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Hertfordshire AL4 8AN, UK
www.ufaw.org.uk

Animal Welfare 2014, 23: 369-379
ISSN 0962-7286
doi: 10.7120/09627286.23.4.369

How should the welfare of fetal and neurologically immature postnatal animals be protected?

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Abstract

Legal protection of the welfare of prenatal animals has not previously been addressed as a discrete subject within the academic literature on animal welfare, ethics and law. This paper aims to rectify this by reviewing the protections (or absence of protections) provided for fetuses by existing legislation in various jurisdictions, and considering the extent to which legal protection of animal fetuses can be justified on animal welfare grounds. Questions related to the need to protect the welfare of neurologically immature postnatal animals are also considered. We argue that there are reasons to protect animal fetuses, both in order to protect fetuses themselves against possible suffering, and in order to protect the animals which fetuses will become against negative welfare impacts that originate prenatally. We review the science on whether fetuses can suffer, and argue that extant regulations do not fully reflect current scientific understanding. Following the precautionary principle, we further argue that regulators should consider the possibility that fetuses and neurologically immature postnatal animals may suffer due to sub-cortically based 'raw basic affects' (ie relatively undifferentiated experiences of discomfort suggested to be generated by neural processing at levels below the cerebral cortex). Furthermore, we show that there are reasons for affording fetuses protection in order to safeguard the long-term welfare of future animals. However, it may be possible to provide such protection via rules or laws relating to the use of certain techniques and the management of pregnant animals, rather than via direct legal protection of fetuses themselves. In order to provide such protection effectively we need to know more about the relationship between maternal nutrition, stress, exercise, management and fetal health, and about the impact of the timing of a fetal insult on long-term postnatal welfare.

Keywords: *animal welfare, fetal protection, fetal suffering, neurological immaturity, postnatal harms, regulations*

Introduction

Death of antenatal animals may occur across a wide range of animal uses. For example, animal models are used to test the embryotoxic and fetotoxic effects of new human medicines (see reviews by Brent [2004] and the Nuffield Council of Bioethics [2005]); livestock fetuses are co-incidentally killed when their pregnant dams are slaughtered (Mellor & Gregory 2003; Peisker *et al* 2010) and, at that time, some provide biological materials such as fetal calf serum (Jochems *et al* 2002; Mellor & Gregory 2003); and ovariohysterectomy of feral and companion cats which happen to be pregnant results in death of their fetuses (Scott *et al* 2002; Bosch *et al* 2012). Even in sporting situations or during transport, where pregnant animals are physiologically stressed, their fetuses may die or be aborted (National Animal Welfare Advisory Committee 2011).

Humans are inclined to feel protective towards prenatal and neonatal animals (Morreall 1991; Morris *et al* 1995; Mellor *et al* 2010a; Mellor 2013). For example, the idea of livestock fetuses dying *in utero* when their pregnant dams are slaughtered is a matter of concern to many (EFSA 2005a; Peisker *et al* 2010). In Denmark, in 2004, the strength of public feeling about this issue led to a law change that banned the slaughter of pregnant production animals and horses during the last tenth of their pregnancy (LOV nr 269 af 21/04/2004; https://www.retsinformation.dk/Forms/R0710.aspx?id=1807). However, many countries provide no legal protection for prenatal animals, and those that do, usually limit the protection to fetuses after a certain stage of development.

Apart from limited consideration in one paper (Mellor *et al* 2010a), no detailed analysis of the protection afforded prenatal animals appears to exist in the academic literature on animal welfare, ethics and law. For example, a recent report on UK law relating to animal welfare made no mention of prenatal animals (FAWC 2012). This paper aims to rectify this deficit by evaluating the foundations of such legal protection in terms of its justification on scientifically supported animal welfare grounds. We aim to investigate whether our current scientific understanding should lead us to believe that the welfare of fetal, newborn and young animals needs protecting, and if so whether current law adequately provides such protection. Thus, the focus of this paper is on the interplay between the scientific evidence base regarding animal welfare on the one hand, and legislation and public perception on the other. We do not consider other, moral reasons which might also underwrite protection of animal fetuses.

Current laws designed to protect animal fetuses usually identify inclusion criteria based on the earliest developmental age at which forms of consciousness and a related capacity to suffer might first appear, as understood at the time the laws were enacted. In a number of cases, however, our scientific understanding of this issue has subsequently advanced significantly. We argue that the bases for deciding what type of protection prenatal animals should be afforded in welfare laws should be re-evaluated. Following the precautionary principle, we argue further that consideration should be given by regulators to the possibility that fetuses may suffer due to sub-cortically based negative 'raw basic affects', ie relatively undifferentiated experiences of discomfort suggested to be generated by neural processing at levels below the cerebral cortex. Finally, we argue that, irrespective of what the science ultimately comes to determine regarding the capacity of fetuses to suffer, the need (or otherwise) to provide protection for postnatal animals based on negative animal welfare impacts that originate prenatally should also be considered.

Embryos, like fetuses, are potential sentient animals and on those grounds perhaps should also be protected. However, we shall restrict ourselves to considering fetuses, ie prenatal animals in which organogenesis is complete. We concern ourselves here primarily with legal protections based on the concern for animal welfare, though we shall also briefly discuss protections which are provided to fetuses as the result of a primary intent to prevent the spread of disease. Though we recognise that owned animals at least are a form of 'living property' (Favre 2010) and that there are allied legal questions relating to the protection of property rights in prenatal animals (for example frozen embryos), we shall not address legal protection of those property rights.

Key features of current legal protections for prenatal animals

A review of the various national and international laws designed to provide protection for animals in agricultural, companion, clinical and research settings reveals three main approaches to protection of their prenatal forms. Legislation:

- Is ambiguous, in that no mention is made of prenatal animals and it is therefore unclear whether the legislation is meant to apply to them or not; or
- Specifically excludes prenatal animals from legal protection; or
- Affords legal protection to prenatal animals after a specified stage of development.

Examples of such legislation in which the intent to provide protection is ambiguous include the USA's Animal Welfare Act (1966), the UK's Veterinary Surgeon's Act (1966) and the legislation governing protection of animals in the Canadian provinces of Alberta and Prince Edward Island (Animal Health and Protection Act RSPEI 1988). In older legislation, at least, such ambiguity quite possibly simply reflects a lack of consideration given to prenatal animal forms at a time when the scientific consensus was that all fetuses (animal or human) were not sentient, and consideration of animal welfare in general was much less well developed than it now is.

The British Animal Welfare Act (2006) s(1)(3-4) is an example of fetuses or embryos being explicitly excluded from protection. The Japanese Law for the Humane Treatment and Management of Animals (1973, revised in 2000 and 2005) is interpreted as deliberately excluding prenatal forms from protection (H Omoe, personal communication 2013). Such deliberate exclusion seems to be based in the belief that the welfare of prenatal forms does not need protecting, because such forms are incapable of suffering. Section 1 (3-4) of the British Animal Welfare Act (2006), for example, grants national authorities the power to amend the legislation to include prenatal animals should they become convinced "on the basis of scientific evidence, that animals of the kind concerned are capable of experiencing pain or suffering". The clear implication is that those who drafted the legislation were not convinced that such suffering was possible.

However, there are examples of legal protection for prenatal animals after a specified stage of development being provided on a supranational basis (European Directive 2010/63/EU on the Protection of Animals used for Scientific Purposes), a national basis (New Zealand's Animal Welfare Act 1999 [s2:1 (b-d)]) or a devolved basis (The Australian State of Queensland's Animal Care and Protection Act 2001 [s1]). The primary focus of some of these provisions, however, is not a desire to protect the prenatal animals themselves, but rather concern that those animal forms represent a biosecurity risk. This is clear in the Canadian Health of Animals Act 1990, characterised as "An Act respecting diseases and toxic substances that may affect animals or that may be transmitted by animals to persons, and respecting the protection of animals", in which "an embryo and a fertilized egg or ovum" are included in its definition of an animal (s2[1]) because of their potential to transmit disease. Chapter 4 of the World Organisation for Animal Health (OIE) Terrestrial Animal Health Code 2013 (Article 4.7.1) is similarly concerned with animal embryos only in so far as they pose a health risk. Thus, there is no underlying concern expressed for the welfare of the embryo itself. However, the welfare of fetuses during slaughter of their pregnant dams is addressed in Chapter 7 of the same OIE code (Article 7.5.5).

https://doi.org/10.7120/09627286.23.4.369 Published online by Cambridge University Press

Nevertheless, the most common reason for inclusion of prenatal animals after a specified stage of development in animal welfare or protection legislation is the underlying belief that animals in the later stages of prenatal development may be capable of suffering, and therefore require protection. Such motivation is clearly expressed in a 2005 scientific report of the European Food Safety Authority (EFSA 2005b) when the purpose behind the commissioning of the report is described as follows (s1:2:2):

> The definition of 'animal' in the current Directive excludes fetal or embryonic forms.… the Commission asks the European Food Safety Authority to issue a scientific opinion on… the stage of gestation after which the fetus/embryo of the species in question is assumed to be capable of 'experiencing pain, suffering, distress or lasting harm' (EFSA 2005b).

EFSA concluded that the stage of development at which there is a risk of poor welfare when a procedure is carried out on antenatal animals is the beginning of the last third of development for mammals; when a fish, amphibian, cephalopod, or decapod becomes capable of independent feeding, and during the last days before hatching in precocial oviparous species.

The conclusions reached by EFSA underwrote the protections provided for prenatal animals in the European Directive for the Protection of Animals used for Scientific Purposes (2010/63/EU). It is thus clear that the intention of those drafting this European legislation was to protect prenatal animals against suffering, the underlying idea being that if such forms are capable of suffering then legal protection against such suffering is called for. The scientific evidence base for suffering in prenatal animals used to draft such legislation is discussed below.

Similarly, the protections provided in the New Zealand 1999 Animal Welfare Act for any mammalian fetus, or any avian or reptilian pre-hatched young that is in the last half of its period of gestation or development, resulted from a general concern about the treatment of prenatal animals. The Animal Welfare Bill as it was originally proposed applied only to postnatal animals. However, the Bill was amended to include the protections for prenatal forms outlined above in response to submissions that animals before birth may be sensitive to noxious stimuli and that manipulation of these animals, including research manipulations, should be covered by the Act. Such submissions were made in the context of unease at the time in New Zealand about research/teaching on pre-hatched eggs and unborn fetuses, maceration/destruction of unhatched chicken eggs, and blood harvesting from fetuses during slaughter of pregnant dairy cattle (KE Littin, personal communication 2013).

A science-based review on whether or not fetuses may suffer

We have shown above that when legal protections are provided for prenatal animals they are most commonly motivated by a concern that such animals may be able to suffer when exposed to noxious stimuli. In order to assess whether such concern is in fact justified on animal welfare grounds, we need to answer two questions: (i) what do we mean by 'suffering'; and (ii) do fetuses have the capacity to suffer?

What do we mean by suffering?

Suffering is a generic term usually applied to strongly negative affects experienced by conscious, sentient animals in response to noxious sensory inputs (Mellor *et al* 2009; Mellor 2012). Traditionally, suffering has been equated with pain, but increasingly it has been recognised that suffering may cover a wide range of experiential states (Mellor 2012; Sandøe & Jensen 2013).

Thus, suffering is not a single entity. Its character depends among other things on the sensory modality being stimulated, and it retains that character throughout the range of negative intensities that are equated with different levels of suffering (Mellor *et al* 2009). For example, even though intense thirst at its upper extreme may often be described in terms of suffering, it continues to be experienced as thirst.

Do fetuses have the capacity to suffer?

Much of the scientific debate about whether or not fetuses have the capacity to suffer has centred around the questions of (i) whether suffering is a cortical phenomenon which is critically dependent on neural processing by the cerebral cortex (Mellor *et al* 2005, 2010a,b; Mellor & Diesch 2006, 2007; Mellor 2010), or may be sub-cortically based (Merker 2007) and (ii) whether, once pathways between the sub-cortical nervous system and the cerebral cortex are fully established, consciousness is necessary in order for suffering to occur.

Three phases of neurological development may be identified: first, the development of connectivity of sensory nerves to the spinal cord and the early development of lower brain centres; second, the connection of peripheral nerves to interacting lower brain centres; third, integrated neural processing of sensory inputs involving interactivity between the thalamus and the cerebral cortex via thalamo-cortical connections. In a key series of articles, Mellor and colleagues developed a scientific argument that fetal suffering can occur only when the development of thalamo-cortical connections between the cerebral cortex and sub-cortical regions of the brain which determine the onset of consciousness becomes advanced (Mellor *et al* 2005; Mellor & Diesch 2006, 2007), and even then only if the fetus (or neonate) is conscious (Mellor *et al* 2005; Mellor & Diesch 2006, 2007; Mellor 2010). Cortically based consciousness is considered to be a prerequisite for the ability to suffer, consistent with the view taken by the Royal College of Obstetricians and Gynaecologists (RCOG) (2010) in relation to the ability of human fetuses to feel pain. However, the *capacity* for consciousness does not necessarily imply that fetuses are conscious, and unless they *are* conscious (it is argued) they will not suffer.

The questions relevant to whether fetuses ought to be protected on animal welfare grounds then become:

- At what stage of fetal development are the thalamo-cortical connections between the sub-cortical nervous system and the cerebral cortex functional, ie when do animal fetuses develop the *capacity* for consciousness (and thus the *capacity* to suffer); and
- Do animal fetuses *actually* become conscious, and if so, when?

doi: 10.7120/09627286.23.4.369

Potential for fetal cortically based consciousness

In humans, sub-cortical-cortical neural connections are established after about 24 weeks of the 40-week gestation (Royal College of Obstetricians and Gynaecologists 2010). For animals, Mellor *et al* (2009, 2010b) distinguished three classes of young in terms of their neurological maturity at birth: exceptionally immature, moderately immature, and mature (examples of which are marsupial joeys, rat pups and lambs, respectively). Mellor and colleagues emphasised that the establishment of neural connections between the cerebral cortex and sub-cortical regions of the brain was an important determinant of the onset of consciousness in all three classes of young. This occurs several months or days to weeks *after* birth in the two neurologically immature groups, and some weeks *before* birth in the mature group (Mellor *et al* 2009, 2010b). Thus, on this basis, fetuses of the two neurologically immature groups do not have the capacity for consciousness (and thus for suffering) before birth, whereas members of the neurologically mature group do.

Do fetuses actually become conscious, and if so, when?

Such a conclusion about the variation in prenatal capacity for consciousness and suffering might lead us to conclude that legislation should reflect such differences in neurological maturity between animal fetuses. However, further evidence suggests that this may not be so, because even those young in which neurological maturity is sufficient to support forms of consciousness that depend on cerebral cortical processing before birth (Mellor *et al* 2005; Mellor & Diesch 2006, 2007) remain unconscious until after birth (Mellor *et al* 2005; Mellor & Diesch 2006, 2007; Mellor 2010).

Evidence used by Mellor and colleagues to support the argument that animal fetuses which will become neurologically mature by the time of birth will nevertheless remain unconscious until then included the continuous presence, until after birth, of EEG traces that are inconsistent with cortically based consciousness (Mellor *et al* 2005), and the observation that such fetuses cannot be aroused from their sleep-like states of unconsciousness by noxious stimuli that awaken sleeping newborns of the same species (Mellor *et al* 2005). Moreover, in this neurologically mature class, fetal unconsciousness was attributed to the prenatal operation of a suite of at least eight *in utero* neuroinhibitors which act on the fetal cerebral cortex until immediately after birth (Mellor *et al* 2005; Mellor & Diesch 2006, 2007; Mellor 2010). One of these factors (adenosine) has a graded capacity ranging from mild inhibition to complete shutdown of cerebrocortical function, and two others (allopregnanolone and pregnanolone) are well-established anaesthetic/analgesic steroids that are synthesised by and act on the fetal brain (Mellor *et al* 2005; Mellor & Diesch 2006). In the two immature classes of neurological development defined above, fetal unconsciousness was attributed to cerebral immaturity assessed both anatomically and bioelectrically (EEG) soon after birth (Mellor *et al* 2010a,b).

Based on EEG results, similar mechanisms involving *in ovo* neuroinhibitory mechanisms are thought to exist in the pre-hatched domestic chick, which is neurologically mature at hatching (Mellor & Diesch 2007). However, hen-chick vocal interactions just before hatching suggested that further evaluations were required to clarify the situation late in incubation (Mellor & Diesch 2007).

Mechanisms moderating fetal oxygen consumption are also relevant to the question of fetal consciousness and the need to protect fetuses on animal welfare grounds. Mellor (2010) reported that there is an 'emergency mechanism', demonstrated in neurologically mature fetuses, which protects them against irreversible cortical damage during transient hypoxic/anoxic episodes. Within 60–90 s of onset, this mechanism virtually abolishes cortical oxygen consumption (Hunter *et al* 2003a) by shutting down electrocortical activity, ie the EEG becomes isoelectric (Mallard *et al* 1992; Bennett *et al* 1999; Hunter *et al* 2003b). Provided that oxygen supply is reinstated within 5–6 min, the EEG and cortical oxygen consumption usually return to normal. The existence of such a mechanism may also be relevant to concerns about the welfare of mature fetuses after the permanent cessation of placental oxygen supply following maternal death or slaughter (Mellor & Gregory 2003; Mellor 2010). An isoelectric EEG in the mature, intact brain is widely considered to be incompatible with consciousness (Bager *et al* 1992; Baars 2001; Boveroux *et al* 2008; Johnson *et al* 2012). The rapid appearance of such an EEG in fetuses left *in utero* (Mellor 2010) after their dam dies raises the possibility that the mechanism which reduces fetal cortical oxygen demands in the face of low oxygen supply might also minimise or prevent noxious experiences in fetuses whose dams have died, *providing* that the fetus is left *in utero* or is otherwise prevented from successfully breathing air (Mellor 2010).

The implication of the body of work by Mellor and colleagues is that animal fetuses do not seem to suffer prior to birth, either because their neurological development is insufficiently mature to enable them to do so, or because, although thalamo-cortical connections are well established, they remain unconscious until after birth due to neuroinhibition. If this is correct, then there would seem to be no welfare-based need to provide legal protection for animal fetuses for their own sake.

However, the argument that animal fetuses do not suffer prior to birth and that there is therefore no need to protect them for their own sake depends upon consciousness and the associated ability of animal fetuses to suffer being cortical phenomena. In the next section, we shall discuss whether consciousness as it applies to animal fetuses, neonates and young animals *does* have essential cortical elements, or whether consciousness might sometimes be sub-cortically based (Merker 2007).

Potential for sub-cortically based consciousness

It has been proposed that in spite of a lack of the functional capacities of the mammalian cerebral cortex in some vertebrate species, neurophysiological manifestations of conscious awareness can nonetheless occur via a system in the upper brainstem (Merker 2007). This system, which extends from the roof of the midbrain to the basal dien-

https://doi.org/10.7120/09627286.23.4.369 Published online by Cambridge University Press

cephalon, is a product of evolution and performs key roles in controlling actions and in instituting conscious perception (Merker 2007). Thus, it is said to integrate and govern the output of the cerebral hemispheres, including those cortical regions implicated in attentional and conscious functions. Furthermore, this system is hypothesised to function in the absence of cortical input, and hence may itself generate a subsidiary form of awareness. If so, this would explain the orienting, exploring, consuming and defensive 'purposive' behaviours exhibited by some hydranencephalic human infants and some mammals after experimental decortication (Merker 2007; Panksepp 2007).

Thus, Merker argued that the neural mechanisms underlying conscious function might not require connectivity as evidenced by thalamo-cortical interactivity — in other words, consciousness might not require cortical processing to become manifest. If consciousness (and therefore the ability to suffer) does not require cortical processing, then it would follow that we should not be basing our provision of protection for animal fetuses solely on evidence of cortically based consciousness.

Various objections to the notion of sub-cortically based consciousness may be mounted. First, Merker's (2007) hypothesis implies that neurological development and sequencing of connectivity between different brain regions exhibits uniformity across species as each phylogenetic stage is reached during development, but such uniformity of phylogenetic staging during ontogeny is not borne out by observation (Kluge & Strauss 1985; Smith 1997; Karlan & Krubitzer 2007; Kalinka & Tomanceck 2012). Second, the evidence provided by hydranencephalic infants or decorticated animals may be criticised on the grounds that residual functional cortical tissue may be present (Freeman 2007). Moreover, remnant tissues in congenitally malformed or lesioned brain areas exhibit a remarkable capacity for neuroplastic enhancement of their operational efficacy and roles beyond those present in the normally formed or non-lesioned brain (Shewmon *et al* 1999; Rorden & Karnath 2004; Doidge 2008) — so what occurs in abnormal brains may not reflect what occurs in normal brains.

Even if sub-cortically based consciousness can occur in certain circumstances (eg following decortication), it is questionable whether it is likely to occur in the brains of healthy and intact animals, because where thalamo-cortical connectivity is fully functional cortically based consciousness may anyway always supersede any such sub-cortically based consciousness. It may thus be argued that, once thalamo-cortical connectivity is well established in fetuses, the question of whether or not they manifest forms of consciousness from that stage of pregnancy onwards is most appropriately addressed by focusing on evidence of their cortical function (because that would always supersede sub-cortical function). As outlined above, in neurologically mature animal fetuses, the capacity for such cortically based consciousness exists before birth (although consciousness in such fetuses is neurologically inhibited until after birth), whilst in young that are, respectively, neurologically exceptionally or moderately immature at birth, thalamo-cortical connectivity is not established until months or days to weeks after birth. This leaves open the question of whether or not some forms of sub-cortical consciousness exist in animal fetuses, neonates and young before the stage at which thalamo-cortical connectivity becomes established — whether that be prior to or after birth. If so, such sub-cortical consciousness may be worthy of our consideration.

Potential for suffering in neurologically immature fetuses and postnatal young

Once animals exhibit effective sub-cortical-cortical interactivity after birth, whether this manifests after minutes to hours, days to weeks or months, they are capable of experiencing a wide range of negative effects (Mellor & Stafford 2004; Mellor *et al* 2009). These effects may include breathlessness, thirst, pain, hunger, nausea, dizziness, debility, weakness and sickness (which are associated with sensory inputs generated internally), and anxiety, fear, frustration, helplessness, loneliness and boredom (associated mainly with the animal's cortically based cognitive assessment of its external circumstances) (Mellor 2010, 2012). Such young would thereafter have the capacity to suffer, with the level of suffering being describable in terms of the character, intensity and duration of the negative affect(s) in question (Mellor *et al* 2009).

Merker's (2007) hypothesis, together with Panksepp's (2007) commentary on it, suggest that prior to this stage the young might manifest states of sub-cortical consciousness that confer a limited capacity to have relatively undifferentiated negative experiences of discomfort ('raw basic affects'). During this stage, an absence of cortically based cognitive influences makes it likely that such raw affects would be generated almost entirely by sensory inputs associated with specific attributes of the young's internal functional state. Although such proposed experiences would be unpleasant, it is not known whether or not their character, intensity and duration would be sufficient to constitute suffering. Thus, the possibility that suffering may occur during this stage of neurological development can, at this point in time, neither be ruled in, nor ruled out.

Prenatal factors that may adversely affect the postnatal welfare of offspring

We wish now to address the question of whether there are reasons unrelated to suffering before birth which might require us to protect animal fetuses. Even if it was demonstrated that fetuses could not suffer as a result of any invasive procedure or other harm that might be imposed on them, would there nevertheless be good reasons to afford them protections because of likely untoward impacts on the welfare of the same individual after birth?

Our answer to this question is that even in the face of documented evidence that prenatal animals cannot suffer, there are compelling welfare reasons to afford legal protection to those prenatal forms because of their potential to become postnatal, sentient animals. These reasons relate not to the (possible) moral worth of the postnatal animal (which is outside the scope of this paper), but to the fact that insults which occur to prenatal animals may have detrimental effects on their postnatal welfare, and thus provide justification for protecting animal fetuses in welfare law.

Such insults to the fetus may occur directly (for example, via biopsy sampling or surgical procedures applied to the fetus), or indirectly (for example, if the pregnant dam is undernourished). In human medicine, it is established that the fetus withdraws from and launches a stress response to needle puncture from 18 weeks of gestation onwards (Gitau *et al* 2004). Invasive procedures result in increased cerebral bloodflow and increased levels of circulating catecholamines and cortisol (hormones indicative of stress). Similar changes occur in response to non-painful noxious stimuli such as hypoxia. This suggests that even if the fetus is not consciously experiencing an insult (either because thalamo-cortical connections are not fully developed or because the fetus is not 'awake'), it is reacting at some level to the insult.

Furthermore, studies on neonatal and prematurely born humans and animals suggest that physiological reactions to potentially damaging stimuli, *even if not consciously perceived at the time*, "may cause permanent changes in the nervous system" which persist "...for the rest of (the person's) life" (Rawlinson 1996). Thus, peripheral nerve injuries to neonatal rats which evoke no behavioural changes at the time of injury cause delayed hypersensitivity to pain (Beggs *et al* 2012; Vega-Avelaira *et al* 2012) and altered sensory and nociceptive processing and motivational behaviour later in life (Low & Fitzgerald 2012). Children born at less than 26 weeks of gestation who were exposed to potentially painful and stressful medical procedures in the post-partum period had reduced sensitivity to thermal insult which may have impacted upon pain responses in later life compared to controls (Walker *et al* 2009). In sheep, castration within 12 h of birth without analgesia may cause sustained hypersensitivity to pain (McCracken *et al* 2010).

Though such studies were carried out on neonates rather than fetuses, their message across a variety of species is that invasive procedures stimulate nociceptors and cause a surge of information along nerve tracts which, *even if pain is not perceived at a cortical level* can cause short-term physiological changes to parameters such as bloodflow and hormone release, and may affect physiological responses to pain in long-term, postnatal life. However, concluding on this basis that invasive fetal procedures would have similar effects postnatally does not allow for the potential impact of the markedly different levels of endogenous anaesthesia/analgesia that are known to operate before and after birth, especially in young that are neurologically mature at birth (Mellor *et al* 2005). Therefore, studies of the postnatal pain-related consequences of invasive fetal procedures are required. As yet, none have been found.

More is known about the impact of indirect prenatal insults to the fetus which arise from maternal factors. In human medicine, it is established that maternal mal- or under-nutrition during pregnancy or placental insufficiency can cause fetal genetic 'reprogramming' which increases the offspring's chance of suffering from coronary heart disease, diabetes, hypertension and stroke in later life (Rawlinson 1996; Belkacemi *et al* 2010; Barker & Thornburg 2013). Studies of animals subject to under-nutrition *in utero* also show that long-term changes occur in the structure of key organs such as the kidney and pancreas (Langley-Evans & McMullen 2010). Some nutritionally restricted fetuses and newborns that nevertheless survive birth and early postnatal life display easy-to-recognise compromise to cardiovascular, metabolic, pancreatic, renal or other functions much later in life (McMillan & Robinson 2005). Furthermore, if a female animal is undernourished during pregnancy the ability of that animal's offspring to nourish its own fetuses during pregnancy may be impaired (Rawlinson 1996). Finally, maternal illness and weight loss during pregnancy is likely to have an adverse effect on the long-term health of the equine fetus (Ousey *et al* 2008). Conversely, over-feeding of mares during pregnancy has been shown to cause developmental orthopaedic disease in some of their offspring (Vander Heyden *et al* 2012).

The maternal disorder need not be purely physical in origin to cause long-term harm to the health of offspring: studies in both animals and humans have shown that maternal anxiety is correlated with fetal neurological development and postnatal behaviour (Sarkar *et al* 2008). Stress-induced increases in human maternal and fetal plasma cortisol and corticotrophin hormone levels during pregnancy are related to postnatal behavioural disorders including attention and learning deficits, generalised anxiety and depression, which can be induced by prenatal stress in rodents and non-human primates (Weinstock 2008). In farm animal species, maternal stress during pregnancy affects the ability of offspring to cope with their social, physical and infectious environment (Rutherford *et al* 2012).

There thus seems to be a real risk that what happens to a prenatal animal can have a negative impact on that animal's postnatal health and welfare which, if we are concerned about animals having "lives worth living" (FAWC 2009), might require us to provide protection for animal fetuses during the prenatal period.

Animal welfare implications

Protecting the welfare of fetuses

Protection of prenatal animal forms for their own sake makes sense only if one accepts that there is at least a scientific possibility that they can suffer. The review of the scientific evidence base above suggests that suffering dependent upon cortically based consciousness is unlikely to occur unless thalamo-cortical connections are well established *and* neuroinhibition of cortical consciousness is abolished. However, there is a so-far unproven possibility that suffering may occur as the result of sub-cortically based consciousness and experience of negative raw affects, before the developmental stage at which the capacity for cortically based consciousness is established. When this could occur (if it does) varies from some time before birth to days/months after birth, depending on how neurologically mature the animal is at the time of birth.

https://doi.org/10.7120/09627286.23.4.369 Published online by Cambridge University Press

Consideration should be given, therefore, to whether or not regulations designed specifically to protect the fetus itself against adverse welfare outcomes of investigatory manipulations or natural occurrences should be modified to take account of the possibility of sub-cortical consciousness and potential suffering arising from the experience of negative raw basic affects. Prenatal welfare protection of fetuses for their own sake would not appear to be necessary for young that are neurologically exceptionally immature at birth, because we would not expect either cortical or sub-cortical mechanisms of consciousness to be functional in such animals until some time after birth. No regulatory change from an exclusive postnatal focus of protection would appear to be required for young that are neurologically exceptionally immature at birth, as is the case for example with the provision for marsupial joeys in the New Zealand Animal Welfare Act (1999).

Protection might be considered if sub-cortical consciousness were shown to occur and to begin before birth in young born moderately immature neurologically (which seems likely in some species). Current regulatory protections from half-way through pregnancy of such mammalian young are likely to appropriately accommodate the stage at which the hypothesised sub-cortically based conscious experience of raw basic affects might first become manifest. Untoward impacts on the welfare of postnatal young that are born both neurologically exceptionally or moderately immature, such that all or part of the period of sub-cortical consciousness, if it exists, would occur after birth, could be addressed effectively by affording those young the same welfare protections from birth as are afforded neurologically mature young from birth.

For neurologically mature young, we know that the capacity for cortically based consciousness exists for some time before birth (though they remain unconscious). The possible capacity for sub-cortical consciousness developmentally precedes the capacity for cortical consciousness. It follows that, if we are concerned about the possibility of suffering due to sub-cortically based consciousness and experience of negative raw affects, limiting protections to the last half of pregnancy would not be sufficient protection for fetuses that are neurologically mature at birth. Indeed, arguably, if we accept that the expression of cortically based consciousness is over-ridden by neuroinhibition in neurologically mature fetuses until birth so that they could not suffer and therefore do not need to be protected during that later stage of pregnancy, there may nevertheless be a need to provide protection during the earlier period in which sub-cortical consciousness and the potential to suffer due to negative raw affects may occur. However, definitive information on the stage of pregnancy at which the possible sub-cortical consciousness and experience of negative raw basic affects might begin in such fetuses appears to be lacking.

Notwithstanding how scientific questions about sub-cortical consciousness and whether negative raw basic affects constitute suffering are ultimately resolved, decisions about regulatory protection of fetuses might be complicated by the possibility that some fetal experience of raw basic affects may ultimately be beneficial in welfare terms. *In utero* experience of such negative affects may be an obligatory early part of the development of mechanisms that involve affectively motivated behaviours which are essential for survival after birth. Examples of such behaviours include postnatal breathlessness-motivated gasping to correct otherwise lethal compromise to oxygen supply and thirst-motivated, water-seeking and drinking behaviours to correct potentially fatal dehydration (Denton *et al* 2009). If this were shown to be the case, the best that regulation might be expected to achieve in this context would be to minimise negative extremes of raw basic affects, not to eliminate them from their integral developmental role during the period of sub-cortically based consciousness.

Protecting the welfare of future animals

Even if one is convinced that prenatal animals cannot suffer, there is good reason to afford protection to animal fetuses not for their own sake, but in order to provide coherent protection of the welfare of the animals which they will become.

Currently, we can think about the effects of fetal insults on the welfare of the animal which the fetus becomes as falling into three categories. First, there are well demonstrated and easily recognised life-threatening postnatal outcomes that occur in the neonatal period in most young which are affected as fetuses. An example would be respiratory failure caused by induction of premature birth by maternal hormone injections before the necessary prenatal surge in maturation of the fetal lungs and other tissues has become sufficiently advanced to secure survival (Liggins 1994; Mellor 2013).

The second category represents dysfunctional states, manifesting with variable severity, which are likely to affect a smaller proportion of animals that are insulted prenatally. An example is nutritionally restricted fetuses and newborns that nevertheless survive birth and early postnatal life, but then display easy to recognise compromise to cardiovascular, metabolic, pancreatic, renal or other functions much later in life (McMillan & Robinson 2005).

The third category is possible situations where the likely occurrence, severity and proportion of animals affected have yet to be clarified. These situations are illustrated by the as yet undocumented proposition (discussed above) that nociceptor stimulation during invasive procedures on the fetus might initiate a cascade of events within the nervous system that could lead to heightened pain sensitivity after birth (Rawlinson 1996).

The range of postnatal outcomes arising from prenatal insults is diverse, complex in aetiology, and variable in terms of the proportion of animals which will be affected postnatally following such prenatal insults. Furthermore, there may be situations in which we know that a prenatal event is likely to cause compromised postnatal welfare, but the use of the animal renders this knowledge relatively unimportant. For example, there is no need to protect fetuses for the sake of the long-term welfare of the animals they are going to become if they are to be killed shortly after birth anyway. To extend this slightly further, given the common requirement that laboratory animals (apart from Great Apes) must be killed at the end of invasive experiments conducted on them, there is less need to protect them in their prenatal form from an insult which causes welfare problems late in life than there would be to protect the fetuses of non-laboratory animals that are expected to live a long life following the same insult.

Such complexities hinder the formulation of precisely targeted and clearly stated legislation or regulations focused specifically on the fetus which would improve postnatal welfare. The answer may be to protect lifetime welfare not by direct regulation of what is done to fetuses, but by alternative mechanisms which protect against fetal insult.

There may be circumstances in which we need to protect animals against being created by certain techniques. The obvious example here is the use of somatic cell nuclear transfer ('cloning') to create mammalian embryos, where it is recognised across a number of species that the technique used to create an embryo can result in welfare problems for the postnatal animal which that embryo becomes (see, for example, Renard *et al* 2001; Houdebine *et al* 2008). This can be dealt with by technique-based legislation, rather than by legal protection of animal fetuses and, indeed, this is the approach being used by the European Commission in its proposed ban on the cloning of farm animals (European Commission, IP/13/1269 18/12/2013).

Where the insult to the fetus is indirect (via maternal mechanisms) rather than direct, protection against fetal insults causing poor welfare in future animals could be provided by safeguarding the management of pregnant animals, without a need to provide protection for their fetuses *per se*. For example, knowledgeable monitoring and management of potentially negative nutritional, environmental and health impacts on the dam, fetus and newborn, directed at confirmed or likely adverse effects of particular husbandry or investigatory manipulations, can already be implemented to good effect (eg Mellor 1988; Eales *et al* 2004; Mellor & Stafford 2004; Mellor *et al* 2009). Also, any pain that might be caused to fetuses during invasive procedures could be ameliorated by requiring that, beforehand, general anaesthesia administered to the dam be given sufficient time to act on the fetus (Mellor & Gregory 2003), thereby ensuring that the anaesthetic standard applied to fetuses would approximate to that widely accepted for postnatal animals.

Such protection could be achieved by the enforcement of codes of conduct and local rules rather than by primary legislation. For example, the protection of livestock young from adverse consequences of premature birth induced by transport stress can be achieved via welfare code recommendations that transport during the last 10–33% of pregnancy be avoided (eg NAWAC 2011; OIE Terrestrial Animal Health Code 2013, Article 7.3.7). Similarly (though perhaps inadvertently, since it is likely that the primary consideration was the welfare of the dam), the protection of equine fetuses and their future welfare from the untoward consequences of racing stress is facilitated by limiting racing to the first one-third or so of pregnancy (British Horseracing Authority 2014).

For such a regulatory approach to the protection of animal fetuses to safeguard lifelong welfare to work, however, more evidence on the effects of maternal stress (physiological and psychological) will be required. For example, little is known about the effects of maternal exercise on animal fetuses. Lack of fitness amongst sedentary pregnant women is detrimental to the health of their children (for a review, see Sui & Dodd 2013). Pregnant sporting animals, in contrast, are trained and compete at levels of fitness not attributable to the majority of pregnant women. In human medicine, it is recognised that maternal exercise can have negative as well as positive effects on the immediate and long-term health of offspring (Hopkins *et al* 2010; Hopkins & Cutfield 2011). Further investigation into such effects in animals would help to inform decisions about when the 'cut-off' point for animals racing, or competing under International Equestrian Federation (FEI) rules (http://www.fei.org/sites/default/files/2014_Veterinary_Regulations_clean.pdf, section 2[e]) should be. Furthermore, if protection of prenatal forms via the management of pregnant dams is to be used to safeguard the welfare of future animals, we need much more information about the relationship between the stage of pregnancy at which an insult occurs, and the effect of an insult to the fetus on long-term welfare of a future animal. Only then will we be able to answer the question of whether animal embryos as well as fetuses should be protected.

Conclusion

Current legal protection of animal fetuses and young does not fully reflect current scientific understanding or uncertainty about neurological pathways and associated abilities to suffer. We suggest that the precautionary principle be applied to the protections afforded prenatal and postnatal animals that may exhibit the hypothesised sub-cortically based consciousness and the attendant potential to suffer due to negative raw basic affects. This might be especially important with neurologically exceptionally and moderately immature young after birth, and would harmonise with our strong genetically embedded emotional desire to care for and protect vulnerable young (Morreall 1991; Morris *et al* 1995; Mellor *et al* 2010a; Mellor 2013).

In order for animal welfare legislation to be effective overall it is necessary for it to be coherent in the sense of the protection of postnatal animals being provided for, in part at least, by the protection of their prenatal forms. Regarding the question of adverse postnatal consequences of prenatal impositions on the fetus, safeguards that primarily focus on techniques, or on the pregnant dam before birth and on the dam and her offspring after birth provide pragmatic means of affording protection where primary legislation is unlikely to be able to do so. Where potential adverse outcomes are understood and anticipated, they can be detected and managed effectively. Existing legal provisions for protecting the welfare of postnatal animals at any age would then usually be sufficient, if assiduous attention is given to potentially affected offspring during periods of their anticipated heightened vulnerability to harm. However, the success of this approach across species is dependent upon continued research into the effect and timing of prenatal insults on postnatal welfare.

https://doi.org/10.7120/09627286.23.4.369 Published online by Cambridge University Press

Acknowledgements

We thank Dr Kate Littin, Senior Adviser, Animal Welfare, Ministry for Primary Industries, New Zealand, for providing contextual comment on the development of the Animal Welfare Act 1999. We thank Dr Hiromi Omoe of the Japanese Science and Technology Foresight Center National Institute of Science and Technology Policy (NISTEP) Ministry of Education, Culture, Sports, Science and Technology, for help with the interpretation of the Japanese Law for the Humane Treatment and Management of Animals. Madeleine Campbell is funded by The Wellcome Trust as a Biomedical Ethics Fellow.

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