Genetics and Reproduction

Review

Water Buffaloes in Cuba III. Fetal Programming, Birth and Weaning Weights

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ABSTRACT

Background: Fetal programming was a term used first in humans, then it spread thanks to different research done on domestic animals to determine the effects on the progenies of nutrition during the early, intermediate, and final stages of gestation, and their short-term repercussions on the productive, reproductive, and immunological parameters, such as birth and weaning weights. **Aim:** To present this concept and analyze birth and weaning weights as reference information for buffalo progenies. **Development**: This paper deals with the concept of fetal programming and its impact on raising; the weight-related data collected upon buffalo calving were shown. **Conclusions:** The scientific evidence demonstrated the relevance of the nutritional state of the cows during fertilization and gestation, as well as the low weaning weights of the progenies. It means that a change of mindset is necessary in livestock raising, by considering this scenario as a starting point to produce offspring with the proper weight required for further production and reproduction.

Keywords: Buffaloes, fetal programming, birth weight, weaning weight (*Source MeSH*)

INTRODUCTION

The conditions of mammal development during gestation and the neonatal period are known to affect post-calving health over time. This phenomenon is associated with changes in gene expression due to epigenetic mechanisms induced by the environment (Robles and Chavatte-Palmer, 2017).

In Cuba, the terms epigenetics and fetal programming have undergone little development in livestocking. Hence, their relevance in animal production, particularly in birth weight and weaning, must be referred to when evaluating young animals.

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DEVELOPMENT

Buffalo efficiency in Cuba is slowly declining; the emphasis on technical analyses is made in relation to the traits that indicate the beginning of the reproductive life of males and females, so two previously transcendental stages are often overlooked mistakenly. 1) The state of the cow throughout gestation; 2) The periods following calving, which are linked to the calf's early puberty, sexual maturity and sacrifice age of males.

This paper will refer to the concept of fetal programming and the results achieved in Cuba in terms of birth weight and weaning, due to their importance for the stability of the buffalo progeny and their contribution to human nutrition. The scientific information about this topic and its impact on the different functions and animals is broad (Kiefer and Perrier, 2019; Takeda *et al*., 2019; Mi *et al*., 2021; Breton *et al*., 2021); however, only a few topics are reviewed.

Epigenetics, fetal or development programming

Epigenetics refers to the study of factors regardless of the elements of classic genetics, but which interact in gene expression. These elements are determined by environmental factors and underlying genotypes that influence the phenotypical expression of livestock (milk production, wool quality, disease resistance, growth, and development). They intervene in the determination of ontogeny or organism development, from the fertilization of the zygote in sexual reproduction to its senescence, and heritable regulation of gene expression without changes in the nucleotide sequence (Lacal and Ventura, 2018; Skvortsova Iovino and Bogdanović, 2018; Maldonado *et al*., 2019; Beaujean *et al.*, 2020; Wu and Sirard, 2020; Breton *et al.*, 2021; Ibeagha-Awemu and Yu, 2021; Peral-Sanchez *et al*., 2022). Figure 1 shows a scheme of the epigenetic factors in animal production. Intergenerational epigenetics represents the transmission of epigenetic marks from one generation to the other (Pang *et al.*, 2017).

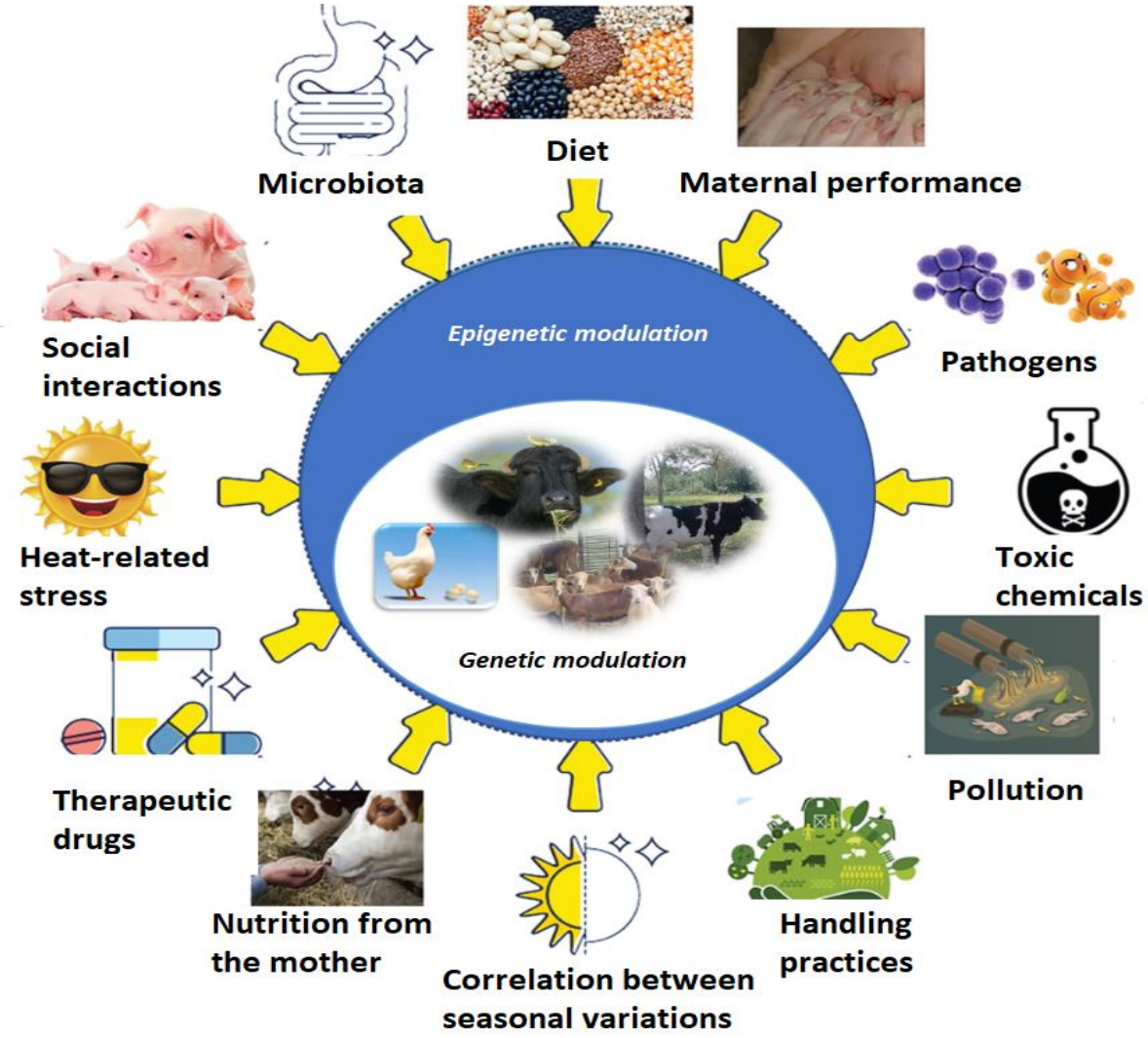

Figure 1. Epigenetic factors that respond to external and internal environmental factors, and interact with the underlying genotype, influencing the outcome of the genotype (Ibeagha-Awemu and Yu, 2021).

According to Anastasiadi *et al.* (2021), the consequences of the epigenomic variation vary depending on the sources (intrinsic, genetic, extrinsic); environmental predictability is a key factor to determine the consequences of epigenetic heredity on the phenotype and aptitude. The authors consider that epigenetic heredity is another piece of the puzzle of non-genetic heredity, though prevalence, sources, persistence, and phenotypical consequences of epigenetic marks on the taxa are still uncertain.

The term development or fetal programming emerged as a part of the epigenetic effects; it was coined by Dr. David Barker, in England, and relied on epidemiological data associated with the effects of pre-natal malnutrition on human health over time (Khanal and Nielsen, 2017; Reynolds *et al*., 2019).

Fetal programming is the set of stimuli received along the intrauterine life, which can interfere with fetal development and have permanent consequences during adulthood (Abruzeese *et al*., 2018; Lunesu *et al*., 2020). In other words, the exposure to certain factors during this period of susceptibility can modulate development processes linked to the formation of the phenotype of adults. Due to their extent, several studies were conducted on domestic animals to observe the effects of nutrition during early, mid, and late stages of gestation on the progenies, and their long-term repercussions on the productive, reproductive, and immunological parameters (Torres Diez, 2018), and the changes caused by heat stress (Wu, Zhang and Li, 2020).

Although no references were found in relation to this topic in water buffaloes especially, various authors focused on the following stages of conception in other ruminants, and demonstrated that development programming, at least in terms of maternal nutritional effects, begins in early gestation (Crouse *et al*., 2017; McLean *et al*., 2017).

The impact on prenatal malnutrition is shaped by the moment of gestation it occurs, the intensity of nutritional restriction, and the duration of the restriction period. In the first half of gestation, the fetus's nutritional requirements are relatively low, it is the stage of maximum growth and vascularization of the placenta and fetus organogenesis, which is critical for normal growth and development throughout an individual's life (Reynolds and Vonnahme, 2016).

The progenies under nutritional restrictions during the first half of gestation (though appropriate , to the end of that period) may be born with normal weights. However, they carry many of the phenotypical characteristics of congeners with nutritional restrictions throughout gestation. Some of these are economically important traits, such as perinatal mortality, dysfunction of essential organs, reduced postnatal growth, and loss of the animal's productive features (meat) (Greenwood Calyton, and Bell, 2017).

The potential of muscular growth depends on the proper formation in the prenatal period, since there is no increase in their numbers after birth, compared to the quantity of muscle fibers. Costa *et al.,* (2021a), claimed that in grazing gestating ruminants, nutritional restriction due to forage seasonality may affect the development of their descendants. Hence, the nutrients from the mother are used for the formation of vital fetal tissues, rather than secondary tissues, such as the skeletal muscles, thus reducing meat-producing efficiency. The damage caused by the protein restriction in beef-producing cows in the middle of their gestation entails a lasting reduction of the number of muscle fibers in the progeny, besides altering the metabolism of the glycolytic-type fiber muscle in an early stage of life, which can be reverted depending on the postnatal scenario.

Similarly, the energy restriction during the last stage of gestation contributes to the low regulation of genes involved in the oxidative metabolism, consequently favoring the low efficiency of the glycolytic metabolism in the skeletal muscle of calves (Sanglard *et al*., 2018); however, the newborn goats from mothers with nutritional restrictions at different stages of gestation did not show phenotypic differences in the muscle (Costa *et al*., 2019).

In that sense, Costa, Gionbelli and Duarte (2021b) highlighted that the nutritional manipulation in the intrauterine period contributes to creating favorable traits in the quality of meat, such as marble-like form and tenderness.

Insufficient nutrition or excessive availability also alter the epigenetic state of *in vivo* and *in vitro* germinal cells, and the transmission to further generations (Guo, Luo, and Lin, 2020). There are studies that link both conditions prior mating to a deficient quality of oocytes, lower fertilization and embryonic rates, and the progenies could have lower antral follicle counts (Mossa *et al*., 2015), an age increase on first calving, greater number of services by conception, lower weight gain, dystocia and infertility due to slower physiological development than the animals whose mothers underwent a normal gestation in terms of nutrition.

The milk-producing cows losing weight at the time of conception generate compromised embryos and progenies with a unique metabolic mark. A similar phenomenon has been associated with different culture conditions and *in vitro* fertilization. Hence, the embryo behaves in economy mode, with the reduction of translation, cell cleavage and the production of triphosphate adenosine are reduced to adjust to the environment perceived. Few epidemiological studies have been conducted in bovines to evaluate if these changes require more analysis to associate specific molecular changes in embryos with visible consequences ahead in their lives (Sirard, 2021). The same occurs with the vulnerability of the epigenome to drastic changes of temperature during the pre-implanting period (de Barros and Paula-Lopes, 2018). Donkin and Barrès, (2018) said that like the somatic cells, the epigenome of spermatozoa is dynamically reactive to a wide variety of environmentally-stressing factors.

As to milk production, upon observing the productive performance during the first lactation of calves whose mothers were producing during the confirmation of gestation there was a trend toward a decline of the total production during the first lactation (18 kg), and less duration of lactation (23 days), in contrast to the animals conceived by animals that were not lactating. It may be explained by the fact that the nutritional requirements of gestating and producing cows were partially met (González-Recio, Ugarte and Bach, 2012).

Birth weight (BW)

Birth weight shows the nutritional level of the mother during gestation, though fetal programming might occur regardless of the birth weight (Reynolds and Caton, 2012; Reynolds *et al*., 2019). In Cuba, the progenies from Buffalypso x Carabao weighed between 37.9 and 42.2 kg on a diet of fodder, molasses, urea, and supplements (García *et al*., 2003). In the province of Pinar del Rio, the overall mean was 37.8±0.03 kg (Fraga, González, and Gutiérrez, 2006), higher than the one reported by Martínez *et al*. (2009) in Granma, with 36.82±3.1 kg, and the Maraguan Company (Camaguey province), whose average was 32.0±0.2 kg (Ceró *et al*., 2017). The results coincided with reports from Brazil involving the calves from Jaffarabadi, Mediterranean, and Murrah, with birth weights of 36.43; 39.79 and 37.63 kg, respectively (Mendes *et al*., 2017).

Weaning weight (WW) and mean daily gain (MDG)

In herds where the cows are not milked and the calves have access to greater amounts of milk, the nutritional state is better, the weaned animals have greater weight and reach sexual maturity or sacrifice weight quickly.

Upon the implementation of artificial rearing of buffaloes, the calves must have a very strong maternal instincts, the mother-progeny bond developed since birth, with a slower learning period when compared to crossbreeds. This entails greater time to learn to drink the mothers' milk artificially. Therefore, the separation of the buffalo mothers from their progenies is more stressing to both than the case of *Bos taurus* calves, though it does not affect the health and immune system of the progenies significantly (Bharti *et al*., 2015).

Kumar *et al*. (2017) said that in two groups of Murrah buffalo calves fed by their mothers (G1), and artificially raised after birth (G2), the calves' weight was significantly lower in G2 at 180 days after birth lower than G1 (113.12±2.81 vs 122.77±2.63 kg, respectively $p<0.05$). Therefore, natural lactation has a positive effect on calf body weight gain.

The characteristics of buffalo progenies in Cuba in succeeding years, showed shortcomings in handling pre-weaning, low nutritional level of the cows, poorly managed natural pasture, stall of zootechnical flows, and *a priori* completion of the milk production plans, which led to violations of proper progeny feeding when drying the cows, all have affected the weaning weight.

The preferred WW in Cuba are low: 122.0±0.3 kg in 255 calves from four dairies in the province of Granma (Méndez and Fraga, 2010), and Maraguan (Ceró, Guevara and Cáceres, 2013). These authors found that in 768 weaned animals between 2006 and 2010, the average weight was 107.2±1.35 kg, lower than the reports from the literature in Latin America. In a dairy Brazilian Murrah herd, with animals grazing on *Brachiaria brizantha* cv. Marandu, supplemented with maize or sorghum silage, the WW at 8 months was 170.30±24.12 (Andrade, 2011), in buffaloes raised on different farms in Colombia, aged 270±19 days, it was 182±42.46 kg (Bolívar *et al*., 2012).

In a company in Camaguey province, the MDG at weaning was 407 g/day in female animals, whereas it was 419 g/day in the male animals. According to the lactation number of buffalo cows, the progenies from first-calving cows reached 369 g/day, whereas the two with the most calvings reached 394-446 g/day (Ceró *et al*., 2017). Under these conditions, the cows will hardly get to 400 kg live weight to begin reproduction at 2 years of age, as established in Cuba in 2009. Then the minimum zootechnical indicators for buffalo herds were set, requiring 550-600 kg/day gains. The findings tell that at 24 months of age, the males and females will be below the optimum weight to start their reproductive cycles. Weaning at 170 kg at nine months with milking mothers, guarantee 440 kg animals in 24 months; while the in ones that consumed all the milk, the relative weight was 480 kg in 20 months.

CONCLUSIONS

The elements found in the literature indicate that the effects on the future progenies begin at the moment of begetting. Hence care must begin when the cow is fertilized. The technical analyses at this time are very convenient, based on the body condition of the mother-to-be. Promoting an optimal uterine environment will not only ensure successful fetal development, but also enhance postnatal performance and development, reducing the risk of disease occurrence in the adult animals, and finally, promoting proper environmental conditions so the cows have the necessary well-being. These should be art of the common practice of buffalo raising in Cuba.

The information published on the birth and weaning weights is not enough to determine the possible epigenetic effects on the calves when fertilization occurs in their mothers. It is recommended to include epigenetic studies (fetal programming) in further research studies in livestocking, as well as a topic in subject Genetics in the Veterinary Medicine Degree.

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AUTHOR CONTRIBUTION

Conception and design of research: AMV; redaction of the manuscript: AMV.

CONFLICT OF INTERESTS

The author declares the existence of no conflicts of interest.