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Farm animal welfare: assessing risks attributable to the prenatal environment

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Abstract

An ever-expanding scientific literature highlights the impact of the prenatal environment on many areas of biology. Across all major farmed species, experimental studies have clearly shown that prenatal experiences can have a substantial impact on outcomes relevant to later health, welfare and productivity. In particular, stress or sub-optimal nutrition experienced by the mother during pregnancy has been shown to have wide-ranging and important effects on how her offspring cope with their social, physical and infectious environment. Variation in the conditions for development provided by the reproductive tract or egg, for instance by altered nutritional supply or hormonal exposure, may therefore explain a large degree of variation in many welfare- and productivity-relevant traits. The scientific literature suggests a number of management practices for pre-birth/hatch individuals that could compromise their later welfare. Such studies may have relevance for the welfare of animals under human care, depending on the extent to which real life conditions involve exposure to these practices. Overall, the findings highlight the importance of extending the focus on animal welfare to include the prenatal period, an aspect which until recently has been largely neglected.

Keywords: *animal welfare, early life, farming, foetal, gestation, prenatal*

Introduction

The existence of variation, whether within an individual over time or between individuals in different litters, pens, farms or production systems, is of fundamental importance in animal welfare research. Suffering, a critical component of most definitions of animal welfare, can only be a property of the individual. Yet individual variation is often overlooked in the search for average treatment effects (Provenza 2008). Questions as to why particular combinations of genotype and environment cause a phenotypic outcome indicative of reduced welfare are clearly important. One possibly important source of individual variation within animals, beyond that attributable to genetic variation, is the prenatal environment (Braastad 1998; Lay 2000). From a welfare perspective, environmental effects that occur prior to birth or hatch have received less consideration than postnatal events, although they are now coming to prominence. This area is of particular interest, as many of the traits that can be affected by early life experiences, such as stress reactivity, behaviour, and immune function, are highly relevant to the ability of animals to exist under human management conditions and avoid states of suffering.

The transition from prenatal to neonatal life is clearly an important one for all living individuals. Mellor and Diesch (2006) have argued that this is the point at which animals become capable of suffering. However, even if individuals are not conscious of a variable prenatal environment it can still dictate how successful they are at coping with later life (Braastad 1998). Since most farmed species are relatively precocial at birth it is also during the prenatal period that many key systems develop and become functional. Therefore, set-points and response thresholds may be permanently affected by variation in experience around this time. This highlights the need to consider the implications of the prenatal period for the future welfare of individuals.

This paper will discuss the possible contribution of variation in the prenatal environment to animal welfare outcomes in a variety of farmed species. The starting points for this discussion are the following two simple suppositions. Firstly, that there are a number of experimental studies showing that early life factors can cause changes during later life that are relevant for animal welfare. Secondly, despite these studies, there is some genuine uncertainty about the extent to which such factors matter in real life, ie under commercial farming conditions.

This paper will briefly review progress so far in terms of the animal welfare interest in early life experiences. This will lead to an appraisal of the current state of knowledge in the area. Finally, consideration will be given regarding the direction the field should take to elucidate the true animal welfare relevance of prenatal effects.

Prenatal development and postnatal health and welfare

It is worth noting at the start that early life really does mean early. Indeed, factors affecting mothers in the peri-conception period can impact on offspring development (Ashworth *et al* 2009). For the purposes of this paper, discussion will be restricted to the prenatal period, from conception to birth (point of hatch in birds, or the point of first feeding in fish).

The knowledge base across all areas of biology, on the relationship between prenatal conditions and offspring outcomes, has expanded greatly in the last two decades. Aside from the growing farm animal production/welfare literature, research into prenatal experiences is conducted in three broadly distinct fields: human epidemiology, behavioural ecology, and laboratory/biomedical studies. There is often little cross-fertilisation between these different fields yet theory and data from all of them can provide useful information for farm animal studies. These fields also often use different terminology yet all build on the basic premise that animals can 'inherit' aspects of their biology from one or both parents by means outwith their genotype (eg Jablonka & Lamb 2005).

Human epidemiology

There has been substantial interest in recent decades in the contribution of the prenatal environment to human health outcomes. The identification by Barker and others of an association between reduced foetal growth (using birth weight as a proxy measure) and chronic ill health later in life (Barker *et al* 1989a,b) was seminal and led to what became known as the 'thrifty phenotype hypothesis' (Hales & Barker 2001). Central to this idea is the concept that negative outcomes of prenatal nutrition may depend on the mismatch between the signals a foetal organism receives (based on the status of its mother) and the postnatal environment it finds itself in. Since the prenatal environment is to some degree dictated by the dam's external environment, the experienced prenatal environment may provide information about the likely postnatal environment. This may allow foetuses to predict what their postnatal environment will be like. In wild animals this ability allows individuals to fine tune their biology, beyond the template laid down by their genotype as a result of natural selection, to the specific environment they are likely to face during their life. Such effects have been termed 'predictive adaptive responses' (Bateson *et al* 2004; Gluckman *et al* 2005). However, in circumstances where that prediction proves incorrect, alterations to phenotype may be detrimental to postnatal health. Whilst the predictive adaptive responses theory emerged in relation to human nutritional studies, it may equally provide a useful framework for understanding foetal responses to a broad range of maternal challenges in humans and in animals.

Barker's data were based on natural variation in human population cohorts. However, other human epidemiology studies have exploited large cohorts of individuals that have systematically experienced altered prenatal conditions, often as a result of tragedies experienced by their mothers. In terms of prenatal nutrition, perhaps the most widely studied of these is the Dutch hunger winter cohort (Lumey *et al* 2007). Towards the end of the Second World War a large proportion of the population of The Netherlands experienced a period of severe famine as the retreating German army cut off food supply lines. As a consequence, many individuals were severely malnourished and mortality levels in the population were extremely high. Beyond these immediate effects, children born to mothers who survived the winter and were pregnant during the period of famine, have been found to have a variety of physical health impairments (eg metabolic disorders), and also effects on mental health, such as increased risk of affective disorders (Brown *et al* 1995).

Research has also addressed the impact that stress can have on foetal development through studies that have followed particular cohorts of offspring whose mothers experienced acute periods of stress, for instance during the World Trade Centre attacks in 2001 (Yehuda *et al* 2005), or during the Quebec ice storm in 1998 (Laplante *et al* 2008). In the latter example, 'Project Ice Storm' investigated the consequences for offspring born to mothers who where pregnant during a severe ice storm that affected large areas of Quebec and neighbouring provinces in Canada in 1998. More generally, studies have investigated 'natural' variation in maternal stress levels (for instance, caused by death or serious illness in the family: Khashan *et al* 2011), or in the degree of depression or anxiety experienced by mothers (eg Field *et al* 2006).

Despite the focus on either nutritional factors or emotional stressors in individual studies, in reality it is often very difficult in epidemiological studies to separate out the contribution of each of these factors. This is also an issue in experimental animal studies as factors that are emotionally stressful may impact on feed intake and conversely, in some cases, restriction of nutrition may be actively distressing — for instance if it involves hunger.

Behavioural-evolutionary ecology

Evolutionary ecology studies in this area, typically discussed under the heading of maternal effects (eg Mousseau & Fox 1998) have examined the adaptive significance of early life effects and more generally their possible contribution to evolutionary change (eg Wolf & Wade 2009). There are numerous examples of such studies in the literature, two of which are briefly discussed here.

Shine and Downes (1999) manipulated different aspects of maternal experience in a lizard species (*Pseudemoia pagenstecheri*) and demonstrated some degree of specificity between maternal treatment and offspring outcomes. For instance, offspring born to mothers that were exposed to predator odours had longer tails, which was suggested to increase the effectiveness of tail autotomy as a predator avoidance tactic. Maternal exposure to the predator scent also increased offspring responsiveness to the same odour, an effect which was not seen in response to other maternal manipulations (eg of food supply or environmental condi-

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tions). Storm and Lima (2010) demonstrated not only that exposing gravid crickets (*Gryllus pennsylvanicus*) to a predator odour altered the anti-predator behaviours of their offspring but that this also enhanced offspring survival under predation risk. The existence of such adaptive maternal effects does not of course imply that all changes to offspring phenotype are beneficial in the wild.

Laboratory/biomedical studies

The literature on prenatal effects as studied, primarily in rodent species, under laboratory conditions is too vast to review here, however, reviews in this area are frequent (Charil *et al* 2010; Brunton & Russell 2011). The studies have most commonly been conducted in a biomedical context, under the broad heading of 'foetal programming', although this term has been criticised (Bateson 2007). Their contribution has largely been a greater understanding of physiological mechanisms. For instance, identifying the role of the enzymes 11-beta-hydroxysteroid dehydrogenase type 1 and type 2, particularly in neural or placental tissue, in regulating the foetal impact of maternal stress (Diaz *et al* 1998; Welberg *et al* 2000) provided an important contribution to understanding the physiological basis regarding periods of foetal sensitivity to maternal stress and how this itself might be altered as a consequence of maternal treatments (Welberg *et al* 2005).

The broad fundamental understanding of rodent physiology and the range of associated measurement techniques, in addition to their short generation time, means that such work can progress rapidly. However, in terms of possible translational impact (either for human relevance or to inform large animal studies) rat and mouse models of prenatal stress may be limited, since these species have a relatively immature state of brain development at birth. Other model systems are clearly warranted to examine the impact of prenatal stress. For example, guinea pigs (*Cavia porcellus*) have been used due to their longer gestation period and more precocial offspring (Kapoor *et al* 2009).

Prenatal contributions to farm animal welfare: where are we now?

Interest in prenatal effects on animal welfare started to expand in the last decade of the 20th century. Braastad's (1998) review paper discussed the impact of prenatal stress on behaviour in laboratory and farmed animals. This paper mostly included information from studies in laboratory rodents or primates, reflecting the general lack of studies in livestock or other farmed species at that time. However, since then a large number of studies have started to investigate prenatal effects in a variety of farmed species (predominantly sheep and pigs, but also in cattle, poultry and fish). These studies have led to a general understanding of some of the ways that prenatal development can be affected by maternal nutrition, maternal stress or health status, other maternal factors (such as age or temperament) and also how individuals can be affected by the composition (numbers, sex) of littermates in the uterine environment. Additionally, the work in this area has provided a broad understanding of how alterations to prenatal development, brought about by the factors mentioned above, subsequently impacts upon postnatal biology in areas including; stress physiology, physical development, reproductive biology, behaviour, metabolic function and immune function.

From an animal welfare perspective, there are several categories of maternal experiences that may have relevance as prenatal challenges for their offspring. In addition, the other offspring experiences such as their *in utero* littermates and their experiences at the point of birth are also relevant. To illustrate the range of maternal experiences, farmed species and outcomes, a selection of relevant studies are discussed here, under eight broad categories of factors that may influence prenatal development:

Social environment

The social environment is crucially important for all farmed species, and social stressors are widely recognised as being amongst the most potent that can be applied to animals. Farm animals may be kept in groups of inappropriate size or composition, or may be subject to regular or intermittent mixing with unfamiliar individuals. For example, research (Jarvis *et al* 2006; Rutherford *et al* 2009; Ashworth *et al* 2011), using a model of social stress in pregnant pigs, has shown a range of offspring outcomes, such as decreased weight gain post-weaning, altered reproductive function, increased stress reactivity, increased behavioural responses to pain and other negative behavioural outcomes.

Housing system

Physical aspects of any housing system have the potential to affect maternal welfare and as a consequence may affect their offspring. In some cases there may be direct evidence that a particular housing system for gestating animals affects offspring phenotype. For instance, Sorrells and colleagues (2006) found that piglets born to gilts housed individually had a lower bodyweight at day 35 than piglets born to group-housed gilts. Campbell and co-workers (1994) found that a two-week period of confinement stress caused an elevation of circulating cortisol levels in rainbow trout (*Oncorhynchus mykiss*) and brown trout (*Salmo trutta*) and that this had a negative effect on survival rates in the offspring of confined fish.

Feeding method and nutrition

The plane of nutrition and feeding method for gestating animals will likely be an important factor that could act as a hazard in many systems. Equally, there is a widespread interest in dietary supplements aimed at enhancing offspring performance and health. Consequently, the impact of maternal nutrition on offspring biology has been the most widely studied example of prenatal effects. During pregnancy it is common in pigs (*Sus scrofa*), cattle (*Bos primigenius taurus*) and sheep (*Ovis aries*) for mothers to experience a degree of food restriction and possibly weight loss as an inherent part of the production cycle. Effects on offspring may be mediated by specific nutritional deficits, or possibly via the stress-response system, where feed restriction is stressful for the mothers. Chadio and colleagues (2007) kept pregnant ewes on a 50% nutrient-restricted diet early in gestation and found an increased HPA responsiveness in their offspring tested at two months of age. Moreover, Rooke *et al* (2010) recently showed that Suffolk lambs born to ewes that were undernourished during the first ninety days of gestation had higher worm burdens at around six weeks of age than lambs born to ewes fed to requirements. Interestingly, in the same experiment, there were breed-related differences, with lambs born to undernourished Blackface ewes not showing the effect observed for the Suffolk lambs. In addition to the overall level of maternal nutrition, the method of feeding may also have an effect on offspring. Janczak and others (2007) found that offspring from hens exposed to an unpredictable feeding regime had elevated tonic immobility durations, putatively indicating increased fear.

Human contact and husbandry treatments

Some animals may experience husbandry interventions whilst pregnant that could be acutely stressful. More generally, the quality of stockhandling that an animal is exposed to has an impact on welfare, and is likely to be an important source of stress during pregnancy (Lay *et al* 2008). Coulon *et al* (2011) recently demonstrated that aversive handling of ewes during pregnancy increased fearfulness in their offspring. Alternatively, Roussel-Huchette *et al* (2008) reported an apparent reduction in lamb fear levels when their pregnant mothers had been repeatedly isolated and transported during the last six weeks of gestation. This study highlights the fact that relationships between maternal treatments and offspring outcomes can be complicated and it is not always the case that treatments that negatively impact on maternal welfare also have negative offspring outcomes. Indeed, this latter point raises the issue that certain management practices applied during gestation may result in a conflict by negatively impacting maternal welfare but having a positive effect for subsequent offspring welfare.

Environmental parameters

Various environmental/climatic factors have the potential to act as early life hazards. For instance, temperature and humidity levels prior to birth or pre-hatch in oviparous species may have an important influence on offspring biology. This may occur through a direct effect on thermotolerance (Yahav *et al* 2004) or could represent a more general stress effect (Collier *et al* 1982). In extensively maintained species, such as sheep and beef cattle, climate may pose a threat if pregnant animals are exposed to conditions outside of their thermo-neutral zone, particularly if variation in day-to-day conditions prevents acclimatisation. Such issues may come to increased prominence in the future as global warming starts to affect the environmental conditions that livestock are exposed to.

Prenatal photoperiod has been shown to affect various measures of piglet immune function and also circulating cortisol levels (Niekamp *et al* 2006). Other environmental factors such as air or water quality could also affect maternal state, with knock-on effects on offspring function. For example, a recent finding in mice (*Mus musculus*), showing that air pollution prior to conception can influence prenatal survival and foetal size (Veras *et al* 2009) points towards the possibility that wider aspects of the environmental experience during gestation can alter offspring development.

A possible issue for many farm animals could be whether the degree of environmental stimulation experienced by mothers impacts on their developing offspring. For example, Maruoka *et al* (2009) found that the degree of maternal environmental enrichment experienced by mice during gestation affected their offspring's brain development and behaviour in an open field. Specifically, female offspring of mothers kept in an enriched environment had lower anxiety levels compared to offspring of mothers kept in barren conditions. Given that the degree of environmental stimulation is a cause for concern for many farm animals this finding could have wider implications. This has not been widely studied, although Beattie *et al* (1996) found that the offspring of gilts reared under barren conditions fought more as juveniles compared to offspring from gilts reared in enriched pens.

Infectious environment and maternal health status

Experimental studies in rodents (Meyer *et al* 2007) have shown that stimulation of the maternal immune system can cause variation in offspring biology. This could occur directly via maternal-offspring immune communication, or more generally poor maternal health status may have an indirect effect on offspring functioning (eg via maternal condition or stress status). For example, maternal endotoxin exposure during late pregnancy has been found to affect offspring HPA function in sheep (Fisher *et al* 2010). Moreover, other sheep studies have shown that ewes infected with sheep scab or mange give birth to lambs with lowered birth weight (Sargison *et al* 1995; Fthenakis *et al* 2001), while Wassink *et al* (2010), found that treatment of footrot during pregnancy increased lambing rate in ewes. This study raises a particularly pertinent question for many farm animals, namely whether pain experienced by the mother, for instance as a consequence of lameness, could act as a significant stressor affecting offspring development, beyond any effect mediated by reduced feeding and body condition? Less obviously, perhaps, treatments applied to remedy maternal ill health could affect developing offspring (Burke *et al* 2005).

Intrauterine position or crowding

In addition to purely maternal effects, littermates may be an important source of variation in the *in utero* environment. A number of studies have shown, either through natural variation or artificial manipulation, the impact that intrauterine sex ratio, and the sex of adjacent individuals within the uterus, can have on development (Ryan & Vandenbergh 2002). Perhaps of greater relevance within agriculture is litter size, since this has been a trait that has been subject to deliberate selection in many animal breeding programmes and has also been affected by improved nutrition and management in many farmed species. Litter size is of particular interest in pigs where it has been the subject of genetic

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selection. There has been much discussion about the consequences of large litter size in pigs in relation to intra-uterine crowding (Foxcroft *et al* 2006). One immediately obvious effect of increasing litter size is decreasing average birth weight (Roehe 1999). Birth weight, within breed, has been associated with a number of alterations to biology. For instance, Poore and Fowden (2003) found that low birth weight piglets have a higher HPA reactivity. Delayed neonatal behaviours such as reaching the udder and sucking have been described in lambs with low birth weights or from larger litter sizes (Dwyer 2003). In fact, in lambs, there was a separate effect of litter size over and above birth weight for behaviour and thermoregulation that suggests larger litters are affected more than would be predicted from birth weight alone (Dwyer 2003). In the human literature, the association between birth weight and postnatal outcomes has been widely discussed. One interesting line of this discussion is the issue of whether birth weight is a causal factor in determining outcomes or whether low birth weight and the later outcomes are correlated due to their both having causal relationships to an impaired uterine environment (Wilcox 2001).

Birth experiences

Finally, the end point of the prenatal period — the birth process itself — can dictate later biological functioning, as shown in studies of the long-term outcomes of Caesarean sections (Daniel *et al* 1999, 2008), or difficult births. In cattle, for example, dystocia has been shown to impact negatively on neonatal thermoregulation (Stott & Reinhard 1978; Adams *et al* 1995), uptake of immunoglobulins (Vermorel *et al* 1989; Bellows & Lammoglia 2000; Waldner & Rosengren 2009), behavioural vitality (Adams *et al* 1995; Bellows & Lammoglia 2000; Hickson *et al* 2008) and on health outcomes (respiratory and digestive diseases: Lombard *et al* 2007).

Knowledge gaps

Whilst research on prenatal effects in farmed species has rapidly developed and contributed to a wider understanding of the issue, there are still a number of important areas where information is sparse. At a fundamental level, relatively little is known about the mechanisms whereby a maternal experience is transferred to the offspring in domesticated species. However, this knowledge may not be critical in determining welfare relevance. The issues identified below are those where further study would be beneficial to determine the animal welfare significance of these challenges.

Genotype effects

To properly understand the relevance of prenatal effects it is necessary to identify possible specific populations of individuals that may be either more or less susceptible to the effects of any particular hazard. Many prenatal effects can be considered as a subset of environmental influences on phenotype (albeit a particularly pertinent subset since these effects may last for the rest of the animal's life). In the same way that genotype (at breed or individual level) can impact on how animals are affected by the postnatal environment, the impact of the prenatal environment may also interact with genetics. Lindqvist and others (2007) used an unpredictable light-dark rhythm to generate stress in parental White Leghorn (a highly selected domestic breed) or the relatively unselected Red Jungle Fowl *(Gallus gallus*) chickens. The treatment affected parents of both breeds, and their offspring were then studied. While white leghorn offspring from stressed parents showed learning deficits, red jungle fowl offspring from stressed parents were not affected. Correlated differential gene expression was seen in white leghorn stressed parents and offspring but, in line with the behavioural data, not in red jungle fowl. The authors suggest that domestication may actually have resulted in animals with "an increased capacity to respond to environmental stress by affecting offspring phenotypes in captivity". This could have occurred either as a by-product of other selection or may have been an important trait in increasing the ability of early domesticated species to adapt to the unnatural environments they were placed in. The findings of Rooke *et al* (2010) can also be interpreted in a similar fashion, since the more highly selected sheep breed (Suffolk) appeared more susceptible to the negative influence of maternal under-nutrition than the Blackface breed, which can be considered a 'wilder' animal that exists in a state closer to ancestral progenitors.

Such results tentatively suggest that domesticated species, particularly those that have been highly selected, could be more sensitive to early-experience effects than wild equivalents. So, although domestication has, on average, reduced traits such as fear, the potential for individual variability remains. Lankin (1997) similarly found a wider range of behavioural reactivity in more selected sheep breeds compared to less selected breeds.

Exposure prevalence and sensitive periods

The critical determinant of whether the scientific literature on prenatal effects is relevant for animal welfare under commercial conditions is the extent to which gravid animals are regularly exposed to similar challenges under normal farm conditions. However, in many cases, relatively little is known about the prevalence with which pregnant animals are exposed to particular stressors or experience periods of sub-optimal nutrition. Another important issue is the timing/duration of stressor application needed to bring about a welfare relevant offspring change and how this varies between species depending on differing time courses of foetal development. At present, the information on this is very patchy and hard to interpret so more work in this area would be very useful. However, several studies clearly show that specific maternal challenges may have an increased effect at particular points of pregnancy (eg Jarvis *et al* 2006). This information is clearly an important contributor along with exposure prevalence to determine the true relevance of prenatal effects. Although, to some extent, the whole of pregnancy (and before) can be considered environmentally sensitive, the degree of sensitivity and the postnatal phenotype generated vary as gestation progresses. Therefore, predicting postnatal outcomes is difficult. The

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issue is further complicated by the fact that different types of stressors may produce distinctly different outcomes in offspring animals (eg as seen by Shine & Downes 1999).

Protective or susceptibility factors

Biological mechanisms do exist that act to buffer the impact of maternal experience on developing individuals. For instance, in relation to stress, the presence in placental tissue of 11-beta-hydroxysteroid-dehydrogenase type 2, an enzyme that converts cortisol/corticosterone to the inactive form cortisone, acts as a partial protection against high maternal glucocorticoid levels (Brunton & Russell 2008). The level of expression of this enzyme in the placenta can change over the course of pregnancy or in response to external challenges, with implications for the degree of protection provided to foetuses (eg Welberg *et al* 2005). Beyond this specific example, there will likely be a whole range of factors that dictate the extent to which maternal challenges transmit to their offspring. For instance, recent mechanistic work (Sferruzzi-Perri *et al* 2011) has shown that the level of IGF2 expression in the placenta may mediate the extent to which maternal under-nutrition impacts upon offspring biology.

Another area where there is only a limited understanding in farmed species is the extent that offspring sex impacts on the outcomes of a maternal challenge. Broadly speaking, laboratory studies suggest that males appear more at risk of functional deficits (for instance in cognition) whilst females appear more at risk of alterations to emotionality (Weinstock 2007). It has been suggested that male offspring may be more at risk of negative health outcomes as a consequence of maternal under-nutrition because male foetuses place a greater demand on maternal nutrients (Eriksson *et al* 2010). Störmer (2011) also identified males as being more at risk of negative effects of early life stress. Conversely, females may be more at risk of prenatal stress increasing behavioural and stress reactivity, possibly as an adaptive strategy to guard against predation. Sex-biased prenatal effects could dictate the degree to which these factors are considered important in agriculture. For instance, in dairy farming or egg production, where male offspring are not useful within the production system, any treatment that impacted on males would be taken less seriously than one which impacted upon females.

Maternal or paternal age has also been shown to contribute to offspring outcomes (eg in quail [*Coturnix coturnix japonica*]: Guibert *et al* 2011). Older parents are not always a bad thing though. Eisenberg (2011) notes that telomere length in sperm increases with age in humans, and suggested that this could be a form of predictive adaptive response signalling to offspring that longevity is possible in the current environmental conditions (telomere length being associated with energetically costly immune responses). In younger fathers, shorter telomeres may promote a phenotype that devotes less energy to immune defences in favour of a quick reproductive strategy.

True prenatal effects?

Broadly speaking, there are two possible ways that a treatment experienced by a pregnant mother could affect her offspring's biology in its postnatal life. Firstly, there is what could be called a 'pure' prenatal effect. Here, the impact on the mother transfers to the offspring and the offspring's biological function is altered in a long-term or permanent fashion. This could be due to a pathological effect, or as a consequence of a trade-off made by the offspring, or as a form of predictive adaptive response (Monaghan 2008). Alternatively, apparent prenatal effects could arise if the mother's own biology is affected beyond the immediate period of the challenge such that she behaves differently following parturition or physiologically affects her offspring through lactation. Indeed, studies have shown that stress or under-nutrition during pregnancy can, for example, alter maternal behaviour (Dwyer *et al* 2003; Ringgenberg *et al* 2012) and this could have effects on offspring that appear to be prenatally mediated.

Braastad (1998) makes the point that to properly establish the existence of a purely prenatal effect, particular experimental designs such as cross-fostering (or artificial rearing) are necessary. However, he further notes that from a practical animal welfare perspective, making a distinction between a pure prenatal effect and a maternal gestation effect carrying-over to the postnatal period is not necessarily important. In fact, most studies conducted in farmed species do not involve experimental designs that allow for prenatal and postnatal carry-over effects to be properly distinguished. Furthermore, manipulations such as cross-fostering can often have substantial effects on biology in their own right, which complicates the interpretation of such studies.

Interaction of effects with the postnatal environment

A common thread through ecology, laboratory and human epidemiological studies is the idea that variation in the prenatal environment may to some extent provide valuable information for the developing foetus. However, very few studies using prenatal manipulations in farmed species include postnatal environmental treatments. Those involving variable postnatal conditions have mostly been nutritional studies. However, the demonstration of negative prenatal stress effects in a variety of farmed species immediately raises the question of whether a good quality postnatal environment can rescue a negatively affected phenotype, or indeed whether some prenatal effects may make animals better suited to negative environments. Recent work (Emack & Matthews 2011) found that post-weaning environmental enrichment did not ameliorate the impact of prenatal stress in guinea pigs.

True transgenerational effects and epigenetic changes

In general, the studies that have been conducted so far in farmed species have demonstrated carry-over effects of the foetal environment rather than true transgenerational effects. The transfer of a maternal challenge to her developing offspring during gestation cannot be considered a true transgenerational effect because the mother can simply be viewed as the 'environment' of the foetal organism.

The question that has been very interestingly explored in other species, including humans, is circumstances where individuals in subsequent generations are also affected. A human health study in Sweden (Pembrey *et al* 2006) has shown that nutritional effects can have substantial impacts on health over more than one generation. While transgenerational effects largely remain to be explored in farm animals, impacts of feeding during pregnancy have been found on grand-offspring in sheep (eg Blair *et al* 2010).

In laboratory-based studies, transgenerational effects are often associated with true epigenetic alterations, for instance through histone modification or alterations to DNA methylation, which affect patterns of gene activation (see Bonduriansky & Day 2009). Offspring from mothers affected by the Dutch hunger winter have been shown to have such changes (Tobi *et al* 2009).

However, beyond a basic interest in biological function, the demonstration of true transgenerational effects in farmed species would be important for determining the practical welfare relevance of such effects. If particular maternal experiences propagate through several subsequent generations this could magnify greatly the possible numbers of individuals affected.

Discussion

The importance of the prenatal period in defining how individuals respond to their environment throughout life is clear. Early experiences act to alter set-points, feedback efficiency, and thresholds for change. A number of experimental studies in farm animals have clearly shown that early life experiences can have a substantial impact on outcomes of great relevance to later health, welfare and productivity. In particular, stress or under-nutrition experienced by the mother during pregnancy has wide-ranging and important effects on how her offspring cope with their social, physical and infectious environment. A fuller understanding of how management during gestation relates to the welfare and productivity of their offspring will benefit both animal welfare and farm efficiency. In many cases there may be practical implications for management and husbandry practices, either to avoid detrimental long-term effects or to actually improve the ability of animals to achieve a good standard of welfare in a range of environments.

The impact of the prenatal environment on later biology could occur as a consequence of damage to normal function, ie if a severe challenge causes a permanent dysfunction in a particular body system. An alternative possibility is that some changes in functioning occur due to an evolved mechanism that allows the individual to closely match their phenotype to prevailing environmental conditions. From this viewpoint the dam can be seen as a complex sensory organ that the developing progeny use to gather information about their (likely) future environment. Although imperfect, any information the developing individual can gain about the external environment is highly valuable in allowing trait plasticity. During prenatal life, although the information an individual has at its disposal is limited, the utility of any such early information is high (Dufty *et al* 2002). However, in the unnatural captive situation the information gained in this way may be inevitably incorrect or the normally adaptive strategies adopted as a consequence may be detrimental (eg increased fearfulness or stress reactivity). There is also some evidence that highly selected domesticated breeds may be more susceptible to early life effects (Lindqvist *et al* 2007; Rooke *et al* 2010) perhaps because normal constraints on making phenotypic errors have been removed or because intense artificial selection has decreased the ability of individuals to adapt to challenges.

Since early experiences play an important role in determining how capable or otherwise animals are at coping with their social and physical environment the obvious corollary of the negative outcomes identified in many studies is that optimal prenatal management could play an important role in supporting positive welfare in any given production system. Lay (2000) raises the possibility that animals could be deliberately 'programmed' for a specific livestock system. Although fitting the system to the animal may be better in the long run, fitting the animal to the system may be a pragmatic necessity. D'Eath *et al* (2010) have recently reviewed the ethical implications of genetically selecting animals for particular behavioural patterns that suit them to unnatural farm production environments. Similar issues could arise from the idea of manipulating animal phenotype through prenatal effects, particularly if the benefit to the offspring occurs at the expense of the mother (eg mid-pregnancy shearing of sheep increases lamb birth weight, but may place ewes at risk of cold stress: Corner *et al* 2006). However, in many cases, there may be win-win scenarios for mothers and their progeny, or neutral changes for mothers may produce progeny benefits. For instance, Oostindjer *et al* (2010) have shown benefits of adding a flavouring to the diet of pregnant sows not only on their offspring's willingness to feed post weaning but on other aspects of their behaviour (decreased oral manipulation and aggression post weaning). Studies in sheep in Australia have also found that allowing pregnant ewes to graze on saltbrush improved their offspring's ability to graze on this pasture (Chadwick *et al* 2009).

In light of the experimental work detailed above, it is clear that prenatal effects could explain variations in welfare-relevant postnatal outcomes. However, the relationship between cause and effect may be hidden from view not only because they are separated in time, but also because they can be separated spatially. For instance, between different buildings, or often between different farms, or indeed, in some cases, such as the common international trade in fish eggs or weaner pigs, between different countries. The next stage of necessary research will identify where the findings from experimental research have direct relevance in real life. From a production perspective, Blair and others (2010) have also pointed out the fact that the experimental studies

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in this area have so far failed to yield a clear consensus that could be translated into useful advice for farmers or priorities for further research.

It is worthwhile saying that, of course, at the extremes such effects clearly do matter. For example, White *et al* (2010) identified a link between periods of drought during gestation for cattle in Australia and the occurrence of a severe physical problem, congenital chrondrodystrophy. But, more generally, it is necessary to question the importance of prenatal effects, and in what instances changes could be made to mitigate any negative effects. Experimental efforts to identify where early life effects impact on welfare in farmed species are important. However, of greater importance, is using that knowledge to improve animal welfare, and where possible farm production efficiency. Ultimately, our aim should be to move the 'goal posts' for welfare standards to include care of pregnant mothers for their offspring's development and welfare, as well as their own.

Animal welfare implications

The existence of early experience effects on many traits that are important for welfare may make attributing environmental causality to welfare problems harder. For instance, we might end up saying that individuals in housing system 'X' appear to have increased stress reactivity or altered immune function or a particular behaviour profile, and a large part of this could be accounted for by the experiences the animal had before it was even born. On-farm surveys of animal welfare often find substantial variation within particular farm production systems. Whilst epidemiological analyses of such data often allow many causal explanatory factors to be uncovered, these studies rarely investigate the role of the prenatal environment (as assessed by the housing and husbandry standards that apply to the dam) in determining welfare outcomes. The possible importance of welfare standards for gestating animals, not merely for their own welfare, but for the welfare of the developing next generation is widely unappreciated within most farming systems and indeed the extent to which these effects may explain variations in outcomes in intensive rearing situations remains unknown. This is largely because, to date, most considerations of the effects of prenatal stress or under-nutrition have been carried out in controlled settings very often with experimental challenges that may not relate to actual commercial practices. Controlled studies are necessary but not sufficient in moving towards a better understanding of the welfare significance of prenatal conditions. Although controlled experiments are extremely valuable in highlighting the possible range of effects and elucidating mechanisms, they do not aid recognition of their effects on-farm or allow evidence-based recommendations on how animals should be treated during gestation for the benefit of their offspring. In many farming systems breeding animals often receive less consideration than the production animals they produce. Whilst some studies do address realistic commercial practices, information is lacking on the extent to which such practices occur in most commercial systems. Further efforts are therefore required to properly establish the true importance of prenatal effects under real life conditions. However, there remains a strong likelihood that animal welfare could be improved in many farming systems by paying closer attention to how breeding animals are housed and managed.

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