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Assessing the Welfare of Transgenic Animals

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Summary

Techniques for the scientific assessment of the welfare of animals have developed rapidly in recent years and many of these can be applied to genetically modified animals. Each modified strain should be compared with unmodified strains using measures of physiology, behaviour, anatomy, immune system function, pathological change, growth, reproduction and longevity. Using a wide range of measurements, any increased levels of pain, fear or distress should be revealed. There may also be indications of the extent to which the welfare of such individuals can be good.

A potential problem in using some welfare assessment techniques is that the animal may be affected by the genetic modification in a way which alters the aspect of its biology which is being measured. For example, if a preference is tested but the relevant sensory functioning has been genetically altered or if an adrenal response is to be measured and adrenal functioning has been changed in the modified animals, then the measurement procedure would be invalid. Such problems must be considered wherever the welfare of transgenic animals is to be assessed.

Every person who works with transgenic animals should be aware of how to assess their welfare and should act so as to avoid or minimise poor welfare. When a transgenic animal has been developed, details of any effects of the genetic manipulation on the welfare of the animal should be part of the specification available for potential users. Whilst there is some legislation concerning the welfare of animals which are part of experiments, in most countries the only legislation relevant to their welfare after this is of a general nature, for example that concerning cruelty to animals. Such legislation is not adequate for transgenic animals. The legislation should stipulate that no genetically modified animal should be permitted to be used commercially until comprehensive studies of the welfare of the animal have been carried out during two generations and continuing for maximum commercial life. The decision as to whether the use of the modified animal is permitted should depend upon whether there is a net benefit for the welfare of all animals including humans. A commercial profit is not sufficient justification for modifying an animal in such a way that its welfare is poor.

Introduction

If animals are to be produced as a consequence of transgenic procedures, two important questions need to be answered. These are - whether or not there are positive or negative effects on welfare and the magnitude of those effects? Hence it is essential to use a definition of welfare which allows scientific measurement. The welfare of an animal is its state as regards its attempts to cope with its environment (Broom 1986). This state refers to the amount of difficulty which the individual has in trying to cope with its environment and the extent to which it is failing to cope. When it fails to cope, or seems likely to do so, it is said to be stressed. The state of the animal includes the feelings of the individual, which may be good feelings or suffering (Broom 1995b). In order to be a useful scientific concept, we must be able to think of welfare as varying over a range from very good to very poor.

There is a rather small range of measures which give us information about welfare at the good end of the scale (Table 1), but a much longer list of measures which can tell us about how poor the welfare of the animal is (Table 2). All of these measures and the concept of welfare are explained in detail by Broom (1991) and Broom and Johnson (1993).

Table 1. Measures of good welfare

Variety of normal behaviours shown
Extent to which strongly preferred behaviours can be shown
Physiological indicators of pleasure
Behavioural indicators of pleasure

(from Broom and Johnson, 1993)

Table 2. Measures of poor welfare

Reduced life expectancy
Reduced ability to grow or breed
Body damage
Disease
Immunosuppression
Physiological attempts to cope
Behavioural attempts to cope
Behavioural pathology
Self narcotization
Extent of behavioural aversion shown
Extent of suppression of normal behaviour
Extent to which normal physiological processes and anatomical development are prevented.

(from Broom and Johnson, 1993)

Measurements of animal welfare should be made in an objective, scientific way. Once they are made, moral judgements concerning what is acceptable can be made more easily. However, the process of scientific evaluation should be kept separate from the moral judgement.

Conventional Breeding and Welfare

Conventional breeding methods can change animals in such a way that they have more difficulty in coping or are more likely to fail to cope (Broom 1994, 1995a). One example of such an effect is the sensory, neurological or orthopaedic defect found commonly in certain breeds of dog. Others are the effects of the genes promoting obesity in mice, double muscling linked to parturition problems in cattle and many examples of selection promoting fast growth and large muscles in farm animals. Modern strains of pigs have relatively larger muscle blocks, more anaerobic fibres and smaller hearts than have the ancestral strains (Dämmrich 1987). They are more likely to die or to become distressed during any activity. Modern broiler strains grow to a weight of 2 - 2.5 kg in 37 days as compared with 12 weeks thirty years ago. Indeed, the maturation age is decreasing by one day per year at present. Their muscles and guts grow very fast, but the skeleton and cardiovascular system do not. Hence, many of the birds have leg problems, such as tibial dyschondro-plasia or femoral head necrosis, or cardiovascular malfunction which may cause ascites.

It is clear that the welfare of meat producing animals, which are growing too fast for their legs and heart, is becoming poorer and poorer because of this genetic selection and that the continuation of this trend is morally wrong. The competitive nature of the industry makes it difficult for individual producers to take action to reverse the trend, but many of them are now breaking the cruelty laws. This point is made here because there is pressure on those concerned with genetic engineering to make such animals grow even faster.

The Welfare of Transgenic Animals

In this section it is emphasised that transgenesis can result in better welfare, in no change from the average for unmodified animals, or in poorer welfare. Some of the points concerning welfare assessment are explained in more detail later in this paper.

Some genetic manipulations can be beneficial to the modified animals. If genes conferring disease resistance are inserted into the genome of an individual, for example in the work on avian leucosis virus resistance, then the welfare of the modified individual is better than that of the unmodified individual. If the animal can cope with disease challenge better then its welfare is slightly improved for most of the time and very much improved in the circumstance where disease challenge occurs.

When the transgenic animal is modified so that it can produce a novel protein in its blood or milk, there may be no effect at all on its welfare. However there could be some adverse effect and the predictability of that effect will vary according to the precision of the transgenesis procedure. Gene transfer by introducing embryonic stem cells into a blastocyst are more predictable in their effects than the introduction of genetic material by microinjection.

The production of disease susceptible animals by transgenesis, so that the animals can be used in medical research, will result in poorer welfare whenever the gene is expressed. The extent of the poor welfare will differ considerably according to the level of expression and the disease state.

If, as discussed in one of the preceding chapters, the animals produced as a result of transgenesis were modified in a way which increased their growth rate, or the growth of a particular organ, or differential growth in such a way that an already productive genetic strain was made even more productive, there is a serious risk that the welfare of the animals would be worse as a direct consequence of the manipulation. Those carrying out such work should consider whether the animals are already close to some biological limit on adaptability before proceeding.

Genetic manipulation could affect: - sensory functioning; the structure of bones or muscles; hormone production; detoxification ability; neural functioning etc. The question which must be considered is not whether or not there is a change but whether there is a change which affects the animal's welfare. In some cases, any effects of the genetic modification on the welfare of other individuals must be considered.

In a study of the effects of transgenesis on welfare, control animals which have not been modified should also be used. A wide range of measures of welfare are necessary because the actual effects on the individual will seldom be known and also because species and individuals vary, both in the methods which they use to try to cope with adversity and in the measurable signs of failure to cope. A simple welfare indicator could show that welfare is poor, but absence of an effect on one indicator of poor welfare does not mean that the welfare is good. For example, if the major effect of a manipulation was a behavioural abnormality or an increase in disease susceptibility but only growth rate was measured, then a spurious result could be obtained. The choice of measurements should include the main methods of assessing poor welfare which are mentioned here. Often it will be obvious from a preliminary study of morphology, or a clinical examination, which measurements of function or of pathology will be most relevant.

The effects of genetic manipulation may not be apparent at all stages of life, so the animal must be studied at different stages including the oldest age likely to be reached during usage. Some effects may be evident in the second generation but not in the first, so modified animals should be studied for two generations.

Measures of Welfare

Preference Studies

As listed in Table 1, an important technique in welfare research is the measurement of the strength of animal preferences. Studies of positive preferences involve choice tests, often with some operant technique being used to indicate how hard the individual will work to obtain a particular resource or have the opportunity to carry out a certain behaviour (Dawkins 1983, Arey 1992, Manser *et al.* 1995). A possible problem which must be considered when using such methods is that the sensory or motor ability of the animal might be altered by the transgenesis. Positive preferences could on occasion give ambiguous results, but in general it would be expected that what is important to normal animals would also be important to transgenic animals. Studies of aversion and its strength would be of value in studies of transgenic animals. If, for example, the modified animal were

changed so that bright light was aversive, the extent of the aversion could be measured in studies of actual movement away from light, of reluctance to be moved towards a well lit place or of some specific task which had to be performed in order to avoid the onset of bright light.

Reproductive Success

Some zoo animals cannot breed when potential breeding partners are present, because of an inadequacy in their environment. The welfare of these animals is less good than that of animals which can breed. Inability to reproduce would be an indicator of poor welfare in transgenic animals.

Growth, Weight Loss, Mortality and Life Expectancy

If control animals can grow or maintain weight in a given situation but modified animals fail to grow or lose weight, this would indicate poorer welfare in the latter. Abnormal weight gain could also indicate a problem. It is important to use a biologically relevant control in such studies. An animal could be losing weight because it is lactating or is a reproductively active male, like a red deer in rut. On the other hand, an animal which is in the pre-hibernation condition could put on a great deal of weight.

Measures of mortality rates have long been used in studies of the effects of housing conditions or management methods on animal welfare. As Hurnick and Lehman (1988) have pointed out, a housing condition, management method or treatment which resulted in the animal having a lower life expectancy indicates poorer welfare with that condition or treatment. Indeed a human who died early because of some form of self abuse or an energetic life style would be considered to have been under greater stress than a similar but longer lived person. Other examples include cetaceans which die early in poor zoo conditions and dairy cows which do not live as long under the very high production conditions of recent years as they did when their metabolic pace of life was lower (Agger 1983, Broom 1993).

Physiological Measures

Aspects of normal physiological functioning, for instance of the kidneys, could be affected in some genetically modified animals. Some of the abnormalities would be detected by clinical examination but others require specific tests to be carried out for detection.

Several physiological measurements are of value in assessing the extent to which emergency responses have been used by an individual. When there is a short-term problem, the individual may increase its heart rate and adrenal activity. Transgenic animals could be tested in situations in which control animals would show a known mean level of physiological response in order to ascertain whether or not those situations caused them more problems. It

might also be useful to investigate longer term usage of adrenal cortex responses by means of dexamethasone and adrenocorticotrophic hormone challenge tests (Dantzer and Mormède 1983, Mendl *et al.* 1992).

A further method of coping with adversity is to use endogenous opioids in the brain to self narcotise. The welfare of individuals which have to do this is less good than that of those who do not. The measurement of levels of plasma opioids appears to give little information about this coping method and the experimental use of opioid antagonists is difficult to interpret. However, studies of opioid receptor density may prove useful in welfare assessment (Zanella *et al.* 1991).

Measures of Immune System, Disease and Injury

When animals show substantial adrenal cortex responses, this is often associated with some degree of immunosuppression (Kelley 1985, Siegel 1987). There are also other mechanisms by which difficult conditions lead to impairment of immune system function. Measurements of immunosuppression include antigen challenge tests, lymphocyte stimulation tests *in vivo*, lymphocyte proliferation tests *in vitro* and specific tests of natural killer cell or macrophage efficacy (Broom and Johnson 1993). If a genetically modified animal had less efficient immunological defences than an unmodified control, then it would be coping less well with its environment so its welfare would be less good. Disease always indicates some effect on welfare, so if that animal was also diseased and suffering then its welfare would be considerably worse. One of the first steps in assessing the welfare of a modified animal is to carry out a thorough clinical examination.

Injury also means poor welfare, the extent depending on the magnitude of the injury and the amount of associated suffering. A predisposition to injury because of weakness of some kind also indicates reduced ability to cope with the environment and hence poor welfare. Hens in battery cages (Knowles and Broom 1990, Norgaard-Nielsen 1990) and sows in stalls (Marchant and Broom 1994, 1996) have weak bones because they get insufficient exercise. If a transgenic animal had thin skin, weak bones or some other effect which predisposed the individuals to injury, then its welfare would be less good than that of controls.

Behavioural Measures

Abnormalities of behaviour are often the easiest indications of poor welfare to recognise and are an integral part of a proper clinical examination. However, careful behaviour recording is also important in welfare assessment and no attempt to assess welfare would be complete unless such recording were carried out. In order to recognise problems in carrying out normal movements, the observer must first establish which movements occur and

with what frequency in normal individuals. When Andreae and Smidt (1982) wanted to assess the extent of abnormality of standing and lying movements occurring in young bulls kept on slippery slats they compared these movements with those of bulls on non-slippery floors. In a study of the extent of walking abnormalities in broiler chickens (Kestin *et al.* 1994) classified locomotor ability by its difference from normality and reported that the majority of birds had some locomotor problem before they reached slaughter age.

In studies of the effects of inadequate housing conditions where the animal has insufficient control over important events in its life, stereotypies are sometimes shown. These repeated, relatively invariant movements with no obvious function are readily recognised. Examples are route-tracing in zoo animals, water spout circling in laboratory rodents and crib-biting in horses. Other abnormalities of behaviour include self mutilation, excessive aggression, unresponsiveness, and attention to localised sources of irritation or pain. For further details see Broom and Johnson (1993).

Progress in Welfare Assessment of Transgenic Animals

Some clinical examination will have been made of most transgenic animals and in the more extreme cases where welfare is obviously poor, the experimental study will have been terminated. However, no comprehensive study of the welfare of a transgenic animal has been published. This represents a serious failing on the part of researchers, administrators and governments who have allowed developments to proceed to the point where some of these animals are being used commercially or in medical research. The results of studies of the welfare of the animal should be put in the specification of the animal prepared for subsequent users.

Legislation Required

During experimentation on transgenesis, there is legislation about animal experimentation in the European Union which requires that some account should be taken of the welfare of the animal. Research workers need to consider the welfare of the animal carefully and should be able to justify all of their actions to a member of the general public.

It will not be adequate to depend upon the moral consciences of those who use transgenic animals and specific legislation is needed concerning testing before usage. There is EU legislation relating to human health and

preservation of the environment. There should also be legislation requiring that no genetically modified animals should be used commercially unless their welfare has been assessed using an adequate range of measures at suitable intervals throughout life and on through the next generation. If there is a net benefit for the welfare of animals, including humans, then the genetic manipulation should be permitted. This is a stricter criterion than just to say that any harm to the animal must be weighed against any benefit because this latter criterion could allow severe effects solely for financial gain. Modifications of animals which are carried out for commercial purposes only but which result in poor welfare, should not be permitted. There is legislation stating that genetically modified animals cannot be used unless specific permission is given in the Netherlands. The EU and other countries should be following that lead. If such action does not occur quickly it will become more difficult as economic pressures build up.

References

Agger JF (1983) Production disease and mortality in dairy cows. Analysis of records from disposal plants from 1969-1982. In: Proceedings of the 5th International Conference on Production Diseases in Farm Animals. Uppsala, pp 308-311.

Andreae U, Smidt D (1982) Behavioural alterations in young cattle on slatted floors. In: Disturbed Behaviour in Farm Animals (Bessei, ed). Stuttgart, Eugen Ulmer.

Arey DS (1992) Straw and food as reinforcers for prepartal sows. Applied Animal Behaviour Science 33, 217-26.

Broom DM (1986) Indicators of poor welfare. British Veterinary Journal 142, 524-526.

Broom DM (1991) Animal welfare: concepts and measurement. Journal of Animal Science 69, 4167-4175.

Broom DM (1993) A usable definition of animal welfare. Journal of Agricultural and Environ-mental Ethics 6, supplement 2, 15-25.

Broom DM (1994) The effects of production efficiency on animal welfare. In: Biological basis of sustainable animal production. Proceedings of the 4th Zodiac Symposium EAAP, Publication 67 (Huisman, EA, Osse JWM, Van der Heide D, Tamminga S, Tolkmap BL, Schouten WGP, Hollingsworth CE, Van Winkel GL, eds). Wageningen: Wageningen Pers, 201-210.

Broom DM (1995a) Measuring the effects of management methods, systems, high production efficiency and biotechnology on farm animal welfare. In: Issues in Agricultural Bioethics, (Mepham TB, Tucker GA, Wiseman J, eds) Nottingham: Nottingham University Press, pp 319-334.

Broom DM (1995b) Animal welfare defined in terms of attempts to cope with the environment. Acta: Agriculturea Scandinavica Section A, Animal Science 45 (in press).

Broom DM, Johnson KG (1993) Stress and Animal Welfare. London: Chapman and Hall. 211 pp.

Dämmrich K (1987) Organ change and damage during stress - morphological diagnosis. In: Biology of Stress in Farm Animals: an Integrated Approach (Wiepkema PR, Van Adrichem PWM, eds). Dordrecht: Martinus Nijhoff, pp 71-81.

Dantzer R Mormède P (1983) Stress in farm animals: a need for re-evaluation. Journal of Animal Science 57, 6-18.

Dawkins M (1983) Battery hens name their price: consumer demand theory and the measurement of animal needs. Animal Behaviour 31, 1195-1205.

Hurnik JF, Lehman H (1988) Ethics and farm animal welfare. Journal of Agricultural Ethics 1, 305-18.

Kelley KW (1985) Immunological consequences of changing environmental stimuli. In: Animal Stress (Moberg GP, ed), Betheseda MD: American Physiological Association, pp 193-223.

Kestin SC, Adams SJM, Gregory NG (1994) Leg weakness in broiler chickens, a review of studies using gait scoring. In: Proceedings of the 9th European Poultry Conference, Glasgow, 7-12th August 1994. Volume II, WPSA, pp 203-206.

Knowles TG, Broom DM (1990) Limb bone strength and movement in laying hens from different housing systems. Veterinary Record 126, 354-356.

Manser CE, Morris TH, Broom DM (1995) An investigation into the effects of solid or grid cage flooring on the welfare of laboratory rats. Laboratory Animals 29, 353-363.

Marchant JN, Broom DM (1994) Effects of housing system on movement and leg strength in sows. Abstract in: Applied Animal Behaviour Science 41, 275-275.

Marchant JN, Broom DM (1996) Effects of dry sow housing conditions on muscle weight and bone strength. Animal Science 62 (in press).

Mendl M, Zanella AJ, Broom DM (1992) Physiological and reproductive correlates of behavioural strategies in female domestic pigs. Animal Behaviour 44, 1107-1121.

Norgaard-Nielsen G (1990) Bone strength of laying hens kept in an alternative system, compared with hens in cages and on deep litter. British Poultry Science 31, 81-89.

Siegel HS (1987) Effects of behavioural and physical stressors on immune responses. In: Biology of Stress in Farm Animals (Wiepkema PR, Van Adrichem PWM, eds), Current Topics in Veterinary Medicine and Animal Science, Dordrecht: Martinus Nijhoff, pp 39-54.

Zanella AJ, Broom DM, Hunter JC 1991. Changes in opioid receptors of sows in relation to housing, inactivity and stereotypies. In: Applied Animal Behaviour: Past, Present and Future (Appleby MC, Horrell RI, Petherick JC, Rutter SM, eds). Potters Bar: Universities Federation for Animal Welfare, pp 140-141.