous cow colostrum, indicating that colostrum quality is altered, maybe for other components (Kume and Tanabe, 1993).

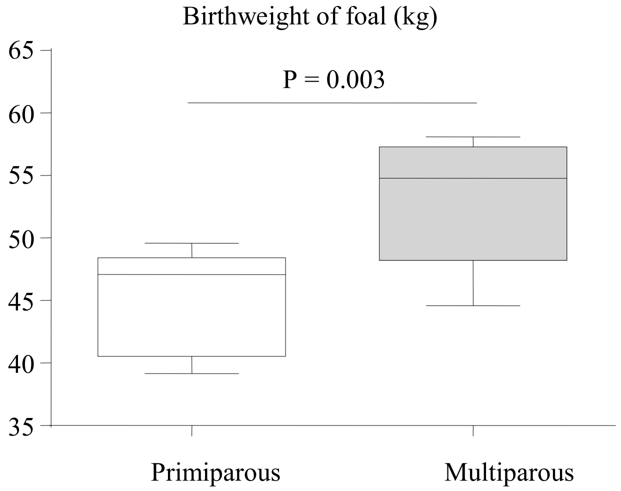

Figure 2. Birthweight of foals depending on the parity of the mare. Data derived from Doreau *et al.* (1991); Lawrence *et al.* (1992); Wilsher and Allen (2003); Elliott *et al.* (2009); Meirelles *et al.* (2017).

Practical implications for embryo transfer

The data presented above show clear evidence that maternal size and nutrition may influence offspring size but also metabolism and production. Other production and health traits, such as immunity, feeding behavior but also fertility may also be affected (Chadio and Kotsampasi, 2014; Chavatte-Palmer *et al.* 2014). This pleads for a very careful choice of embryo recipients in terms of breed and size but also underlines the importance of the management of these animals before and during pregnancy. The molecular basis for these effects is epigenetic mechanisms (Gonzalez-Recio *et al.*, 2015; Triantaphyllopoulos *et al.*, 2016). Future research is needed to explore if epigenetic markers could be used as predictors of long term outcomes in offspring.

References

Allen W, Wilsher S, Tiplady C, Butterfield R. 2004. The influence of maternal size on pre- and postnatal growth in the horse: III postnatal growth. *Reproduction,* 127:67-77.

Biensen NJ, Wilson ME, Ford SP. 1999. The impacts of uterine environment and fetal genotype on conceptus size and placental vascularity during late gestation in pigs. *J Anim Sci,* 77:954-959.

Bispham J, Gopalakrishnan GS, Dandrea J, Wilson V, Budge H, Keisler DH, Pipkin FB, Stephenson T, Symonds ME. 2003. Maternal endocrine adaptation throughout pregnancy to nutritional manipulation: Consequences for maternal plasma leptin and cortisol and the programming of fetal adipose tissue development. *Endocrinology,* 144:3575-3585.

Bossaert P, Leroy J, Vliergher S, Opsomer G. 2008. Interrelations between glucose-induced insulin response, metabolic indicators and time of first ovulation in high-yielding dairy cows. *J Dairy Sci,* 91:3363-3371.

Chadio S, Kotsampasi B. 2014. The role of early life nutrition in programming of reproductive function. *J Dev Orig Health Dis*, 5:2-15.

Chavatte-Palmer P, Debus N, Dupont,C, Camous S. 2014. Nutritional programming and the reproductive function of the offspring. *Anim Prod Sci*, 54:1166-1176.

Chavatte-Palmer P, Richard C, Peugnet P, Robles M, Rousseau-Ralliard D, Tarrade A. 2015. The developmental origins of health and disease: importance for animal production. *Anim Reprod Sci,* 12:505-520.

Chavatte-Palmer P, Tarrade A, Rousseau-Ralliard D. 2016. Diet before and during pregnancy and offspring health: The importance of animal models and what can be learned from them. *Int J Environ Res Public Health,* 13:E586. doi: 10.3390/ijerph13060586.

Cymbaluk N, Laarveld B. 1996. The ontogeny of serum insulin-like growth factor-I concentration in foals: effects of dam parity, diet, and age at weaning. *Domest Anim Endocrinol,* 13:197-209.

Da Silva P, Aitken RP, Rhind SM, Racey PA, Wallace JM. 2003. Effect of maternal overnutrition during pregnancy on pituitary gonadotrophin gene expression and gonadal morphology in female and male foetal sheep at day 103 of gestation. *Placenta*, 24:248-257.

De Koster JD, Opsomer G. 2013. Insulin resistance in dairy cows. *Vet Clin North Am Food Anim Pract,* 29:299-322.

Doreau M, Boulot S, Martin-Rosset W. 1991. Effect of parity and physiological state on intake, milk production and blood parameters in lactating mares differing in body size. *Anim Prod,* 53:111-118.

Elliott C, Morton J, Chopin J. 2009. Factors affecting foal birth weight in Thoroughbred horses. *Theriogenology,* 71:683-689.

Evans AC, Mossa F, Walsh SW, Scheetz D, Jimenez-Krassel F, Ireland JL, Smith GW, Ireland JJ. 2012. Effects of maternal environment during gestation on ovarian folliculogenesis and consequences for fertility in bovine offspring. *Reprod Domest Anim*, 47(suppl. 4):31-37.

Ferrell CL. 1991. Maternal and fetal influences on uterine and conceptus development in the cow: I. Growth of tissues of the gravid uterus. *J Anim Sci,* 69:1945-1953.

Field ME, Anthony R V., Engle TE, Archibeque SL, Keisler DH, Han H. 2015. Duration of maternal undernutrition differentially alters fetal growth and hormone concentrations. *Domest Anim Endocrinol,* 51:1-7.

Ford SP, Hess BW, Schwope MM, Nijland MJ, Gilbert JS, Vonnahme KA, Means WJ, Han H, Nathanielsz PW. 2007. Maternal undernutrition during early to mid-gestation in the ewe results in altered growth, adiposity, and glucose tolerance in male offspring. *J Anim Sci*, 85:1285-1294.

Funston RN, Summers AF, Roberts AJ. 2012. Alpharma Beef Cattle Nutrition Symposium: implications of nutritional management for beef cow-calf systems. *J Anim Sci*, 90:2301-2307.

Gardner D, Tingey K, Van Bon B, Ozanne S, Wilson V, Dandrea J, Keisler D, Stephenson T, Symonds M. 2005. Programming of glucose-insulin metabolism in adult sheep after maternal undernutrition. *Am J Physiol Regul Integr Comp Physiol,* 289:947-954.

González-Recio O, Ugarte E, Bach A. 2012. Trans-generational effect of maternal lactation during pregnancy: a Holstein cow model. *PLoS One,* 7:e51816.

Gonzalez-Recio O, Toro MA, Bach A. 2015. Past, present, and future of epigenetics applied to livestock breeding. *Front Genet*, 6:305. doi: 10.3389/fgene.2015.00305.

Hoffman ML, Rokosa MA, Zinn SA, Hoagland TA, Govoni KE. 2014. Poor maternal nutrition during gestation in sheep reduces circulating concentrations of insulin-like growth factor-I and insulin-like growth factor binding protein-3 in offspring. *Domest Anim Endocrinol,* 49:39-48.

Hoffman ML, Peck KN, Forella ME, Fox AR, Govoni KE, Zinn SA. 2016. The effects of poor maternal nutrition on postnatal growth and development of lambs. *J Anim Sci*, 94:789-799.

Huang Y, Zhao JX, Yan X, Zhu MJ, Long NM, McCormick RJ, Ford SP, Nathanielsz PW, Du M. 2012. Maternal obesity enhances collagen accumulation and cross-linking in skeletal muscle of ovine offspring. *PLoS One,* 7:1-8.

Joubert D, Hamond J. 1958. A crossbreeding experiment with cattle, with special reference to maternal effect in South Devon-Dexter crosses. *J Agric Sci*, 51:325-341.

Kamal MM, Van Eetvelde M, Depreester E, Hostens M, Vandaele L, Opsomer G. 2014. Age at calving in heifers and level of milk production during gestation in cows are associated with the birth size of Holstein calves. *J Dairy Sci,* 97:5448-5458.

Kamal MM, Van Eetvelde M, Bogaert H, Hostens M, Vandaele L, Shamsuddin M, Opsomer G. 2015. Environmental factors and dam characteristics associated with insulin sensitivity and insulin secretion in newborn Holstein calves. *Animal,* 9:1490-1499.

Kawashima C, Munakata M, Shimizu T, Miyamoto A, Kida K, Matsui M. 2016. Relationship between the degree of insulin resistance during late gestation and postpartum performance in dairy cows and factors that affect growth and metabolic status of their calves. *J Vet Med Sci,* 78:739-745.

Kertz AF, Reutzel LF, Barton BA, Ely RL. 1997. Body weight, body condition score, and wither height of prepartum holstein cows and birth weight and sex of calves by parity: a database and summary. *J Dairy Sci,* 80:525-529.

Khanal P, Husted SV, Axel AMD, Johnsen L, Pedersen KL, Mortensen MS, Kongsted AH, Nielsen MO. 2014. Late gestation over- and undernutrition predispose for visceral adiposity in response to a post-natal obesogenic diet, but with differential impacts on glucose-insulin adaptations during fasting in lambs. *Acta Physiol,* 210:110-126.

Kleemann DO, Kelly JM, Rudiger SR, McMillen IC, Morrison JL, Zhang S, MacLaughlin SM, Smith DH, Grimson RJ, Jaensch KS, Brien FD, Plush KJ, Hiendleder S, Walker SK. 2015. Effect of periconceptional nutrition on the growth, behaviour and survival of the neonatal lamb. *Anim Reprod Sci,* 160:12-22.

Klewitz J, Struebing C, Rohn K, Goergens A, Martinsson G, Orgies F, Probst J, Hollinshead F, Bollwein H, Sieme H. 2015. Effects of age, parity, and pregnancy abnormalities on foal birth weight and uterine blood flow in the mare. *Theriogenology*, 83:721-729.

Kume S, Tanabe S. 1993. Effect of parity on colostral mineral concentrations of Holstein cows and value of colostrum as a mineral source for newborn calves. *Journal of dairy science*, 76:1654-1660.

Laporte-Broux B, Roussel S, Ponter A, Perault J, Chavatte-Palmer P, Duvaux-Ponter C. 2011. Short-term effects of maternal feed restriction during pregnancy on goat kid morphology, metabolism, and behavior. *J Anim Sci,* 89:2154-2163.

Laporte-Broux B, Roussel S, Ponter A, Giger-Reverdin S, Camous S, Chavatte-Palmer P, Duvaux-Ponter C. 2012. Long-term consequences of feed restriction during late pregnancy in goats on feeding behavior and emotional reactivity of female offspring. *Physiol Behav,* 106:178-184.

Lawrence L, DiPietro J, Ewert K, Parrett D, Moser L, Powell D. 1992. Changes in body weight and condition of gestating mares. *J Equine Vet Sci*, 12:355-358.

Long NM, George LA, Uthlaut AB, Smith DT, Nijland MJ, Nathanielsz PW, Ford SP. 2010. Maternal obesity and increased nutrient intake before and during gestation in the ewe results in altered growth, adiposity, and glucose tolerance in adult offspring. *J Anim Sci,* 88:3546-3553.

Long NM, Rule D, Tuersunjiang N, Nathanielsz P,

Ford S. 2015. Maternal obesity in sheep increases fatty acid synthesis, upregulates nutrient transporters, and increases adiposity in adult male offspring after a feeding challenge. *PLoS One*, 10:e0122152.

Lopez-Tello J, Arias-Alvarez M, Jimenez-Martinez M-A, Garcia-Garcia R-M, Rodriguez M, Lorenzo Gonzalez P, Bermejo-Poza R, Gonzalez-Bulnes A and Garcia Rebollar P. 2017. Competition for materno-fetal resource partitioning in a rabbit model of undernourished pregnancy. *PLoS One*, 12:e0169194.

Meirelles MG, Veras MM, Alonso MA, de Fátima Guimarães C, Nichi M, Fernandes CB. 2017. Influence of maternal age and parity on placental structure and foal characteristics from birth up to two years of age. *J Equine Vet Sci,* 56:68-79.

Mohrhauser DA, Taylor AR, Underwood KR, Pritchard RH, Wertz-Lutz AE, Blair AD. 2015. The influence of maternal energy status during midgestation on beef offspring carcass characteristics and meat quality. *J Anim Sci,* 93:786-793.

Opsomer GA, Van Eetvelde M, Kamal MA, Van Soom A. 2017. Epidemiological evidence for metabolic programming in dairy cattle. *Reprod Fertil Dev,* 29:52-57.

Peugnet P, Wimel L, Duchamp G, Sandersen C, Camous S, Guillaume D, Dahirel M, Dubois C, Jouneau L, Reigner F, Berthelot V, Chaffaux S, Tarrade A, Serteyn D, Chavatte-Palmer P. 2014. Enhanced or reduced fetal growth induced by embryo transfer into smaller or larger breeds alters post-natal growth and metabolism in pre-weaning horses. *PLoS One,* 9:e102044.

Peugnet P, Mendoza L, Wimel L, Duchamp G, Dubois C, Reigner F, Caudron I, Deliège B, Toquet M-P, Richard E, Chaffaux S, Tarrade A, Lejeune J-F, SerteynD, Chavatte-Palmer P. 2016. Longitudinal study of growth and osteoarticular status in foals born to between-breed embryo transfers. *J Equine Vet Sci,* 37:24-38.

Philp LK, Muhlhausler BS, Janovska A, Wittert GA, Duffield JA, McMillen IC. 2008. Maternal overnutrition suppresses the phosphorylation of 5'-AMP activated protein kinase (AMPK) in liver, but not skeletal muscle, in fetal and neonatal sheep. *Am J Physiol Regul Integr Comp Physiol*, 295:1982-1990.

Pillai S, Jones A, Hoffman M, McFadden K, Reed S, Zinn S, Govoni, K. 2017. Fetal and organ development at gestational days 45, 90, 135 and at birth of lambs exposed to under- or over-nutrition during gestation. *Translational Animal Science*, 1:16-25.

Pool-Anderson L, Raub R, Warren J. 1994. Maternal influences on growth and development of full-sibling foals. *J Anim Sci,* 72:1661-1666.

Prezotto LD, Camacho LE, Lemley CO, Keomanivong FE, Caton JS, Vonnahme KA, Swanson KC. 2016. Nutrient restriction and realimentation in beef cows during early and mid-gestation and maternal and fetal hepatic and small intestinal in vitro oxygen consumption. *Animal*, 10:1-9.

Reed SA, Raja JS, Hoffman ML, Zinn SA, Govoni KE. 2014. Poor maternal nutrition inhibits muscle development in ovine offspring. *J Anim Sci Biotechnol*, 5:43. doi: 10.1186/2049-1891-5-43.

Sen U, Sirin E, Ensoy U, Aksoy Y, Ulutas Z, Kuran M. 2016. The effect of maternal nutrition level during mid-gestation on postnatal muscle fibre composition and meat quality in lambs. *Anim Prod Sci,* 56:834-843.

Sinclair KD, Rutherford KMD, Wallace JM, Brameld JM, Stöger R, Alberio R, Sweetman D, Gardner DS, Perry VEA, Adam CL, Ashworth CJ, Robinson JE, Dwyer CM. 2016. Epigenetics and developmental programming of welfare and production traits in farm animals. *Reprod Fertil Dev*, 28:1443-1478.

Summers AF, Meyer TL, Funston RN. 2015. Impact of supplemental protein source offered to primiparous heifers during gestation on I. Average daily gain, feed intake, calf birth body weight, and rebreeding in pregnant beef heifers. *J Anim Sci,* 93:1865-1870.

Tischner M. 2000. Maternal influence on pre- and postnatal growth of foals born after embryo transfer. *J Reprod Fertil Suppl*, 56:705-708.

Triantaphyllopoulos KA, Ikonomopoulos I and Bannister AJ. 2016. Epigenetics and inheritance of phenotype variation in livestock. *Epigenetics Chromatin* 9:31. doi: 10.1186/s13072-016-0081-5.

Vazquez J, Esteller-Vico A, Irizarri A, Liu I, Troedsson M. 2015. Influence of stallion, donor and recipient mare's height and parity in foal height from birth to three years old in an embryo transfer program. A retrospective study. *In*: Proceedings of the 4th International Congress of the World Equine Veterinary Association (WEVA), 2015, Guadalajara, Mexico. Guadalajara: WEVA.

Wallace J, Milne J, Adam C, Aitken R. 2017. Impact of donor and recipient adiposity on feto-placental growth in adolescent sheep. *Reproduction*, 153:381-394.

Walton A, Hammond J. 1938. The maternal effects on growth and conformation in Shire horse-Shetland pony crosses. *Proc R Soc London*, 125:311-335.

Whorwood CB, Firth KM, Budge H, Symonds ME. 2016. Maternal undernutrition during early to midgestation programs tissue-specific alterations in the expression of the glucocorticoid receptor, 11-hydroxysteroid receptor in neonatal sheep. *Endocrinology*, 142:2854-2864.

Wilsher S, Allen W. 2003. The effects of maternal age and parity on placental and fetal development in the mare. *Equine Vet J*, 35:476-483.

Wilson TB, Faulkner DB and Shike DW. 2016. Influence of prepartum dietary energy on beef cow performance and calf growth and carcass characteristics. *Livest Sci,* 184:21-27.

Zachut M, Honig H, Striem S, Zick Y, Boura-Halfon S, Moallem U. 2013. Periparturient dairy cows do not exhibit hepatic insulin resistance, yet adipose-specific insulin resistance occurs in cows prone to high weight loss. *J Dairy Sci,* 96:5656-5669.

Zhang L, Long N, Hein S, Ma Y, Nathanielsz, Ford S. 2012. Maternal obesity in the ewe results in reduced fetal pancreatic β-cell numbers in late gestation, and decreased circulating insulin concentration at term. *Domest Anim Endocrinol,* 40:30-39.

Zoch ML, Clemens TL, Riddle RC. 2016. New insights into the biology of osteocalcin. *Bone,* 82:42-49.