Original Article

Restricted feeding of goats during the last third of gestation and trans-generational effects on plasma progesterone in their female offspring

Andrew A. Ponter[1,2*] Bérengère Laporte[3] Sabine Roussel[3,4] Winai Kaewlamun[1,5]
Pascale Chavatte-Palmer[1,2] Christine Duvaux-Ponter[3]

Abstract

Feeding levels can vary in goat farms for several reasons. Underfeeding of gestating dairy goats can occur and may influence fetal follicle development and future reproductive performance in their offspring. The objective of this experiment was to study the effect of restricted feeding during the last third of gestation on some reproductive parameters in female offspring (F1). Two feeding groups were formed using 60 Alpine and Saanen dairy goats to produce the F1 female offspring. The control group (C, n = 30) was fed to requirements. The restricted group (R, n = 30) was given the same diet, but the quantity corresponded to 50% of the amount given to the C group between -8 and -4 weeks, 60% between -5 and -4 weeks, 70% between -4 and -3 weeks and 80% from -2 weeks to parturition. Estrus was synchronized at 7 months of age in female F1 goats born to C (n = 17) or born to R goats (n = 15) with a progestagen-impregnated sponge and prostaglandin F2α and eCG injections, and the goats were inseminated. Serial blood samples were collected over this period. After mating, plasma progesterone rose more slowly to reach a maximum plateau concentration in females born to R goats compared to females born to C goats ($P < 0.05$). The lag time was approximately 2 days. There was no difference in dam F0 prolificacy (C, 2.4 ± 0.6 vs. R, 2.1 ± 0.8, $P > 0.05$), length of gestation (C, 151 ± 2 days vs. R, 151 ± 2 days) and kid mortality rate (mummified fetuses, stillbirth or death in first 48h) between the groups. However, birth weight was lower in R kids compared to C kids (4.0 ± 0.11 kg vs. 4.5 ± 0.10 kg, $P = 0.007$). In conclusion, maternal feed restriction during late pregnancy modified progesterone patterns after insemination in female offspring, although there was no effect on reproductive success.

Keywords: female offspring, goat, late gestation, progesterone, restricted feeding

[1]*Ecole Nationale Vétérinaire d'Alfort, BREED, 94700 Maisons-Alfort, France*
[2]*Université Paris-Saclay, UVSQ, INRAE, BREED, 78350 Jouy-en-Josas, France*
[3]*Université Paris-Saclay, INRAE, AgroParisTech, UMR Modélisation Systémique Appliquée aux Ruminants, 91120, Palaiseau, France*
[4]*Université de Brest, CNRS, IRD, Ifremer, LEMAR, Plouzané F-29280, France*
[5]*School of Agricultural Resources, Chulalongkorn University, Bangkok, Thailand*
***Correspondence:** andrew.ponter@vet-alfort.fr* (A.A. Ponter)
Received November 12, 2024
Accepted February 27, 2025

Introduction

Nutritional requirements during the last third of gestation are very high in small ruminants due to the high prolificacy of these animals. In goats, the conceptus acquires 80% of its birth weight in the last 2 months of gestation (Conway *et al*., 1996). In order to cover the requirements for fetal growth, the goat must either eat more or mobilize its reserves. Feed intake can be low at the end of gestation. This is due to compression of the rumen by the fetuses and under-development of the rumen papillae (which reduces the rate at which the products of fermentation are absorbed, Mayer *et al*., 1986). Moreover, breeding to produce kids in the winter is concomitant with a shortage of forages. In addition, the use of poor-quality conserved feedstuffs and feed cost-cutting by farmers can negatively impact dietary supply.

It is now well established that an individual's phenotype can be modified by a nutritional insult in early life, for example, in utero or in the post-natal period. Indeed, a mismatch in pre- and post-birth nutrition appears to be particularly dangerous for an individual. Both hypertension/blood pressure (Eriksson *et al*., 2000; Ben-Shlomo *et al*., 2008) and coronary events (Barker *et al*., 2005) occur more frequently if an individual's growth is limited in utero and there is then a subsequent phase of catch-up in growth after birth. The links between *in-utero* nutrition and non-communicable diseases involving the cardiovascular system or metabolism are well established (Barker and Osmond, 1986). However, the link between maternal diet and the subsequent fertility of offspring is not clearly demonstrated, although recent reviews (Wathes, 2022; Yao *et al*., 2021; Akbarinejad and Cushman, 2024) have shed light on the situation. The number of ovarian follicles is set during fetal life in precocial species such as the goat (Da Silva *et al*., 2002). Therefore, it is likely that in utero, feeding level is more important than post-natal feeding in influencing follicle reserve in this species. In addition to studies on females, the effect of gestational nutritional programming on male progeny has been recently reviewed by Ghasemi *et al*. (2024).

Several studies in sheep have investigated the link between in-utero nutrition and subsequent fertility, ovarian development, and ovulation rate. Gunn *et al*. (1995) concluded from their study that under-nutrition in late gestation/early lactation reduced lifetime reproductive performance in their offspring. Embryo/fetal losses were affected since there were no residual differences in live weight, body condition score, and ovulation rate in their offspring. However, Rae *et al*. (2002a) concluded from their experiment that under-nutrition between mating and day 95 of gestation reduced the ovulation rate in their offspring. In another experiment, Rae *et al*. (2001) showed that gestational under-nutrition reduced the transition of primordial follicles into primary follicles compared to controls. The transition from primordial to primary follicles starts at around 90d of gestation in sheep (McNatty *et al*., 2000). The objective of the present experiment was to study the effect of restricted feeding of dams on their prolificacy and the post-mating progesterone concentrations in their female offspring (F1).

Materials and Methods

The experiments were carried out according to French legislation on animal experimentation (code rural: articles R 214-87 to R214-94) in line with the European Convention for the Protection of Animals used for scientific purposes (EU Directive 2010/63/EU for animal experiments). The scientist in charge of the experiment was licensed to perform experiments on animals, and the staff who applied the experimental procedures attended a special course approved by the French Ministry of Agriculture.

Animals and diets: The feeding system used for the dams has been described previously (Laporte *et al*., 2011). Briefly, sixty Alpine and Saanen dairy goats were used for the experiment. Goats were synchronized prior to mating. Following AI, all the goats were given free access to a total mixed ration (TMR), water, and a mineral-fortified salt lick. Gestation was confirmed at 60 days by ultrasonography. Starting at 89±3 days of gestation, the goats were allocated to one of two dietary treatments: control (C) or restricted (R) according to breed, age, liveweight (LW), and body condition score (BCS). The composition and proximate analysis of the diets are given in Table 1. The C group (n = 30) was fed ad libitum (5% feed refusals) the diets described in Table 1 for the last third of gestation, and the R group (n = 30) was given the same diets but at a lower level. The restricted group received 50% of the amount of feed given to their control group for 4 weeks, 60% for 1 week, 70% for 1 week, and 80% last 2 weeks of pregnancy.

At birth, kids were immediately removed from their dams and ear-tagged. Two meals of good quality pooled colostrum were given ad libitum on the first day, and a milk replacer was given ad libitum on the following days (dilution 150 g powder/kg water). On the fifth day, the female kids born to C goats (n = 17) or born to R goats (n = 15) were randomly chosen, mixed, and placed together in experimental pens by age (maximum of 4 days between the youngest and the oldest kid) and raised in the same manner. They were weaned at 3 months of age onto a diet of natural meadow hay and a commercial concentrate, with water and mineral and vitamin-fortified salt licks available ad libitum. The diet was designed to cover requirements for the growth of young goats in a commercial goat farm (Agabriel, 2007). Kids were weighed at birth and then regularly to assess their growth rate during the experiment.

Reproduction management: In August, when the young female goats were 7 months of age, estrus was synchronized using a progestagen-impregnated intra-vaginal sponge (40 mg flugestone acetate: CHRONOGEST SPONGE, Intervet, France) starting on day -13. On day -4, injections of PGF2α (Cloprostenol, 50 µg i.m., ESTRUMATE®, MSD Animal Health, France) and eCG (400 UI, MSD Animal Health, France) were given. On day -2, sponges were removed, estrus

was detected on day -1, and insemination was performed on day 0.

Measurements: Blood was collected from the female offspring (F1) for progesterone analysis by jugular venipuncture into heparinized tubes (Venosafe, Terumo, Belgium) before the morning feed, 10 days before starting estrus synchronization and at sponge insertion to check if the goats were already cycling and on days 0, 2, 4, 6, 8, 10, 15 and 20 in relation to mating.

Assays: Plasma progesterone (P4) was analyzed using an enzyme immunoassay (Ovucheck plasma, Biovet). The intra-assay coefficient of variation was 14.4% for < 2.5 ng/mL, 5% between 2.5 and 3.5 ng/mL, and 4.9% > 3.5 ng/mL.

Statistical analysis: Statistical analysis was performed using SAS (SAS Institute Inc., 2014, SAS OnDemand for Academics). Results are presented as Lsmean±SEM. A $P \leq 0.05$ was significant, while $0.05 < P < 0.10$ was considered to be a trend. A *t*-test was performed to study the effect of treatment on dam prolificacy and on the birthweight and liveweight gain of their female offspring.

Statistical analysis was performed using a linear mixed model with the MIXED procedure of SAS software for repeated measures, including a random female effect in all the models (Littell *et al*., 1998). For plasma progesterone (Y), the effects of dietary regimen, breed, sampling time and the interaction sampling time x dietary regimen were tested.

$$Yijkl = \mu + Ti + Bj + Ak + TAik + \mu jl + \varepsilon ijk1$$

In this model, μ represents the overall mean, Ti is the fixed effect of the treatment i, Bj is the fixed effect of the breed j, Ak is the time of sampling as a repeated factor k, and TAik is the interaction between treatment and time. ujkl is the repeated effect of time within animals estimated with a compound symmetrical covariance structure, and εijkl is the residual error. Using SAS, estimates were calculated in order to allow comparisons from time point to time point.

Table 1 Composition and proximate analysis of the diets given to dairy goats during the experimental period.

	-8 to -4 weeks*	-4 to -2 weeks	-2 to 0 weeks	after parturition
Composition (% DM):				
Sugar beet pulp	35.0	30.0	30.0	28.0
Perennial ryegrass hay	25.0	25.0	25.0	17.0
Lucerne hay	29.0	29.0	29.0	32.0
Protein concentrates	0.0	5.0	10.0	17.0
Barley	10.0	10.0	5.0	5.0
Vitamin and mineral mix	1.0	1.0	1.0	1.0
Nutrients (/kg dry matter):				
Net energy (MJ)	5.7	5.6	5.5	5.7
PDIN (g)	72.0	75.0	77.0	84.0
PDIE (g)	82.0	84.0	86.0	90.0
Crude fiber (g)	292.0	285.0	287.0	270.0
Calcium (g)	9.0	8.5	8.7	8.8
Phosphorus (g)	2.0	2.3	2.4	2.8

*weeks in reference to parturition (parturition = 0).
NEL = Net energy for maintenance and lactation
PDIN = true Intestinal Digestible Protein, when fermentable N is the limiting factor
PDIE = true Intestinal Digestible Protein, when fermentable energy is the limiting factor

Result

The plasma progesterone concentrations measured prior to estrus synchronization indicated that none of the female goats (F1) born to the C goats were cycling, while two females born to R goats were cycling (data not shown). All female goats (F1) goats ovulated and subsequently became pregnant. There was no difference in prolificacy measured at birth between the female goats (F1) born to the C and R dams (C, 2.4 ± 0.6 vs. R, 2.1 ± 0.8, $P > 0.05$). Birth weight was lower in R kids compared to C kids (4.0 ± 0.11 kg vs. 4.5 ± 0.10 kg, $P = 0.007$). No differences in average daily weight gain between C and R kids were found thereafter. There was no effect of dietary regimen on the length of gestation in the dams (C, 151 ± 2 days vs. R, 151 ± 2 days). Kid mortality rate (mummified fetuses, stillbirth, or death in first 48h) was not affected by treatment.

Plasma progesterone concentrations rose more slowly to reach maximum levels in females born to R goats compared to females born to C goats ($P < 0.05$, Fig. 1). There was no subsequent difference in P4 concentrations between treatments ten days after insemination.

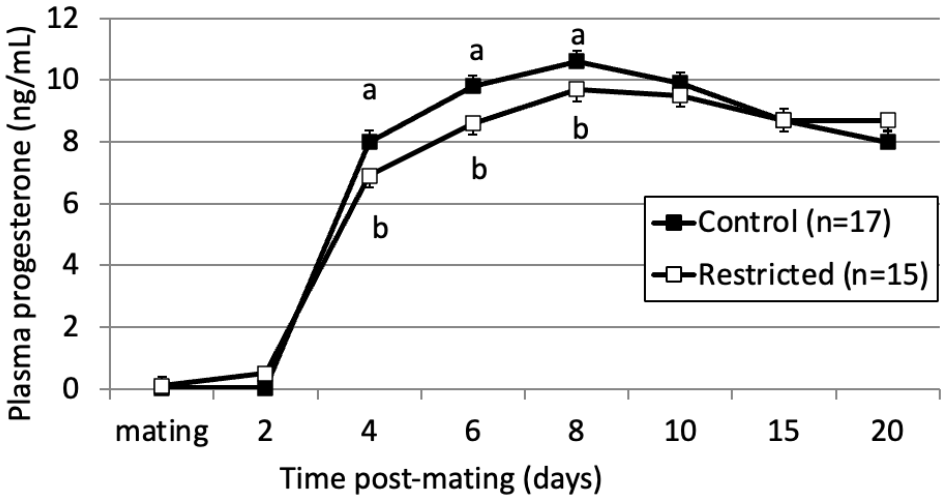

Figure 1 Effect of pregnant dam feeding level on plasma progesterone concentrations in their female offspring after oestrus synchronization and mating at 8 months of age. The C group offspring (n = 17) came from dams given a Total Mixed Ration (TMR) *ad libitum* for the last third of gestation and the R group offspring (n = 15) came from dams given the same TMR but starting from -8wk from parturition the quantity corresponded to 50% (for 4 weeks), 60% (for 1week), 70% (for 1wk) and 80% (for 2 weeks) of the amount given to the C group. a, b significant difference between treatments, $P < 0.05$.

Discussion

It is well established that a relationship exists between a mismatch between pre-natal growth (slow) and post-natal growth (rapid catch-up) and the development of non-transmissible diseases (Barker and Osmond, 1986). Several recent reviews have also studied the effect of developmental programming on reproduction in cattle (Wathes, 2022), in rodents (Yao *et al*., 2021) and the possible involvement of epigenetics on developmental programming (Chavatte-Palmer *et al*., 2018; Akbarinejad and Cushman, 2024). Sinclair *et al*. (2007) concluded that it was evolutionarily logical for poly-ovulatory species to reduce ovulation rate in situations of under-nutrition to maximize the chances of survival of fewer offspring. However, in mono-ovulatory species, the absence of ovulation would be untenable in the long term. The goat, with a prolificacy rate of 1 to 4 per litter, may be intermediate between these two extremes of ovulation rate and therefore be affected by pregnancy under-feeding. Indeed, Gunn *et al*. (1995) and Rae *et al*. (2002a) have shown that the ovulation rate is reduced in adult female sheep that suffer from fetal under-nutrition during folliculogenesis (Rae *et al*., 2001).

Progesterone is a key hormone involved in the cyclic control of reproductive function in the goat (Fatet *et al*., 2011) and other species. In the goat, progesterone is mainly synthesized by the corpus luteum (Thornburn and Schneider, 1972) through the action of several luteal steroidogenic enzymes such as Steroid Acute Regulatory Protein (STAR), cytochrome P450 (CYP17A1, CYP19A1) enzyme and 3β-Hydroxysteroid dehydrogenase (3β-HSD) (Diaz *et al*., 2002). Progesterone concentrations vary due to numerous factors, amongst others: pregnancy (Fatet *et al*., 2011), season (Błaszczyk *et al*., 2004), feeding level (Bloomfield *et al*., 2004), and heat stress (Emesih *et al*., 1995). Some information on ovary steroidogenesis genes and nutritional programming has been published in rats (Harrath *et al*., 2019).

The main finding of the present paper is that after mating, plasma progesterone concentrations rose more slowly to reach a maximum in females born to late gestation feed-restricted goats compared to controls. To our knowledge, this is the first time such a finding has been published on dairy goats. Long *et al*. (2013) showed that in early gestation-restricted sheep, their female offspring had lower concentrations of P4 compared to the control group. Sloboda *et al*. (2009) showed, using the underfed pregnant rat model, that plasma progesterone was significantly lower during proestrus in offspring from under-fed females compared to controls. They also found that females from under-fed dams attained puberty earlier than controls. In the present experiment, we did not confirm the latter finding since only two R females were cycling before estrus synchronization, and none of the C females were cycling. Both Kotsampasi *et al*. (2009) and Grazul-Bilska *et al*. (2014) were also unable to show that puberty occurred earlier in females from under-fed ewes (underfeeding applied between 31-100 days of gestation or 50 days prior to parturition respectively) compared to controls. However, Kotsampasi *et al*. (2009) did show that female lambs born to late gestation underfed dams had fewer CL (diameter 8 to 11 mm) after ovarian cycle synchronization. They speculated that the necessary progesterone support for the maintenance of pregnancy (Niswender *et al*., 2000) was perhaps inadequate. The results from the present experiment did not confirm this since all the F1 goats became pregnant after insemination. Long *et al*. (2010) studied progesterone secretion after natural estrus and used the under-fed ewe model. Under-feeding resulted in a 50% reduction in nutrient supply compared to requirements between 28 and 78 days of gestation. They showed that progesterone concentrations were lower in females from under-fed ewes at 1 and 2 years of age compared to controls and that the females from the under-fed dams produced fewer lambs than the females from control ewes after mating at 2 years of age. Unfortunately, Long's paper does not indicate ovulation rates. Therefore, it is not possible to conclude

if lower P4 was due to reduced corpora lutea numbers or whether low P4 resulted in embryo loss since lamb numbers were reduced in the females from restricted dams compared to controls. It may be that central drivers of reproduction were altered by in-utero under-nutrition, which produced gonadal abnormalities (Rae *et al*., 2001), but the same group (Rae *et al*., 2002b) showed that the abnormalities were not due to changes in pituitary function.

Another possible reason for reduced P4 could be impaired fetal ovary development during the period of maternal under-feeding. The number of antral follicles has been linked to progesterone concentrations after estrus in heifers (Jimenez-Krassel *et al*., 2009). Borwick *et al*. (1997) concluded that under-nutrition of the ewe from the time of mating significantly delays ovarian development in fetal ovaries. For example, they showed that at day 62 of gestation, the process of germ cell degeneration was less advanced in fetuses from underfed ewes compared to controls, where the former had higher oocyte numbers than the latter. The ovaries from the under-fed fetuses also had a greater percentage of meiotic cells than controls. Murdoch *et al*. (2003) showed that oocytes from female fetuses, under-fed during development, had higher levels of oxidative DNA damage compared to oocytes from control fetuses. Using a similar model, Lea *et al*. (2006) showed that genes involved in apoptosis were modified in ovaries from late-term fetuses taken from underfed ewes. They concluded that this might be one of the mechanisms by which the number of primordial follicles is reduced in this type of model. In addition, cell proliferation is reduced by under-feeding during 50-135 days of gestation in primordial, secondary, and antral follicles and in stromal cells and blood vessels in fetal sheep ovaries (Grazul-Bilska *et al*., 2009). Therefore, ovarian follicle numbers appear to be reduced by under-feeding during gestation.

There exists a very high variability in ovary reserves (total numbers of healthy oocytes and follicles [Block, 1953]). Despite the very high variability in antral follicle count (AFC) within individuals (approximately sevenfold difference), it is very repeatable during follicular waves within the same individual (Burns *et al*., 2005). Jimenez-Krassel *et al*. (2009) showed that if the AFC during follicular waves was low, then subsequent P4 concentrations were low, and this was very repeatable. They showed that the low levels of P4 were not linked to the size of the corpus luteum (CL) since it was the same in both AFC groups. However, they did show that CL function was impaired. Using luteal cells isolated from corpora lutea from low and high AFC animals, they showed that basal and LH-stimulated P4 production from 25-hydroxycholesterol (P4 precursor) was lower in low AFC compared to high AFC animals. Neither excess LH nor 25-hydroxycholesterol enhanced P4 production by low AFC luteal cells compared to high AFC luteal cells. They showed that there was a desensitization of luteal cells to LH and 25-hydroxycholesterol, a reduction in steroidogenic acute regulatory protein (StAR) in the CL. In addition, there was a reduced capacity of granulosa cells from dominant follicles to undergo luteinization and produce P4 in low AFC compared to high AFC animals. StAR is the rate-limiting step in steroidogenesis. Therefore, in the present experiment, females from under-fed pregnant dams may have low AFC, which in turn causes low P4. Indeed, Mossa *et al*. (2013) showed that AFC was decreased in heifers born to under-fed pregnant cows. In the present experiment, the under-feeding regimen was started at 90 days of gestation, which corresponds with the phase where there is a transition between primordial and primary follicles in the fetal ovary (Hernandez-Medrano *et al*., 2012). Therefore, underfeeding during this period may have adversely affected AFC in the present experiment by affecting the transition between primordial and primary follicles.

An alternative hypothesis involves differences in steroid synthesis and catabolism. Long *et al*. (2013) concluded from sheep experiments that the decrease in circulating P4 in offspring from early gestation undernutrition appeared to be consistent with the programming of decreased steroidogenic enzyme expression in CL compared to controls. In addition, they concluded that it was not due to a difference in hepatic steroid catabolism.

It is interesting to speculate as to the potential effect of the differences in P4 observed in the present experiment on reproductive function. Menchaca *et al*. (2002) studied the number of ovarian follicular growth waves in goats, i.e., 3 or 4 waves. They showed a relationship between early luteal phase P4 levels and follicular wave turnover. They concluded that higher P4 concentrations may accelerate follicular turnover, probably due to an early decline in the negative feedback action of the largest follicle of the first wave. This would increase the number of waves and result in a 'younger' follicle ovulating. However, Evans (2003) was unable to show, in cattle and sheep, that the age of the ovulatory follicle impacted fertility. This was recently confirmed in dairy heifers and lactating cows, where fertility was not influenced by the number of follicular waves of the ovulatory follicle (Mohammadi *et al*., 2024). Carter *et al*. (2008), confirmed by Okumu *et al*. (2010), showed that elevated P4 in the early luteal phase down-regulates its receptor in the uterine luminal epithelium of cyclic and pregnant heifers. This leads to an alteration in the timing of expression of P4-regulated genes. In their experiment, the effect on the expression of progesterone receptor protein was observed on days 5 and 7. This timing coincides with the difference that we observed in P4 between R and C goats in the present study. The downregulation of P4 receptors is a critical event required for conceptus development, maternal recognition of pregnancy, and implantation. However, unfortunately, we did not follow the gestations of the F1 animals to term in the present experiment.

Limitations to our study: The present study has two weaknesses. The first is due to the relatively small sample size (C, n = 17 vs. R, n = 15). This is often a problem in large animal studies due to limits in experimental facility size and sampling protocols. However, in previous experiments conducted by our team on similar topics, the number of animals that we used was seen to be adequate. The other limitation is the lack of information concerning F1 ovarian follicle

data (number and size). The experiment was designed as a preliminary study to screen for potential areas of research involving in-utero programming of reproductive function. It was not designed to exhaustively study P4 secretion, ovarian structure and function, and pregnancy outcomes since it would have required many more resources than were initially available.

Perspectives: Future experiments are needed to confirm the results of the present study and should include ultrasound measurements of ovarian structures and the number of follicular waves in F1 goats. Other aspects of interest might be the study of reproductive hormone profiles, pregnancy outcomes in the F1 goats, and nutritional mitigating strategies. To date, in farm animals, the paradigm when studying nutritional programming has been to modify global energy/protein/mineral and vitamin supply to the pregnant dam. Future research should perhaps focus on individual nutrients and their action on fetal programming, for example, the supply of starch, fat, and individual essential or non-essential amino acids.

In conclusion, the low P4 concentrations around mating observed in the present experiment in females born to under-fed pregnant goats may result from inappropriate fetal ovary development, resulting in low numbers of follicles. Other maternal stress factors: thermal stress (cold and heat), high altitude (hypoxia), maternal age and breed, and litter size (Beede *et al*., 2019; Reynolds *et al*., 2019; Vautier and Cadaret, 2022; Cushman *et al*., 2024) are known to affect P4 concentrations in female offspring, we do not believe that these factors were important in the present experiment. The rearing conditions were the same for all the animals. Low antral follicle counts during estrous cycles have been shown to be associated with low progesterone levels. This may be one way in which low feeding levels during gestation affect, in a trans-generational way, reproductive efficiency through P4 concentrations. However, we did not measure ovarian structures in the present experiment and cannot, therefore, confirm the possible role of AFC in our results. P4 around the period of fertilization is known to affect fertility through uterine preparation and the histroph environment (Clemente *et al*., 2009) and the timing of ovulation after estrus (Bloch *et al*., 2006). However, in the present experiment, there was no difference in fertility between treatment groups.

Acknowledgment

The authors would like to thank J. Tessier and his team at the goat unit of the Institut National de Recherche pour l'Agriculture, l'Alimentation et l'Environnement (INRAE) for care of the animals and C. Ficheux for technical assistance.

Conflicts of interest: The authors confirm that no conflicts of interest exist.

References

Agabriel J 2007. Alimentation des bovins, ovins et caprins: besoins des animaux, valeurs des aliments: tables Inra 2007. Editions Quae.

Akbarinejad V and Cushman RA 2024. Developmental programming of reproduction in the female animal. Anim Reprod Sci. 107456.

Barker DJP, Osmond C, Forsén TJ, Kajantie E and Eriksson JG 2005. Trajectories of growth among children who have coronary events as adults. N Engl J Med. 353: 1802-1809.

Barker DJ and Osmond C 1986. Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. Lancet. 327: 1077-1081.

Beede KA, Limesand SW, Petersen JL and Yates DT 2019. Real supermodels wear wool: summarizing the impact of the pregnant sheep as an animal model for adaptive fetal programming. Animal Frontiers. 9: 34-43.

Ben-Shlomo Y, McCarthy A, Hughes R, Tilling K, Davies D and Smith DG 2008. Immediate postnatal growth is associated with blood pressure in young adulthood: the Barry Caerphilly Growth Study. Hypertension. 52: 638-644.

Błaszczyk B, Udała J and Gączarzewicz D 2004. Changes in estradiol, progesterone, melatonin, prolactin and thyroxine concentrations in blood plasma of goats following induced estrus in and outside the natural breeding season. Small Rum Res. 51: 209-219.

Bloch A, Folman Y, Kaim M, Roth Z, Braw-Tal R and Wolfenson D 2006. Endocrine alterations associated with extended time interval between estrus and ovulation in high-yield dairy cows. J Dairy Sci. 89: 4694-4702.

Block E 1953. A quantitative morphological investigation of the follicular system in newborn female infants. Acta Anatomica. 17: 201-206.

Bloomfield FH, Oliver MH, Hawkins P, Holloway AC, Campbell M, Gluckman PD, Harding JE and Challis JR 2004. Periconceptional undernutrition in sheep accelerates maturation of the fetal hypothalamic-pituitary-adrenal axis in late gestation. Endocrinol. 145: 4278-4285.

Borwick SC, Rhind SM, McMillen SR and Racey PA 1997. Effect of undernutrition of ewes from the time of mating on fetal ovarian development in mid gestation. Reprod Fertil Dev. 9: 711-715.

Burns DS, Jimenez-Krassel FJ, Ireland JLH, Knight PG and Ireland JJ 2005. Numbers of antral follicles during follicular waves in cattle: evidence for high variation among animals, very high repeatability in individuals, and an inverse association with serum follicle-stimulating hormone concentrations. Biol Reprod. 73: 54-62.

Carter F, Forde N, Duffy P, Wade M, Fair T, Crowe MA, Evans AC, Kenny DA, Roche JF and Lonergan P 2008 Effect of increasing progesterone concentration from day 3 of pregnancy on subsequent embryo survival and development in beef heifers. Reprod Fertil Dev. 20: 368-375.

Chavatte-Palmer P, Velazquez MA, Jammes H and Duranthon V 2018. Review: epigenetics,

developmental programming and nutrition in herbivores. Animals. 12: s363-s371.

Clemente M, de La Fuente J, Fair T, Al Naib A, Gutierrez-Adan A, Roche JF, Rizos D and Lonergan P 2009. Progesterone and conceptus elongation in cattle: a direct effect on the embryo or an indirect effect via the endometrium? Reproduction. 138: 507-517.

Conway MLT, Blackshaw JK and Daniel RCW 1996. The effects of agonistic behaviour and nutritional stress on both the success of pregnancy and various plasma constituents in Angora goats. Appl Anim Behav Sci. 48: 1-13.

Cushman RA, Akbarinejad V, Perry GA and Lents CA 2024. Developmental programming of the ovarian reserve in livestock. Anim Reprod Sci. 264: 107458.

Da Silva P, Aitken RP, Rhind SM, Racey PA and Wallace JM 2002. Impact of maternal nutrition during pregnancy on pituitary gonadotrophin gene expression and ovarian development in growth-restricted and normally grown late gestation sheep fetuses. Reproduction. 123: 769-777.

Diaz FJ, Anderson LE, Wu YL, Rabot A, Tsai SJ and Wiltbank MC 2002. Regulation of progesterone and prostaglandin F2alpha production in the CL. Mol Cell Endocrinol. 191: 65-80.

Emesih GC, Newton GR and Weise DW 1995. Effects of heat stress and oxytocin on plasma concentrations of progesterone and 13, 14-dihydro-15-ketoprostaglandin F2α in goats. Small Rum Res. 16: 133-139.

Eriksson J, Forsén T, Tuomilehto J, Osmond C and Barker D 2000. Fetal and childhood growth and hypertension in adult life. Hypertension. 36: 790-794.

Evans ACO 2003. Ovarian follicle growth and consequences for fertility in sheep. Anim Reprod Sci. 78: 289-306.

Fatet A, Pellicer-Rubio M T and Leboeuf B 2011. Reproductive cycle of goats. Anim Reprod Sci. 124: 211-219.

Ghasemi Z, Masouleh AAM, Ghaleno LR, Akbarinejad V, Valojerdi MR and Shahverdi A 2024. Maternal nutrition and fetal imprinting of the male progeny. Anim Reprod Sci. 107470.

Grazul-Bilska AT, Caton JS, Arndt W, Burchill K, Thorson C, Borowczyk E, Bilski JJ, Redmer DA, Reynolds LP and Vonname KA 2009. Cellular proliferation and vascularization in ovine fetal ovaries: effects of undernutrition and selenium in maternal diet. Reproduction. 137: 699-707.

Grazul-Bilska AT, Neville TL, Borowczyk E, Sharma A, Reynolds LP, Caton JS, Redmer DA and Vonnahme KA 2014. Ovarian and uterine characteristics and onset of puberty in adolescent offspring: effects of maternal diet and selenium supplementation in sheep. Theriogenology. 81: 877-895.

Gunn RG, Sim DA and Hunter EA 1995. Effects of nutrition in utero and in early life on the subsequent lifetime reproductive performance of Scottish Blackface ewes in two management systems. Anim Sci. 60: 223-230.

Harrath AH, Alrezaki A, Alwasel SH and Semlali A 2019. Intergenerational response of steroidogenesis-related genes to maternal malnutrition. J Dev Orig Health Dis. 10: 587-594.

Hernandez-Medrano JH, Campbell BK and Webb R 2012. Nutritional influences on folliculogenesis. Reprod Dom Anim. 47(Suppl 4): 274-282.

Jimenez-Krassel F, Folger JK, Ireland JLH, Smith GW, Hou X, Davis JS, Lonergan P, Evans ACO and Ireland JJ 2009. Evidence that high variation in ovarian reserves of healthy young adults has a negative impact on the corpus luteum and endometrium during estrous cycles in cattle. Biol Reprod. 80: 1272-1281.

Kotsampasi B, Chadio S, Papadomichelakis G, Deligeorgis D, Kalogiannis D, Menegatos I and Zervas G 2009. Effects of maternal undernutrition on the hypothalamic-pituitary-gonadal axis function in female sheep offspring. Reprod Dom Anim. 44: 677-684.

Laporte-Broux B, Duvaux-Ponter C, Roussel S, Promp J, Chavatte-Palmer P and Ponter AA 2011. Restricted feeding of goats during the last third of gestation modifies both metabolic parameters and behaviour. Livest Sci. 138: 74-88.

Lea RG, Andrade LP, Rae MT, Hannah LT, Kyle CE, Murray JF, Rhind SM and Miller DW 2006. Effects of maternal undernutrition during early pregnancy on apoptosis regulators in the ovine fetal ovary. Reproduction. 131: 113-124.

Littell RC, Henry PR and Ammerman CB 1998. Statistical analysis of repeated measures data using SAS procedures. J Anim Sci. 76: 1216-1231.

Long NM, Nijland MJ, Nathanielsz PW and Ford SP 2010. The effect early to mid-gestational nutrient restriction on female offspring fertility and hypothalamic-pituitary-adrenal axis response to stress. J Anim Sci. 88: 2029-2037.

Long NM, Tuersunjiang N, George LA, Lemley CO, Ma Y, Murdoch WJ, Nathanielsz PW and Ford SP 2013. Maternal nutrient restriction in the ewe from early to midgestation programs reduced steroidogenic enzyme expression and tended to reduce progesterone content of corpora lutea, as well as circulating progesterone in nonpregnant aged female offspring. Reprod Biol Endocrinol. 11: 1-10.

Mayer E, Liebich HG, Arbitman R, Haandemeister H and Dirksen G 1986. Nutritionally-induced changes in the rumenal papillae and in their capacity to absorb short chain fatty acids in high producing dairy cows. Proc. 14th World Congress on Diseases of Cattle. 806-817.

Menchaca A and Rubianes E 2002. Relation between progesterone concentrations during the early luteal phase and follicular dynamics in goats. Theriogenology. 57: 1411-1419.

Mohammadi J, Azari M and Kafi M 2024. The fertility of dairy heifers and cows is not influenced by the follicular wave of the ovulatory follicle. J Reprod Develop. 70: 138-143.

Mossa F, Carter F, Walsh SW, Kenny DA, Smith GW, Ireland JLH, Hildebrandt TB, Lonergan P, Ireland JJ and Evans AOC 2013. Maternal undernutrition in cows impairs ovarian and cardiovascular systems in the offspring. Biol Reprod. 88: 1-9.

Murdoch WJ, Van Kirk EA, Vonnahme KA and Ford SP 2003. Ovarian responses to undernutrition in pregnant ewes, USA. Reprod Biol Endocrinol. 1: 6.

McNatty KP, Fidler AE, Juengel JL, Quirke LD, Smith PR, Heath DA, Lundy T, O'Connell A and Tisdall DJ 2000. Growth and paracrine factors regulating follicular formation and cellular function. Mol Cell Endocrinol. 163: 1-20.

Niswender GD, Juengel JL, Silva PJ, Rollyson MK and McIntush EW 2000. Mechanisms controlling the function and life span of the corpus luteum. Physiol Rev. 80: 1-29.

Okumu LA, Forde N, Fahey AG, Fitzpatrick E, Roche JF, Crowe MA and Lonergan P 2010. The effect of elevated progesterone and pregnancy status on mRNA expression and localisation of progesterone and oestrogen receptors in the bovine uterus. Reproduction. 140: 143-153.

Rae MT, Kyle CE, Miller DW, Hammond AJ, Brooks AN and Rhind SM 2002a. The effects of undernutrition, in utero, on reproductive function in adult male and female sheep. Anim Reprod Sci. 72: 63-71.

Rae MT, Rhind SM, Kyle CE, Miller DW and Brooks AN 2002b. Maternal undernutrition alters triiodothyronine concentrations and pituitary response to GnRH in fetal sheep. J Endocrinol. 173: 449-455.

Rae MT, Palassio S, Kyle CE, Brooks AN, Lea RG, Miller DW and Rhind SM 2001. Effect of maternal undernutrition during pregnancy on early ovarian development and subsequent follicular development in sheep foetuses. Reproduction. 122: 915-922.

Reynolds LP, Borowicz PP, Caton JS, Crouse MS, Dahlen CR and Ward AK 2019. Developmental programming of fetal growth and development. Vet Clin North Am Food Anim Pract. 35: 229-247.

Sinclair KD, Lea RG, Rees WD and Young LE 2007. The developmental origins of health and disease: current theories and epigenetic mechanisms. Soc Reprod Fertil Suppl. 64: 425-443.

Sloboda DM, Howie GJ, Pleasants A, Gluckman PD and Vickers MH 2009. Pre- and postnatal nutritional histories influence reproductive maturation and ovarian function in the rat. PLoS One. 4: 1-8.

Thorburn GD and Schneider W 1972. The progesterone concentration in the plasma of the goat during the oestrous cycle and pregnancy. J Endocrinol. 52: 23-36.

Vautier AN and Cadaret CN 2022. Long-term consequences of adaptive fetal programming in ruminant livestock. Front Anim Sci. 3: 778440.

Wathes DC 2022. Developmental programming of fertility in cattle - is it a cause for concern? Animals. 12: 2654.

Yao S, Lopez-Tello J and Sferruzzi-Perri AN 2021. Developmental programming of the female reproductive system - a review. Biol Reprod. 104: 745-770.