Human Health and Animal Production: Nutritional Influences on Reproductive Performance

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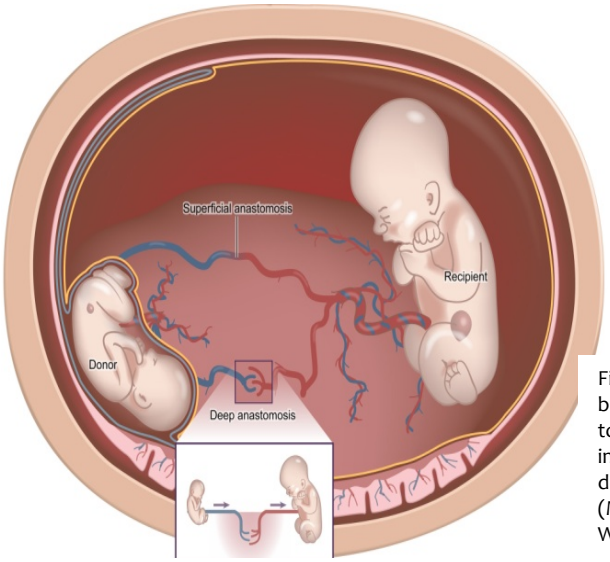

Figure 1. Disproportionate blood transfer from one twin to the other causing impaired growth and decreased development (Medically Speaking, WordPress.com, 2012)

Introduction

Reproductive performance is a fundamental process that has far-reaching effects. In human society fertility can have social implications, but in animal production the number, strength and performance of offspring is vital. This can manifest throughout the features of fertility, from the production of germ cells to the formation of the phenotype.

Significant investment of maternal resources in the growth of the foetus suggests that nutrition can be used as a tool to manipulate reproduction or prevent certain forms of disease in the adult animal. This article summarises research involving nutritional components and their effects on the success of a pregnancy and long term health.

Ovulation

Hormones are the signalling molecules that regulate many physiological processes and are vital to the timing of reproductive life. They are dependent on a variety of environmental cues, such as nutrition, which suggests maternal dietary changes could affect these hormone cycles.

In a study that restricted overall feed intake in sows and rats Almeida *et al.* (2001) observed lowered levels of critical hormones in the first week of oestrus and changes in the FSH/LH (Follicle-stimulating Hormone/Luteinising Hormone) balance in the pre-oestrus period (figures 2&3). However, these hormonal changes were reversed when insulin was injected. This suggests insulin could be injected when feed intake is low to reduce recognition of dietary changes.

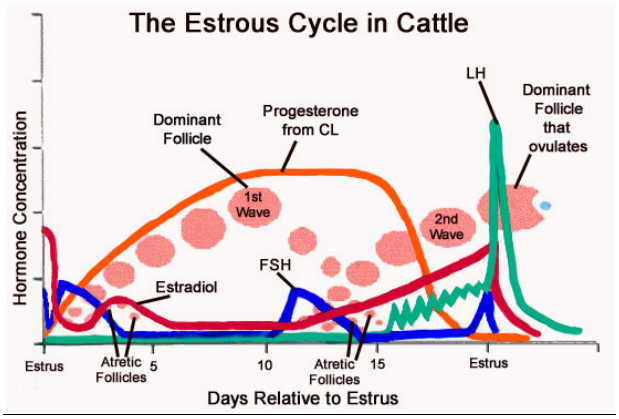

Figure 2. Showing the hormone levels and follicular waves during the oestrus cycle of a cow. FSH stimulates the maturation of germ cells, while an LH surge causes ovulation (Javic and Conroy 2001).

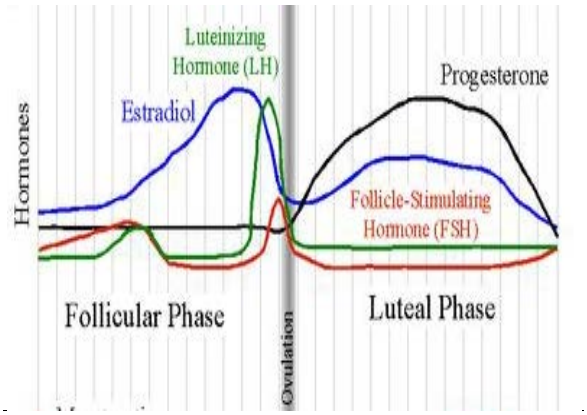

Figure 3. The hormone levels during the menstrual cycle of a human (Deardeuff, L. 2012. WordPress.com)

Specific nutrients of importance seem to be those that interfere with hormonal precursors. For instance *trans* fatty acids interfere with the formation of the precursor arachidonic acid and thus prostaglandins (which regress the corpus luteum and induce labour) have reduced synthesis.

Conception and Embryo Survival

Protein & Carbohydrate

Protein and energy sources are vital to support the extensive cell proliferation and hormone production during initial stages of embryo formation. Abecia *et al.* (1997) found low protein delayed development to blastocyst stage and higher protein expanded the blastocysts with unaffected development.

In the higher stress of intensive animal systems energy supply in excess of 'normal' is recommended to offset increased energy demands. With this adjusted energy method cattle did experience improved fertility, but not pigs. Progesterone concentration was reduced below that required for implantation of the blastocysts (Virolainen *et al.* 2004).

Fats

Obesity is major concern when improving conception rates in humans, as obese women are 3 times more likely to experience fertility problems than those of a healthy weight (Brewer *et al.* 2010). *In vitro* testing suggested hyperlipidaemia increased the expression of apoptoptic genes in blastocyst cells but the *in vivo* tests produced less definitive results due to hormonal involvement (Leroy *et al*. 2010).

During IVF and embryo transfer techniques, the quality of the follicle collected largely depends on the donor's physical condition and improvements have been shown when a dietary fat supplement is given (Santos *et al.* 2008). When an animal is in poor condition with low fat and mineral reserves, hormonal levels change and transfer conditions are not met. Despite close monitoring of both factors problems such as low birth-weight or premature births occur. It is as yet unclear whether these are to do with the condition of the participants or the procedure itself.

Vitamins & Minerals

Dietary antioxidants are one of the most vital components at this stage to combat the free radicals produced during blastocyst formation and to protect oocytes during maturation. Therefore vitamins/minerals (above recommended levels) have been shown to enhance fertility through improved first conception rates (Nocek *et al.* 2006).

Number and Size of Offspring

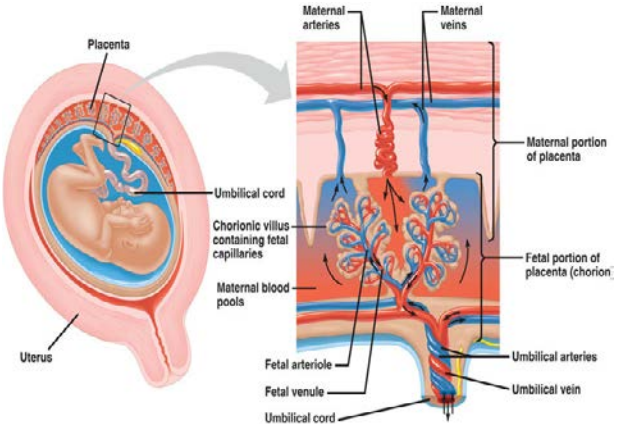

Figure 4. Human placenta showing maternal and foetal blood vessels (Krauz, WordPress Experts, 2011).

Nutrient transfer is a major factor in determining the number of offspring supportable, but due to ovulation rates the number fertilised per cycle is largely species dependant. For example cows produce 1 ovum whereas pigs produce 15-25. However, selective breeding tends to over-ride expected nutritional influences. For instance pigs selected for high prolificacy won't abort embryos unless under severe malnutrition.

Most research in this area has centred on improving pig production by increasing litter size (using vitamin A to reduce embryo re-absorptions) but the only success was with young sows (Lindemann *et al.* 2008).

In mammalian species the placenta (figure 4) is the site of nutrient transfer to a foetus. Diffusion can

become unequal amongst the multiple offspring, which may cause a deficiency in a nutrient. This reduces the growth and is an example of how a 'runt of the litter' is formed.

Human studies largely focus on twins as differences in development can be distinguished between foetal programming (permanent changes in tissues derived at foetal stages) and environmental effects. For instance, some diseases (hypertension, diabetes) are seen in early infancy of just one monozygotic twin. This suggests non-genetic causes for these conditions, such as the altered blood flow shown in figure 1. This reduced growth causes specific disease states due to the less developed organs (Bajoria *et al.* 2001).

Birth-weight and size are the first ways to determine the effects of conditions *in utero*. Nutrition provides the structural components for building tissues, but the uterine capacity determines the maximum size. Well-known cases feature mare ponies and draft horse stallions producing pony sized foals which later grow to draft horse sizes.

The placenta is the first structure affected by nutrition and can adapt its size in order to maintain a constant supply of nutrients to the foetus. Rat studies showed starvation diets during the first trimester produced a larger placenta with average sized progeny (Belkacemi *et al.* 2010). Interestingly, if the nutrient restriction is isolated to the second trimester the offspring become under-weight (Belkacemi *et al.* 2009). This suggests the placenta cannot compensate for severe malnutrition during this period of maximal foetal growth.
During the third trimester, starvation produced smaller placentas with low birth-weight offspring. Hence, it appears that as the placenta grows during the first 2/3 of pregnancy it can adapt its size to maximise nutrient transfer. However, once the placenta is no longer growing it undergoes apoptosis with increased expression of Bcl-2 genes. These genes produce proteins to permeabilize membranes which kill cells in a controlled fashion.

The major foetal hormones involved in pre-natal growth are Insulin-like growth factors (IGF). IGF-2 is active mainly during early gestation and IGF-1 later to promote organ growth. A protein supplement (figure 5) increases the levels of these hormones in the heifer to increase the birth weight of calves.
Maternal protein intake (rats) has been studied in relation to overall tissue formation in terms of 'catch-up growth'. Reduced protein (8-10%) caused a corresponding decrease in the weight of tissues at birth. But once protein was increased the offspring grew to normal gestational size. However the metabolic strain caused by the 'catch-up growth' also reduced the average lifespan of the young. Similar increased birth-weight is also seen with increased protein intake in humans (Ozanne 2001).

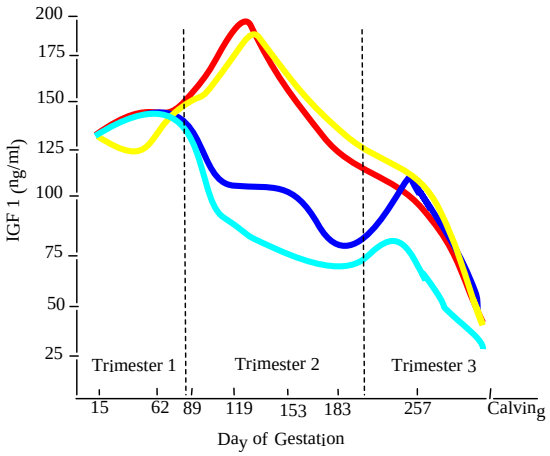

Figure 5. Based on data from Perry *et al.* (2002) showing the trend of IGF-1 levels during bovine gestation in response to protein supplement either high (H) or low (L) protein during the first then second trimester. Red denotes H/H, Yellow shows L/H, Light blue shows L/L and Dark blue shows H/L. Results showed significant differences between high and low protein on day 62 of the first trimester and days 119, 153, 183 of trimester 2. Conclusions suggest protein supplement increases IGF-1 during trimester 2.

Some evidence suggests fat metabolism is affected by maternal diet, most critically the balance of omega-6 and omega-3 fatty acids. Lower omega-3 decreased lipid metabolism by reducing the expression of adipokines in the foetal liver, increasing fat deposition later in life (Hanbauer *et al.* 2009).

Different responses between genders were observed in several maternal nutrient deficiencies. Evolutionary imprints tend to increase growth during male development; therefore a higher plane of nutrition is needed for their support. Evidence suggests this enables gender to be influenced by nutrition, as more females are produced in poor conditions (Maloney *et al.* 2011).

Health of Offspring

Health was considered in terms of the functional capacity of the different organ systems and the diseases associated with the physical changes. The 'thrifty phenotype' theory (Hockaday and Yajnik 2003) suggests the foetus is capable of adapting to malnutrition through altering the level of nutrient related receptors/transporters in a hierarchal order of organs. Thus particular diseases could develop from alterations in maternal diet.

Nervous System. The nervous system is one of the first structures to form and is mainly susceptible to folic acid and fatty acid deficiency. Neural Tube defects (NTDs) (failed closure of the neural tube) lead to diseases such as spina bifida. Folic acid supplement studies demonstrated 40-80% of NTDs cases were prevented if the supplement was taken during conception and early gestation (figure 6). Fatty acids (DHA) also concentrate to promote synapse formation and neurone growth (Cao *et al.* 2009).

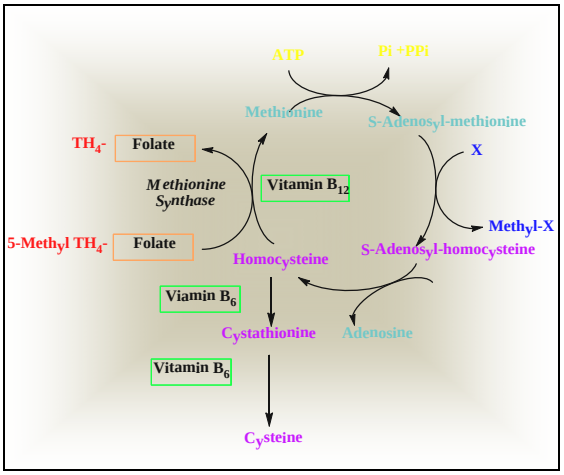

Figure 6. Showing the roles of folic acid and B vitamins in the transfer of methyl groups and the production of cysteine (based on 'Vitamin B9' by Brunstetter, http://blog.bekahbrunstetter.com/?cat=53).

Muscle. Muscle has been extensively studied to improve performance of offspring (animals) or prevent muscle diseases (humans). General under-nutrition caused a permanent reduction in secondary fibres and altered mechanical properties, manifesting later in life as reduced gripping capacity and strength (Ozanne *et al.* 2001).

Skeleton. As expected bone formation is reduced when its structural components (calcium, silicon) are lacking in the maternal diet. This increases the likely-hood of bone diseases (osteoporosis, rickets) as a result of the poor bone strength. Excess fatty acids are of importance with effects relating to oxidative stress on osteoblasts, (figure 7). Addition of quercetin (antioxidant) reversed the effects which confirmed oxidation was the cause (Liang *et al.* 2009).

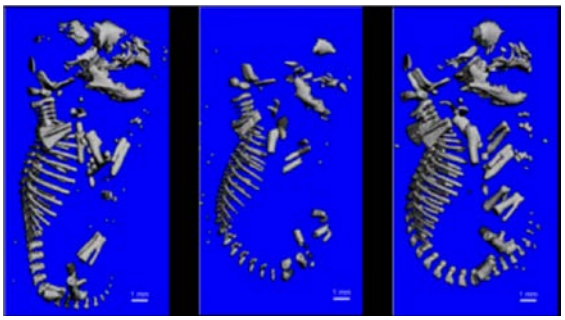

Figure 7. 3D MicroCT imaging of mice foetuses. Control (left), high saturated fat diet (HFD, middle), and high saturated fat diet with quercetin (HFD/Q, right). Foetuses from HFD dams showed lowered total mineralized tissue, while HFD/Q foetuses were similar to controls (Liang et al. 2009).

Kidney and Pancreas. The operation of the pancreas and kidneys rely on the number of functional units, the beta-cells and nephrons, respectively. Reduced energy & protein intake restricts the number of units formed. These changes reduce the capability of the organs and may induce diseases such as hypertension (decreased filtering by nephrons), diabetes (decreased insulin production) seen later in life (Ozanne *et al.* 2001).

Adipose tissue. Adipose tissue is formed from two functional types; Brown adipose tissue (BAT), which generates heat and White adipose tissue (WAT) that acts as an insulator. Both have functions in post-natal protection, however a strategy for improving health later in life would involve altering the ratio of BAT:WAT which is determined before birth. BAT contains UCP (uncoupling proteins) which occur as UCP-1 which oxidises fats and UCP-2 that is associated with obesity. UCP-1 was enhanced under an *ad. lib*. diet, whereas UCP-2 is enhanced under restriction. These pre-natal changes remain throughout life, thus the concept arises that some people could be predisposed to becoming obese (Bispham *et al.* 2005).

Discussion

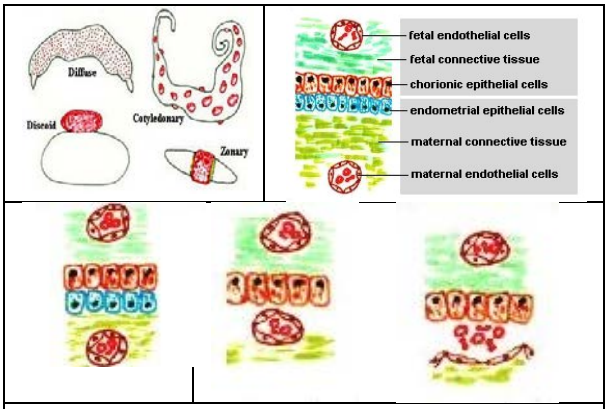

Figure 8. Placental types based on shape and contact points and maternal and foetal layers of blood exchange interactions (Bowen, 2001, http://www.vivo.colostate.edu/hbooks/pathphys/reprod/placenta/structure.html).

These studies cover a variety of models (pigs, rats, humans) with varying methodologies. Nevertheless, the similar results in several models suggest the effects maybe common for mammals. However differing physiology (rumen) and differing reproductive structures (see Figure 8) must also be considered when implementing nutritional strategies.

Applications for this type of research are wide ranging. For humans the uses consist of revised advice tailored to individual needs or prevention of common diseases such as hypertension and obesity. For animals the improvement of performance through better feed efficiency is an important concept. Growth and product yields are almost at physical limits so identifying developmental effects are essential.

Conclusion

The nutritional influences described here clearly demonstrate that reproduction can be manipulated by diet through the relation to body condition and the hierarchy of energy use. Foetal programming features heavily in many analyses as response to nutrients and organ functions are determined during gestation. These far-reaching effects have important implications for improving population health and tailoring diet to individual needs, but more specifics effects could be determined with further epigenetic studies.

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Author Profile

Jennifer is 23 years old and graduated from the School of Biosciences in 2012 with a first class degree, BSc (Hons) in Animal Science. Jennifer is particularly interested in foetal programming and is currently undertaking a PhD at the University of Nottingham.