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Embryonic, Fetal and Post-natal Animal-Human Mixtures: An Ethical Discussion

Overview

The potential power of embryonic and fetal inter-species mixtures became clear about a decade ago in a series of dramatic experiments in which small sections of brains from developing quails were taken and transplanted into the developing brains of chickens. The resulting chickens exhibited vocal trills and head bobs unique to quails, proving that the transplanted parts of the brain contained the neural circuitry for quail calls. It also offered astonishing proof that complex behaviours could be transferred across species [1].

Although moral intuitions about the creation of animal-human mixtures, especially at the embryonic and fetal level, may vary, it is subject to deep ethical concern to many for whom the creation of animals with certain kinds of human characteristics or with human brain and reproductive cells, would be offensive. [2]

In a report published in 2004 and entitled **Reproduction and Responsibility: The Regulation of New Biotechnologies** [3], the **President's Council on Bioethics** of the USA indicated that in the context of procreation - of actually mixing human and non-human gametes or blastomeres [4] at the very earliest stages of embryological development - the ethical concerns raised by violating the animal-human species barrier were especially acute. Thus, the drawing of clear lines limiting permissible research in this area should be specifically considered.

In this respect, the President's Council recommended that one bright line should be drawn at the creation of animal-human embryos, produced by the fertilisation of human eggs by animal (for example, chimpanzee) sperm (or the reverse). This is because the Council accepted that society should not be put into a position to judge the humanity or moral worth of such ambiguous hybrid entities (for example, a "humanzee", the analogue of the mule). Moreover, the Council stated that it did not want to see the possibility of a human being having other than human progenitors (for example, having a monkey as a parent).

Accordingly, the Council recommended that the US Congress should draft legislation to address these biological possibilities and make it illegal to cross this line.

But in a report entitled ***Human Reproductive Technologies and the Law*** [5] prepared in 2005, the **UK House of Commons Science and Technology Committee** went a lot further than the US President's Council. For example, it indicated that the fertilisation of animal eggs with human sperm should continue to be legal in the UK for research purposes and the time limit extended before they are destroyed.

Recommendations of the Scottish Council on Human Bioethics

1. National Ethics Committees of the Council of Europe member states should initiate, as soon as possible, an extensive consultation and reflection relating to the complex ethical questions arising from the creation of animal-human mixtures.
2. The Parliamentary Assembly and the Steering Committee on Bioethics of the Council of Europe should address the ethical issues arising from the creation of animal-human mixtures, as soon as possible, in a Recommendation and/or a legally binding Convention.
3. The placing of a live human embryo into an animal should be prohibited.
4. The placing of live human sperm into an animal should be prohibited.
5. The placing of a live animal embryo into a woman should be prohibited.
6. The placing of live animal sperm into a woman should be prohibited.
7. The creation of an embryo containing cells made up of both human and animal chromosomes should be prohibited.
8. The insertion of a human cell nucleus or chromosomes into a non-human egg stripped of its chromosomes enabling an embryo to exist should be prohibited.
9. The mixing of animal and human gametes should be prohibited.
10. Xenotransplantation should only take place if the procedure respects all national and international legal instruments such as the Council of Europe Recommendation (2003) 10 of the Committee of Ministers on Xenotransplantation.

11. The incorporation of human stem cells into post-natal animals should proceed with extreme caution. Moreover, such a procedure should only take place if it can be demonstrated that the cells cannot contribute to the germline or give rise to specifically human brain functions in the animals.
12. The incorporation of human stem cells into post-blastocyst stages of non-human embryos should only take place if it can be demonstrated that they cannot contribute to the germline or brain cells of the animal.
13. The incorporation of non-human stem cells into post-blastocyst stages of human embryos should only take place if it can be demonstrated that they cannot contribute to the germline or brain cells of the human being.
14. The incorporation of human pluripotent or totipotent stem cells into a non-human blastocyst or its preliminary embryonic stages should be prohibited.
15. The incorporation of non-human pluripotent or totipotent stem cells into a human blastocyst or its preliminary embryonic stages should be prohibited.

Contents

1. Introduction

Crossing the human species barrier is a procedure that has always fascinated humanity. In ancient Egypt, Greece and Rome, for example, sphinxes (human-lion mixtures), centaurs (human-horse mixtures), fauns (human-goat mixtures) and minotaurs (human-bull mixtures) were accepted as being special and endowed with specific powers. And although they were not considered as being part of the human race, they were neither seen as being entirely animal. Indeed, their distinct and solitary status in mythology resulted in them being sometimes rejected as different and portrayed as lonely monsters. This happened, for example, in the myth relating to the minotaur which was eventually destroyed by Theseus.

In this regard, it should be emphasised that the process of interspecies mixing does actually happen in nature. For example, animal-animal mixtures such as mules are derived from interbreeding between two different species. In the case of a mule, chromosomes from a horse and a donkey are brought together through the fusion of horse and donkey gametes in fertilisation to produce an animal whose every cell contains genes from both parental species< [8]. Nevertheless, mixtures between biological species are relatively rare in nature, and most such entities would be less 'fit' than their progenitors.

With respect to animal-human mixing, no evidence of any entities being born has ever been recorded but new developments in crossing the species barrier may no longer limit animal-human mixtures to the domain of mythology. Indeed, procedures have recently been developed by scientists which mix human and animal biological elements to such an extent that it questions the very concept of being entirely human.

For example, concern for animal-human mixtures was raised in 2001by the **UK Animal Procedures Committee** which indicated in its ***Report on Biotechnology*** [9] that though questions may exist as to the likely fate of such animal-human mixtures, there may be a deeper repugnance at the thought of their very existence. Indeed, the committee indicated that the main opposition to animal-human mixtures would probably come from those who wish to maintain real boundaries between human and non-human, and who retain a conviction that 'kinds' are separate creations, each - as it were - designed to embody a particular beautiful form. Thus confusion of 'kinds' may be something which raises concern in a large section of society even though no certainty exists as to the exact identity of these 'kinds' [10,11].

On the other side of the Atlantic, the **President's Council on Bioethics** of the USA indicated in a report entitled ***Reproduction and Responsibility: The Regulation of New Biotechnologies*** [12] and published in 2004, that the crossing of the animal-human boundary was, in some respects, quite complex and subtle but that the mixing of human and animal tissues and materials was not by itself objectionable.

In other words, in the context of therapy and preventive medicine, the President's Council accepted that the transplantation of animal parts to replace defective human ones could be considered as ethical.

Moreover, the Council had no overriding objection to the insertion of animal-derived genes or cells into a human body - or even into human foetuses - where the aim would be to address a serious disease in the patient or the developing child.

Likewise in the context of biomedical research, the US Council did not see anything objectionable in the practice of inserting human stem cells into animals. But in the context of procreation - of actually mixing human and non-human gametes or blastomeres at the very earliest stages of embryological development - the Council indicated that the ethical concerns raised by violating that boundary were especially acute. Thus, the drawing of clear lines limiting permissible research in this area should be specifically considered.

In this respect, the President's Council recommended that one bright line should be drawn at the creation of animal-human embryos, produced by the fertilisation of human eggs by animal (for example, chimpanzee) sperm (or the reverse). This is because the Council accepted that society should not be put into a position to judge the humanity or moral worth of such ambiguous hybrid entities (for example, a "humanzee," the analogue of the mule). Moreover, the Council stated that it did not want to see the possibility of a human being having other than human progenitors (for example, having a monkey as a parent).

Accordingly, the Council recommended that the US Congress should draft legislation to address these biological possibilities and make it illegal to cross this line.

However, a more liberal approach to the creation of animal-human mixtures, especially in the realm of the embryo, was considered in a report entitled ***Human Reproductive Technologies and the Law*** prepared in 2005 by the **UK House of Commons Science and Technology Committee**.

In this report it is somewhat surprisingly indicated that while there is a revulsion in some quarters that animal-human creations appear to blur the distinction between animals and humans, it could be argued that they are less human than fully human embryos and therefore pose fewer ethical problems for research. The report went on to recommend that new legislation should:

a. define the nature of these creations,
b. make their creation legal for research purposes if they are destroyed in line with the current UK 14-day rule for human embryo cultures, and
c. prohibit their implantation in a woman. [13]

Others again, such as bioethicists Jason Scott Robert and Francoise Baylis [14], are unwilling to draw a specific line concerning interspecies mixtures. Indeed they assert that they take "no stance at all" on whether "animal-human mixtures should be forbidden or embraced." This is because they indicate that "the arguments against.creating novel part-human beings.are largely unsatisfactory."

2. Definitions

Because of the different constitutions of the possible animal-human mixtures including the use of eggs and sperm in addition to pluripotent stem cells, the following definitions may be considered:

Animal-Human Chimera [15,16]: A biological organism that is made up of genetically distinct population of animal and human cells. In this context it is possible to define:

- Embryonic or fetal animal-human chimera [17] which is:
  - a human embryo or fetus into which at least one cell of a non-human life form has been introduced; or
  - an animal embryo or fetus into which at least one cell of a human life form has been introduced,
- Post-natal animal-human chimera which is:
  - a human person in which animal cells, tissue or organs have been transplanted (this is defined as xenotransplantation). For example, experiments have been undertaken in the past in which animal hearts have been transplanted into human beings, or
  - an animal in which human cells, tissue or organs have been transplanted.

Animal-Human Hybrid: A biological organism created through the general use of eggs and sperm cells of different animal and human origins. These include: [18]

- a human ovum that has been fertilized by sperm of a non-human life form;
- an ovum of a non-human life form that has been fertilized by human sperm;
- a human ovum into which the nucleus of a cell of a non-human life form has been introduced;
- an ovum of a non-human life form into which the nucleus of a human cell has been introduced;
- a human ovum or an ovum of a non-human life form that otherwise contains chromosomes from both a human being and a non-human life form.

Hybrids blend genetic information from different lines or even species, at a cellular level. They do not present a "patchwork"

appearance, and are not always less fit than their progenitors [19].

3. Legislation

In most countries no guidelines exist which specifically address animal-human mixtures. The following awkward question can therefore be asked: How human must an animal-human mixture be before human legislation applies or more stringent research rules exist?

3.1. International Legislation

Even on the international stage, the existence of animal-human mixtures have not really been considered. For example, most international conventions only address either human or non-human beings but have not yet examined animal-human mixtures. These include:

United Nations: *Universal Declaration of Human Rights* [20]

Article 1 indicates that:

> *All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood.*

Council of Europe: *European Convention on Human Rights and Biomedicine (ETS No. 164)* [21]

Article 1 (Purpose and object) indicates that:

> *Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine.*

Article 11 (Non-discrimination) indicates that:

> *Any form of discrimination against a person on grounds of his or her genetic heritage is prohibited.*

Article 13 (Interventions on the human genome) indicates that:

> *An intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.*

Article 18 (Research on embryos in vitro) indicates that:

1. *Where the lawallows research on embryos in vitro, it shall ensure adequate protection of the embryo.*
2. *The creation of human embryos for research purposes is prohibited.*

Council of Europe: *European Convention for the Protection of Pet Animals (ETS No. 125)* [22]

Article 3 (Basic principles for animal welfare) indicates that:

1. *Nobody shall cause a pet animal unnecessary pain, suffering or distress.*
2. *Nobody shall abandon a pet animal.*

Some texts, however, are beginning to consider animal-human mixtures, including:

Council of Europe: *Embryonic, Foetal and Post-natal Animal-Human Mixtures, Doc. 10716*
11 October 2005, Motion for a resolution presented by Mr Wodarg and others [23].

In this draft document it is indicated that:

> *The Assembly invites the governments of the member states to initiate an extensive consultation and reflection relating to the complex ethical questions arising from the creation of animal-human mixtures.*

The Assembly wants to table its own recommendations concerning animal-human mixtures in order to evaluate the scientific facts, general ethical arguments, different risks and social consequences.

The Assembly recommends to the Committee of Ministers to entrust the Steering Committee on Bioethics of the Council of Europe to address the ethical issues arising from the creation of animal-human mixtures as soon as possible in a

recommendation and/or to insert this task into the ongoing work on additional protocols to the European Convention on Human Rights and Biomedicine.

3.2. National legislation

Canada: *Assisted Human Reproduction Act 2004*

Clause 5 indicates that it is prohibited to: [24]

- *create a chimera, or transplant a chimera into either a human being or a non-human life form; or*
- *create a hybrid for the purpose of reproduction, or transplant a hybrid into either a human being or a non-human life form.*

USA: *Draft Human Chimera Prohibition Act of 2005 (S.1373)* introduced in the Senate of the United States by Mr. Brownback [25]

Indent (a) indicates that, in general, it shall be unlawful for any person to knowingly, in or otherwise affecting interstate commerce:

(1) create or attempt to create a human chimera;
(2) transfer or attempt to transfer a human embryo into a non-human womb;
(3) transfer or attempt to transfer a non-human embryo into a human womb; or
(4) transport or receive for any purpose a human chimera.

Note: In this draft legislation, some animal-human hybrids would come under the definition of a chimera.

United Kingdom: *Human Fertilisation and Embryology Act (1990)*

In the UK, the creation of many animal-human entities would exist in a legal vacuum, apart from the mixing of human gametes with the live gametes of animals to form two cell embryo hybrids which, as indicated by Section 4. (1) (c) of the UK Human Fertilisation and Embryology Act (1990), is possible provided a licence is obtained.

This is confirmed, in the report prepared in 2005 by **House of Commons Science and Technology Committee** entitled ***Human Reproductive Technologies and the Law*** [26] which indicated that the consideration of animal-human chimeras and hybrids is made difficult by the lack of legal definitions. For example, since the UK Act mentions the mixing of human and animal gametes, it may be assumed to have been drafted with the possibility of addressing the crossing of the species barrier. But the Human Fertilisation and Embryology Act (1990) does not, unfortunately, provide adequate clarifications concerning the specific status and nature of the created animal-human entities. Because of this situation, it is also uncertain whether the UK Human Fertilisation and Embryological Authority (HFEA) is even entitled to regulate the creation of most of the animal-human entities being envisaged in research. In other words, whether or not these entities come under the jurisdiction of the HFEA depends on whether or not they are 'human'. And it is probable that controls relating to the creation of such animal-human entities would only exist if the HFEA chooses to consider a broad definition of a human embryo [27].

Recommendations

- **National Ethics Committees of the Council of Europe member states should initiate, as soon as possible, an extensive consultation and reflection relating to the complex ethical questions arising from the creation of animal-human mixtures.**
- **The Parliamentary Assembly and the Steering Committee on Bioethics of the Council of Europe should address the ethical issue arising from the creation of animal-human mixtures, as soon as possible, in a Recommendation and/or a legally binding Convention.**

4. General Ethical Arguments

To many people, the resulting animal-human entities created by crossing the species barrier would give rise to grave and complex concerns. In crossing the species barrier, the definition of 'being human' would no longer be clear cut. Indeed, any ethical appraisal of crossing this barrier should ultimately address the question of whether the introduction of foreign animal parts into the human body modifies a person's identity and the rich meaning of being human. And if modifying a human body with animal parts is indeed being considered, then questions relating to the acceptable limit of such modifications may then be posed. [28]

Many persons believe that the ethical implantation of foreign parts into a human body is related to the degree of change that it may entail in the human identity of the person who receives them [29]. In this respect, it should be noted that not all parts of the human body are generally considered to be equally important in the expression of the identity of the person. Some

body parts exclusively perform their specific function such as the heart which is considered as a biological pump. Others, instead, add to their functionality a strong and personal symbolic element which inevitably depends on the subjectivity of the individual. And others still, such as the brain and reproductive cells, are often considered to be intrinsically linked with the personal identity of a person.

For example, it is suggested that those animal parts which are seen as being purely functional could be transferred into a human person, on a case by case basis, and depending on the specific relation to the symbolic meaning which they take on for each individual person. However concerns are being expressed with the transfer of animal brain and reproductive cells to human persons because of the specific risks connected with such a procedure with respect to human identity< [30,31].

4.1. The transfer of brain cells between humans and animals

In 2005, an interdisciplinary working group in the USA published the results of its consultation on the scientific, ethical, and policy issues raised by research involving the engraftment of human neural stem cells into the brains of non-human primates [32]. The group indicated that the introduction of human cells into non-human primate brains raised questions about the very nature of the moral status of a being [33]. Thus a variety of reasons could be given for according different moral standing to humans and non-human primates. For example, in the Judeo-Christian traditions, humans are set apart by God as morally special and are given stewardship over other forms of life (Genesis 1:26-28). For Kantians, human capacities for rationality and autonomy demand that persons be treated as ends in themselves [34]. Mill, on the other hand, found an especially fecund source of utility in the richness of human mental life [35]. Singer, although strongly defending equal consideration of non-human interests, argues that self-awareness affects the ethically allowable treatment of a creature by changing the kinds of interests it can have [36].

Thus, apart from certain situations in the Judeo-Christian tradition [37], many of the widely accepted candidates for determining moral status involve mental capacities. These include:

- the ability to feel pleasure and pain,
- the use of language,
- rationality,
- the possibility of forming rich and meaningful relationships,
- the potential to have complex emotions, and
- an unparalleled ability to imagine a future and remember the past [38].

Moreover, it is the human brain that enables a person to be aware of himself or herself and his or her own identity. In addition, it is through the mental capacity of human beings that a person can understand concepts such as unconditional acceptance, religions and is able to confer human dignity upon himself or herself as well as upon others.

Therefore, to the extent that a non-human primate attains those capacities, it may be argued that such a creature should be held in correspondingly high moral standing [39]. In other words, if the distinction between the mental capacities of a human individual and an animal is undermined through the creation of an animal-human mixture then the very concept of the existence of specific human dignity and individuality could be questioned.

With respect to the particular kinds of animal-human experiments relating to the brain which should be examined, the interdisciplinary working group proposed the six following factors that research oversight committees and other review groups should use as a starting framework [40]:

1. Proportion of engrafted human cells,
2. Neural development of the animal,
3. Animal species,
4. Brain size of the animal,
5. Site of integration into the animal brain of the human neural stem cells,
6. Brain pathology of the animal.

4.2. The transfer of reproductive cells between humans and animals

Again, one of the defining attributes of being a human person has always been that the individual was created by other human persons. In other words, an important aspect of the identity of a human person is given through knowing who his or her creators really are and that they were human. This is also reflected in that significant interpersonal bonds of mutual belonging are often formed between the creators, on the one hand, and the created person, on the other [41]. This is, for example, understood in the concept that a person is accepted as a royal prince or princess because he or she was created by a king or queen. In other words, it is because a bond of mutual belonging is seen to exist between a son or daughter and his or her parents that the concept of inherited rights and identity is embraced by many societies.

Accordingly, if an entity is accepted as having been created by human and non-human beings, then its whole identity and its

entitlement to human rights and dignity could be challenged.

4.3. Psychological risks

In the case where an animal-human entity is capable of self awareness, he or she would also certainly be under substantial psychological risks. These would probably be related to his or her awareness of his or her unique animal and human origins and identity but also to the manner in which society would perceive, accept and relate to animal-human mixtures. Indeed, being such a mixture would be profoundly different, psychologically, to having, for example, a pig's heart valve implanted, which is basically a more mechanical procedure.

4.4. Biomedical risks

4.4.1. Risks of biological developmental problems

In the first reproductive cloning experiment, in February 1997, Dolly the sheep was created after 277 nucleus fusions took place, whereby 8 embryos were obtained giving only one viable lamb [42]. In the creation of animal-human mixtures, especially at the embryological level, it would be expected that a far greater number of pre- and post-natal developmental biological problems would occur. Thus, any such experiments would be considered as ethically very questionable by the research community and other members of society.

4.4.2. Risks of creating new diseases

It is well known that many animals may harbour in their organs, cells, and genome, microbiological and other entities for which they are healthy carriers because they have developed protective mechanisms, which render them resistant. But some of these entities are capable of crossing the species barrier and developing in the host. The appearance of 'new' diseases after crossing the species barrier is not - alas - a myth : the HIV virus for instance, is very probably of simian origin, and is the cause of a pandemic in which the animal has ceased to play any part [43]. This infectious danger is therefore sufficiently serious to induce physicians and biologists to publicly raise the question of whether it is ethical to allow humankind to run the risk of devastating and uncontrollable pandemics since animal-human mixtures will never concern more than a limited group of procedures [44]. The real issue is whether the risk can be reduced to an acceptable threshold [45].

4.5. Conclusion

One could argue that there may be no ethical concerns (aside from individual biomedical and psychological risks) with the creation of animal-human mixtures if all biological species are freely accorded full and equal rights. However, society does not do this, and it is difficult to evaluate a priori the level of human dignity and hence the extent to which human rights that should be accorded to new animal-human mixtures.

At present society has the following options:

- It can decide not to create certain kinds of animal-human mixtures because it cannot, as yet, deal with the ethical consequences which they initiate. Thus, if the moral status of an animal-human mixture cannot be determined without creating such an entity, then that in itself should be a sufficient argument against creating such an entity on the basis of the precautionary principle.
- It can decide to create certain kinds of animal-human mixtures and kill them before they develop to any advanced stage because society cannot, as yet, deal with the ethical issues which they pose.
- It can decide to create certain kinds of animal-human mixtures and allow them to develop to term. However, society may then agree that they should never have been created in the first place due to biomedical developmental defects, psychological problems or societal inequalities and prejudice.

DEVELOPMENTS IN THE CREATION OF ANIMAL-HUMAN MIXTURES

5. Animal-Human Transgenesis

For many years, scientists have been creating transgenic animals in which some foreign (human or non-human) genes are deliberately inserted into the genome of animals. Mice with human immune-system cells and organ-donor pigs with human genes have thus been created which can also pass on the human genes to subsequent generations.

However, several technical obstacles have limited the amount of human genes that can be expressed in animals such as mice. Indeed, only a few human genes at a time can be successfully inserted into the mouse genome without interrupting essential mouse gene functions or creating a fatal combination.

Other transgenic animals include sheep and goats which can express foreign proteins in their milk. And transgenic chickens

are now able to synthesise human proteins in the 'white' of the eggs which scientists believe may eventually prove to be a valuable source of proteins for human therapy [46].

Specific Ethical Issues

In some quarters, concern has been expressed about the 'humanisation' of animals. But although the genetically modified sheep produced in Scotland or the pigs intended as sources of transplants, may, technically, be considered as 'humanized', in that they produce 'human' proteins rather than ovine or porcine equivalents, the real concern is related to the production of creatures with overtly animal-human properties. It may be that these worries are for the future but it is also true that talk of 'human genes' may be misleading. Indeed the insertion or excision of DNA so as to replicate a human gene may not involve any actual transfer of human material, any more than it encourages the expression of a significantly human feature [47].

However, the SCHB is concerned that the production of creatures with overtly animal-human properties would create grave and complex ethical difficulties. Thus, in the light of the precautionary and proportionality principles it believes that such experiments should only proceed with extreme caution.

6. Animal-Human Gestation

6.1. Placing a human embryo in an animal

The placing of a human embryo into an animal was addressed by the **President's Council on Bioethics** of the USA in its report entitled ***Reproduction and Responsibility: The Regulation of New Biotechnologies*** [48] published in 2004. In this document it is indicated that a bright line should be drawn at the insertion of ex vivo human embryos into the bodies of animals. Thus, an ex vivo human embryo entering a uterus belongs only in a human uterus [49].

In the report prepared in 2005 by the UK **House of Commons Science and Technology Committee** entitled ***Human Reproductive Technologies and the Law*** [50] it is also indicated that the placing of a human embryo in an animal raises difficult ethical issues. These include the special status of the embryo and animal welfare.

However, this committee went on to note that once an embryo had been created but was not required for treatment, it must either be destroyed or used for research. In this regard, the House of Commons committee suggested that it could be argued that its special status demands that it be used for potentially valuable research. In other words, the UK committee suggested that if a spare embryo was made available for research then, because of the respect for the embryo, researchers should ensure that it is used for the best possible ends. And while the committee was aware of no interest from scientists in placing human embryos into animals, it did suggest that it was conceivable that such research could yield valuable insights into the causes of infertility and miscarriage [51].

Moreover, the committee suggested that if the incubation of a human embryo in an animal were to yield valuable information about the causes of infertility, then it could be argued that this is an appropriate use for the embryo and consistent with its status [52].

In this respect, the House of Commons Science and Technology Committee indicated that:

> *"the ethical problems concerning the use of embryos surplus to treatment are not clear cut, particularly if no embryo could be incubated in the animal for longer than the statutory maximum duration for in vitro culture. In considering the subject comprehensively we should not shy away from addressing difficult subjects which may widely be considered 'taboo'." [53]*

Specific Ethical Issues:

The SCHB is concerned that this procedure would create grave and complex ethical difficulties in the manner in which the human character of the human embryos would be considered. There is indeed a risk that human embryos and human foetuses could be considered in the same manner as those of animals (with no special protection being granted) if they were to be found in an animal. This would only further undermine the bestowing of any respect and dignity to human embryos and fetuses.

Thus, in the light of the precautionary and proportionality principles, the SCHB believes that such experiments should not take place. In addition, the SCHB is unaware of any useful scientific benefits arising from such a procedure and there is no virtue in relaxing the current prohibition. It also questions the ethical stance of the House of Commons Science and Technology Committee report.

On the other hand, the SCHB agrees with the UK ***Human Fertilisation and Embryology Act (1990)*** which states in Section 3(3) that:

> *(b) A licence cannot authorise placing a [human] embryo in any animal.*

Recommendation

- **The placing of a live human embryo into an animal should be prohibited.**

6.2. Placing human sperm into an animal

Many national legislations, including the UK Human Fertilisation and Embryology Act (1990) do not specifically mention the placing of human sperm into an animal. However, it is probable that one of the reasons (amongst others) why many countries prohibit bestiality (human-animal sexual activity) is related to the deep revulsion towards the creation of possible animal-human mixtures through the biological placement of human sperm into an animal. For example, in the UK, the Sexual Offences Act 2003 [55] indicates under Section 69 (Intercourse with an animal), paragraph (1) that a man commits an offence if he has sexual intercourse with an animal.

Specific Ethical Issues

The SCHB is concerned that the placing of human sperm into an animal creates very grave and complex ethical difficulties with respect to human dignity. Thus, in the light of the precautionary and proportionality principles it believes that such experiments should not take place.

Recommendation

- **The placing of live human sperm into an animal should be prohibited.**

6.3. Placing an animal embryo into a human

In some countries, such as in the UK, legislation prohibiting the placing of an animal embryo in a human exists [56].

Thus, the UK ***Human Fertilisation and Embryology Act (1990)*** states in Section 3(2) that:

(a) No person shall place in a woman a live embryo other than a human embryo,

Specific Ethical Issues

The SCHB is concerned that placing an animal embryo in a human would create grave and complex ethical difficulties. Thus, in the light of the precautionary and proportionality principles it believes that such experiments should not take place. In addition, the SCHB is unaware of any useful scientific benefits arising from such a procedure and there is no virtue in relaxing the current prohibition.

Recommendation

- **The placing of a live animal embryo into a woman should be prohibited.**

6.4. Placing animal sperm into a woman

In the UK ***Human Fertilisation and Embryology Act 1990*** it is stated in Section 3 (2) that:

(b) No person shall place in a woman any live gametes other than human gametes.

However, it is probable that one of the reasons (amongst others) why many countries prohibit bestiality (human-animal sexual activity) [57] is related to the deep revulsion towards the creation of possible animal-human mixtures through the biological placement of animal sperm into a woman. For example, in the UK, the ***Sexual Offences Act 2003*** [58] indicates under Section 69 (Intercourse with an animal), paragraph (2) that a woman commits an offence if she has sexual intercourse with an animal.

Specific Ethical Issues

The SCHB is concerned that the placing of animal sperm into a woman creates very grave and complex ethical difficulties with respect to human dignity. Thus, In the light of the precautionary and proportionality principles it believes that such experiments should not take place.

Recommendation

- **The placing of live animal sperm into a woman should be prohibited.**

7. Animal-Human Hybrid Embryos

7.1. Embryo containing cells made up of both human and animal chromosomes

7.1.1. Non-human eggs into which human nuclei are inserted

The insertion of human nuclei into non-human eggs has already lead to some concern in the press [59]. This is because of recent research presented by Dr. Orly Lacham-Kaplan [60,61] and her colleagues from the Monash Institute of Reproduction and Development in Australia, in which it was shown that any complete set of chromosomes could, theoretically, be considered as gametes if they were introduced into an egg. Indeed, Dr. Orly Lacham-Kaplan found a way of 'fertilising' non-enucleated mouse oocytes by injecting somatic cell nuclei taken from adult male mice. And following chemical activation of the 'fertilised' oocytes and the extrusion of two secondary polar bodies, embryos could be formed containing two sets of chromosomes which could further develop. Thus, if the nuclei of adult human cells were inserted into non-human eggs, concern may be expected that the human nuclei could, theoretically, 'fertilise' the animal eggs.

Experiments already undertaken

Frog-Human Hybrid Entities [62]

In 2003, a team of scientists at Cambridge University fused the nuclei of adult human cells with frog eggs, with the aim of producing rejuvenated master cells that could be grown into replacement tissues for treating disease. In this experiment some kind of development was initiated, the extent of which makes it impossible to ascertain whether or not fertilisation had been initiated [63].

Specific Ethical Issues

The SCHB is concerned that this procedure would create grave and complex ethical difficulties if frog-human embryos were produced. It questions why human donor nuclei were used rather than those of other mammalian species in order to perform such basic research aimed at better understanding the mechanism of nuclear reprogramming. Thus, in the light of the precautionary and proportionality principles, the SCHB believes that such experiments should not take place.

7.1.2. Animal-Human chromosome transplant

The possibility of transplanting chromosomes between animals and human beings creates new ethical problems as to the manner and extent in which the new beings should be considered and whether they should have animal or even human rights. Human beings normally contain 46 chromosomes of which 23 originate from each parent. A question can then be raised concerning the manner in which an inter-species chromosomal transplantation would affect the way one considers a species. Should a living being be considered to belong to a specific species if the majority of its chromosomes belong to this species? A further question could be considered if a living being was created with chromosomes originating from several different species.

Experiments already undertaken

Mouse-Human Hybrids [64]

In 2005, a team of UK scientists was able to successfully transplant a human chromosome into mice. To create these mice, the team first extracted chromosomes from human cells and sprayed them on to beds of stem cells taken from mouse embryos. Any stem cells that absorbed human chromosome 21 were then injected into three-day-old mouse embryos which were then re-implanted into their mothers. The newly born mice carried copies of the chromosome and were able to pass it on to their own young who contained the human chromosomes in their cells.

Specific Ethical Issues

The SCHB is concerned that this procedure would create grave and complex ethical difficulties if mouse-human embryos were produced containing cells made up of both mouse and human chromosomes. Thus, In the light of the precautionary and proportionality principles the SCHB believes that such experiments should not take place.

Recommendation

- **The creation of an embryo containing cells made up of both human and animal chromosomes should be prohibited.**

7.2. Non-human eggs stripped of their chromosomes into which human nuclei are inserted [65,66]

It has been suggested that the use of non-human oocytes stripped of their chromosomes as recipients of human somatic nuclei with the aim of generating human embryonic stem cell lines without the need for human oocytes may constitute a solution to the problem of limited supplies of human oocytes [67].

In addition, some scientists have indicated that interspecies combinations (human nucleus into non-human oocytes stripped of their chromosomes) could become valuable research tools that may be used to increase understanding of the

reprogramming process of somatic nuclei, which could be a long term solution to the problems of tissue rejections [68].

Experiments already undertaken

Gametal Cow-Human Hybrid Embryos

The company Advanced Cell Technologies was reported, in November 1999, to have created the first human embryo clone using a gametal animal-human hybrid. This was achieved when the nucleus of an adult human cell was inserted into a cow's egg stripped of its chromosomes in order to create a cloned embryo. This embryo was left to develop and divide for 12 days before being destroyed [69,70].

Similarly, Prof. Panayiotis Zavos who runs a fertility laboratory in the USA indicated, in September 2003, that he had created around 200 cow-human hybrid embryos that lived for around two weeks and grew to several 100 cells in size and beyond the stage at which cells showed the first signs of developing into tissues and organs. It was also noted that they appeared to have normal human DNA [71,72].

Gametal Rabbit-Human Hybrid Embryos

In August 2003, Hui Zhen Sheng of Shanghai Second Medical University, China, announced that gametal rabbit-human hybrid embryos had been created by fusing adult human cells with rabbit eggs stripped of their chromosomes. Using donor cells from the foreskins of a five-year old boy, two men and facial tissue from a woman, the researchers created rabbit-human hybrid embryos which developed to the approximately 100 cell stage that forms after about four days of development [73,74,75].

Specific Ethical Issues

First, the SCHB would like to question the scientific merit and validity of these experiments, which either remain unpublished in any peer-reviewed journal (cow-human hybrid embryos) or were published in a relatively minor and obscure journal (Cell Research) in the case of the rabbit-human hybrid embryos.

Second, the medical risks of implanting cells that contain a mixture of animal (and possibly some human) mitochondrial DNA and human nuclear DNA are considerable, given that there are varying degrees of interspecies incompatibility between mitochondrial and nuclear function. Furthermore, it should be noted that mitochondrial dysfunction has been discovered to be a key factor in many neurodegenerative diseases. Since many of the diseases claimed to be treatable by therapeutic cloning are neurodegenerative, using enucleated animal eggs for Somatic Cell Nuclear Transfer (SCNT) would be liable to result in profound medical risks. Similarly, the use of animal eggs for SCNT to treat heart or liver complaints could create a number of difficulties owing to the high level of mitochondrial activity in these organs.

Third, regarding the use of enucleated animal eggs for SCNT for research into diseases, there are so many profound genetic and epigenetic flaws in cloned embryos (even using eggs of the same species), that to use embryos created by interspecies nuclear transfer would be liable to become a study of artefacts. In other words, it would be difficult to interpret the results.

Fourth, there would also be risks of transmission of animal diseases to humans or the creation of new diseases.

Thus, In the light of the precautionary and proportionality principles the SCHB believes that such experiments should not take place.

Recommendation

- **The insertion of a human cell nucleus or chromosomes into a non-human egg stripped of its chromosomes enabling an embryo to exist should be prohibited.**

7.3. Mixing of Animal and Human Gametes [76]

The mixing of animal and human gametes to form animal-human entities is prohibited in a number of countries including Denmark, France and Germany [77] but not in others such as the UK where the fertilisation of animal eggs with human sperm can be used to determine the quality of this sperm.

Experiments already undertaken

Genetic Human-Hamster Hybrid Embryos

The hamster test is a well established test in the UK which gives indications relating to the ability of a man's sperm to penetrate a hamster egg stripped of its outer membrane, the zona pellucida. After fertilisation by the human sperm of the hamster egg, this human-hamster hybrid embryo can be left to develop until the two cell stage for observation.

At the time when the Human Fertilisation and Embryology Act (1990) was put through parliament in the UK, the 'Hamster Egg Penetration Test' (HEPT) in which human sperm is mixed with a hamster's egg, was one of the few valid tests available to measure the viability of some patients' sperm. However, the introduction of Intra Cytoplasmic Sperm Injection (ICSI) and other treatments has now made HEPT effectively obsolete for testing sperm prior to treatment. A similar technique has sometimes been used in the UK for research into the viability of sperm. However, the most recent treatment licence ended in 2003. In effect the UK Human Fertilisation and Embryology Authority no longer offers licences for HEPT to any treatment centres. In addition, the most recent research licence also expired in 2003.

Although currently there are no research projects licensed for HEPT in the UK, the case for use of the technique is still valid. Any research project which intends to use the technique would need to prove that it had considered the ethical implications and that the use of HEPT was necessary or desirable under the purposes for which the HFEA can issue research licences.

Specific Ethical Issues

The SCHB is concerned that this procedure would create grave and complex ethical difficulties. Thus, In the light of the precautionary and proportionality principles it believes that such experiments should not take place. In addition, the SCHB is unaware of any scientific benefits arising from such a procedure and there is no virtue in relaxing the current prohibition. In this respect it concurs with the legislation in Denmark, France and Germany which states that the creation of animal-human hybrid embryos through the mixing of gametes should be prohibited [78].

Recommendation

- **The mixing of animal and human gametes should be prohibited.**

8. Animal-Human Chimeras

Chimeras, unlike genetic hybrids, consist of mixtures of cells, tissue and organs from two different biological entities whether or not they are of the same species. Unlike the situation in hybrids, there is no mixing of genetic material inside the individual cells of a chimera [79]. For example, the 'geep' was a mixture of goat and sheep cells and presents a 'patchwork' appearance [80,81,82]. These experiments demonstrated that sheep and goat blastomeres can form chimeric blastocysts and that such inter-species blastocysts are viable and may give rise to animals which are sheep-goat chimeras. The experiments also demonstrate that a goat fetus can develop to term in a sheep, and a sheep fetus can develop to term in a goat.

8.1. Animal-Human Chimeras Created Through Xenotransplantation

Xenotransplantation (the transplantation of cells, tissues and organs from one species to another) was first considered almost 100 years ago. Since then, there have been sporadic instances of clinical applications in the history of medicine but interest was only rekindled in the early 1990s as a result of new progress in the biomedical sciences. Indeed, because of the great success of allotransplantation (human to human) an ever increasing number of operations are being performed and the need for human transplants now exceeds many times the supply. It is because of this shortage and the possibility for scientists to create a virtually unlimited supply of transplants through the use of animal material, that xenotransplantation is currently being studied as a therapeutic solution to several previously incurable diseases relating to heart, liver, lung and kidney disorders. Additionally, there are other unmet medical needs which could potentially be treated by xenotransplantation such as incurable neurological diseases (Parkinson's and Alzheimer's disease), paraplegia due to spinal cord lesions and pancreatic islet or beta cell transplants for treatment of diabetes.

Xenotransplantation chimeras are also widely used in research and medicine when, for example, the transplantation of (1) human skin onto mice, (2) human tumors onto mice, and (3) human bone marrow into mice is undertaken to provide appropriate models for biomedical examinations.

Specific Ethical Issues

Xenotransplantation raises medical, legal, cultural, religious and ethical issues. And at first, public acceptation of such a procedure was minimal. With time, however, and because of the potential to save lives, xenotransplantation has become more ethically acceptable to most sections of the UK population provided the medical problems of rejection and transmission of disease have been addressed.

Recommendation

- **Xenotransplantation should only take place if the procedure respects all national and international legal instruments such as the Council of Europe Recommendation (2003) 10 of the Committee of Ministers on Xenotransplantation.**

8.2. Animal-Human Embryonic and Fetal Chimeras

The potential power of embryonic and fetal chimeras as research tools became clear about a decade ago in a series of dramatic experiments in which small sections of brain from developing quails were taken and transplanted into the developing brains of chickens. The resulting chickens exhibited vocal trills and head bobs unique to quails, proving that the transplanted parts of the brain contained the neural circuitry for quail calls. It also offered astonishing proof that complex behaviours could be transferred across species [83].

In this context, the discovery of human pluripotent stem cells, such as human embryonic stem cells in 1998, allowed researchers to consider related experiments that might reveal a lot about how embryos grow. This is because the cells found in 5-day-old human embryos multiply prolifically and - unlike most adult cells - have the potential to turn into any of the body's about 200 cell types.

It may eventually be possible for researchers to inject human stem cells into an animal embryo and then transfer that chimeric embryo into an animal's womb. The purpose of this research could include the understanding of the mechanisms by which transplanted cells localise and differentiate in a host and using the cells in preclinical testing. Human cells could also someday be grown into functioning tissue or organs in an animal for later transfer into a patient [84].

Specific Ethical Issues

Although moral intuition about the creation of chimeras may very, it is a subject of deep moral concern to many for whom the creation of animals with certain kinds of quantities of human cells, such as neural or germline cells, would be offensive. Accordingly, such research requires careful consideration and review. Perhaps no organ that could be exposed to human pluripotent stem cells raises more sensitive questions than the animal brain, whose biochemistry or architecture might be affected by the presence of human cells. Similarly care must be taken lest human pluripotent stem cells alter the animal's germline.

Thus, few scientists are eager to do these kinds of experiments without guidance because of the risk that some human cells may find their way to the developing testes or ovaries, where they might grow into human sperm and eggs. For example, if two such mice chimeras were to mate, a human embryo might form which would be trapped inside a mouse.

Various precautions seem reasonable in studies that involve the transfer of human pluripotent stem cells into non-human animals and should be considered in any prior review of a protocol [85]. Questions that have been raised by the US National Academy of Sciences in 2005 in this context include [86]:

- Are human pluripotent stem cells required, or can cells, from other non-human species be used?
- Has sufficient animal work preceded the proposed work involving human pluripotent stem cells?
- If human pluripotent stem cells are to be transferred into an animal embryo or fetus, have studies (for example, with embryonic stem cells from other species or interspecies chimeras) suggested that the resulting creature would exhibit characteristics that would be ethically unacceptable to find in an animal?
- If visible human-like characteristics might arise, have all those involved in these experiments, including animal care staff, been informed and educated about this?

In the light of these questions, the National Academy of Sciences in the USA recommended that: [87]

- Research involving the introduction of human pluripotent stem cells into non-human animals at any stage of embryonic, fetal, or postnatal development should only be permissible after authorisation from an appropriate and independent ethics committee. Particular attention should be paid to the probable pattern and effects of differentiation and integration of the human cells into the non-human tissues.
- Research in which human pluripotent stem cells are introduced into non-human primate blastocysts or in which any embryonic non-human stem cells are introduced into human blastocysts should not be permitted at this time.
- No animal into which human pluripotent stem cells have been introduced at any stage of development should be allowed to breed.

8.2.1. Incorporation of Human Stem Cells into Post-natal Animals

The ethical concerns in the incorporation of human stem cells into post-natal animals relate to the possibility that such cells, because of their potency, could give rise to cells of the germline or the brain.

However, it seems highly unlikely that human stem cells could contribute to the germline after implantation into a post-natal animal because the germline is set aside very early in fetal development [88]. The possibility of contributing to the brain is harder to evaluate. One purpose for introducing human stem cells or human neural progenitor cells into the brain is to have them contribute to repair or regenerative processes and to yield neurons which may, for example, contribute to combating neurodegenerative diseases.

Specific Ethical Issues

The idea that human neuronal cells might participate in 'higher-order' brain functions in non-human animals, however unlikely that may be, raises concerns that need to be considered. Indeed, if such cells are to be used in human therapeutic interventions, it is necessary to know whether they could participate in that way in the context of a treatment [89].

Recommendation

- **The incorporation of human stem cells into post-natal animals should proceed with extreme caution. Moreover, such a procedure should only take place if it can be demonstrated that the cells cannot contribute to the germline or give rise to specifically human brain functions in the animals.**

8.2.2. Incorporation of (1) Human Stem Cells into Post-blastocyst Stages of Non-human Embryos or (2) Non-human Stem Cells into Post-blastocyst Stages of Human Embryos [90]

Experiments incorporating human stem cells into appropriately organised tissues would offer greater opportunities to reveal the potential of such cells. Such experiments have already been undertaken in testing the capacity of neuronal progenitors cells derived in vitro from mouse embryonic stem cells by transplantation into chicken embryos.

Experiments already undertaken

Genetic Human-Mouse Chimeric Fetuses

Recently Scientists at Stanford University injected human neuronal stem cells into mouse fetuses, creating mice whose brains were about 1% human. By dissecting the mice at various stages, the researchers were able to see how the added brain cells moved about as they multiplied and made connections with mouse cells [91]. The same scientists now want to add human brain stem cells that have the defects that cause Parkinson's disease, Lou Gehrig's disease and other brain ailments and study how those cells make connections. Indeed, scientists suspect that these diseases, though they manifest themselves in adulthood, begin when something goes wrong in early development.

Because of this, the Stanford team is also thinking about making chimeric mice whose brains are 100% human. However, they suggest that if the brains look as if it is taking on a distinctly human architecture - a development that could suggest a specific amount of 'humanness' - they could be killed. On the other hand, if they look as if they are organising themselves in a mouse brain architecture, they could be used for research [92,93].

In January 2005, an informal ethics committee at Stanford University endorsed the proposal to create mice with brains made nearly completely of human brain cells. The chairperson of this committee indicated, in this respect, that the board was satisfied that the size and shape of the mouse brain would prevent the human cells from creating any traits of humanity. But just in case, the committee recommended closely monitoring the mice's behaviour and immediately killing any that display human-like behaviour [94].

Genetic Sheep-Human Chimeric Fetuses

In 2001, researchers at the University of Nevada, USA, injected human stem cells coming from bone marrow or umbilical cords into sheep fetuses. The sheep then grew up with a small proportion of human cells throughout their bodies [95].

More recently (December 2003) it was announced that human stem cells which were injected into sheep fetuses were able to produce a surprisingly high proportion of human cells in some organs. In most cases between 7-15% of all the cells in the sheep's liver were human though a few had as much as 40% of human cells [96]. The human cells were injected around halfway through gestation - before the fetus' immune system had learned to differentiate between its own and foreign cells, so that the animal does not reject them, but after the body had formed. This procedure ensures that the resulting animals look like normal sheep rather than sheep-human combinations. The researchers recognised, however, that there was no way for them to determine whether the sheep fetuses had human brain cells [97].

Genetic Monkey-Human Chimeric Fetuses

Researchers have also injected human neuronal stem cells into the skulls of three unborn monkeys. They then showed that these cells were incorporated into the developing brains of the animals [98].

Genetic Pig-Human Chimeric Fetuses

In January 2004, pigs grown from fetuses into which human stem cells were injected were shown to be made up of three kinds of cells. In other words, researchers indicated that they were made up of (1) pig cells, (2) human cells and (3) hybrid cells, the latter being fully fused pig-human cells in which the DNA from both species were mixed at the most intimate level [99].

Specific Ethical Issues

Again, ethical sensitivities arise concerning neuronal and germline cells and are perhaps even more of a concern than in the case of transplantation into a post-natal animals. This is because the human stem cells might be expected to have a greater opportunity to participate in the development of the biological entity.

As a result, the SCHB is of the opinion that more research is required in this area and that such experiments should not take place in the light of the precautionary and proportionality principles.

Recommendations

- **The incorporation of human stem cells into post-blastocyst stages of non-human embryos should only take place if it can be demonstrated that they cannot contribute to the germline or brain cells of the animal.**
- **The incorporation of non-human stem cells into post-blastocyst stages of human embryos should only take place if it can be demonstrated that they cannot contribute to the germline or brain cells of the human being.**

8.2.3. Incorporation of (1) Human Pluripotent Stem Cells into a Non-Human Blastocyst or its Preliminary Embryonic Stages or (2) Non-human Pluripotent Stem Cells into Human Blastocysts or its Preliminary Embryonic Stages

An animal blastocyst or its preliminary embryonic stages into which human pluripotent stem cells are transplanted raises difficult issues because potentially, the developing inner cell mass, the progenitor of the fetus, would consist of a mixture of human and animal cells. At present, it is not possible to predict the extent of human contribution to such chimeras. If the recipient embryo were from an animal that is biologically close to a human, the potential for human contributions would appear to be greater [100].

Experiments already undertaken

Genetic Human-Mouse Chimeric Embryos

In 2003, Scientist at the South Korean firm Maria Biotech, were reported to have injected human embryonic stem cells labelled with a fluorescent protein into 11 mouse blastocysts which later developed. The embryos were then carried by foster mice, whereby five offspring were born with fluorescence in tissues including the heart, bones, kidney, and liver. However, the scientists terminated the project after having to address "severe protests" from the public [101].

Specific Ethical Issues

The SCHB is concerned that this procedure would create grave and complex ethical difficulties. Thus, In the light of the precautionary and proportionality principles it believes that such experiments should not take place. In this respect it agrees with the UK Animal Procedures Committee Report on Biotechnology published in 2001 which indicated that *"No licences should be issued for the production of embryo aggregation chimeras especially not cross-species chimeras between humans and other animals"* [102].

Recommendations

- **The incorporation of human pluripotent or totipotent stem cells into a non-human blastocyst or its preliminary embryonic stages should be prohibited.**
- **The incorporation of non-human pluripotent or totipotent stem cells into a human blastocyst or its preliminary embryonic stages should be prohibited.**

Glossary

blastocyst: a hollow ball of 50 to 100 cells reached after about four to five days of embryonic development just before implantation in the uterus.

blastomere: a single cell in an embryo just after fertilisation.

cell line: cells of common descent and type cultured in the laboratory.

cell nuclear replacement (also called somatic cell nuclear transfer): the procedure of replacing the cell nucleus of an egg with the nucleus from another cell.

cell type: one of over 200 different types of cells in the body, for example blood cells, liver cells, neural cells. Each of these cell types has a different subset of genes switched on ('expressed') and therefore specific characteristics which allow it to serve a specific function in the body.

chimera: an organism composed of cells derived from at least two genetically different cell types. The cells could be from the same or separate species.

clone: a cell or organism derived from and genetically identical to another cell or organism.

cytoplasm: a jelly-like substance, which together with the nucleus which it surrounds, forms the cell.

dedifferentiation: the process of inducing a specialised cell to revert towards pluripotency.

differentiation: the process by which less specialised cells develop into more specialised cell types

DNA: deoxyribonucleic acid-the cell's and the body's genetic material.

ectoderm: the outermost of the three primitive germ layers of the embryo; it gives rise to skin, nerves, and brain.

embryo (human): a human being during the first 56 days of his or her development following fertilisation or creation, excluding any time during which the development has been suspended.

endoderm: the innermost of the three primitive germ layers of the embryo; it later gives rise to the lungs, liver, and digestive organs.

enucleated: from which the nucleus has been removed (usually of an egg).

gamete: the male sperm or female egg.

gastrulation: the procedure by which an animal embryo at an early stage of development produces the three primary germ layers: ectoderm, mesoderm, and endoderm.

genome: the complete genetic material of an individual.

in vitro fertilisation: the fertilisation of an egg by a sperm outside the body.

mesoderm: the midle layer of the embryonic disk, which consists of a group of cells derived from the inner cell mass of the blastocyst; it is formed at gastrulation and is the precursor to bone, muscle, and connective tissue.

morula: a solid mass of 16-32 cells resulting from the cell division of a zygote (a fertilised egg).

multipotent: having the capacity to develop into multiple (but not all) cell types.

oocyte: the female egg.

pluripotent: having the capacity to develop into every cell type in the human body, but not the extra-embryonic tissues such as the placenta and the umbilical cord.

redifferentiation: the process of inducing a dedifferentiated cell to differentiate into a (different) specialised cell type.

stem cell: a cell that has the ability to divide for an indefinite period in vivo or in culture and to give rise to specialised cells.

totipotent: having the capacity to develop into every cell type required for human development, including extra-embryonic tissues.

xenotransplantation: the transplantation of cells, tissue or organs from a donor of one species into a recipient of another species.

zygote: the single cell formed when the male sperm fertilises the female egg.

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1 Balaban, E. (1997) "Changes in multiple brain regions underlie species differences in a complex, congenital behavior". *Proc. Natl. Acad. Sci. U.S.A.* 94(5): 2001-2006.

2 Rick Weiss, Of mice, men and in-between: Scientists debate blending of human, animal forms, Washington Post, 20 November 2004.

3 The President's Council on Bioethics - Reproduction and Responsibility: The Regulation of New Biotechnologies - Washington, D.C., March 2004, http://bioethics.gov/reports/reproductionandresponsibility/chapter10.html

4 blastomere: a single cell in an embryo just after fertilisation.

5 House of Commons Science and Technology Committee, Human Reproductive Technologies and the Law, Fifth Report of Session 2004-05, Vol.I, p 30-32. http://www.publications.parliament.uk/pa/cm200405/cmselect/cmsctech/7/702.htm

6 In this case, it is unclear whether embryos were even created.

7 Ian Sample, Chromosome transplant in mice could provide clue to Down's syndrome illnesses, The Guardian, Friday September 23, 2005, http://www.guardian.co.uk/medicine/story/0,11381,1576717,00.html

8 Guidelines for Human Embryonic Stem Cell Research, National Research Council, National Academy of Sciences, USA, http://www.nap.edu/books/0309096537/html p.32

9 UK Animal Procedures Committee - Report on Biotechnology , June 2001, p.18-20, http://www.apc.gov.uk/reference/biorec.pdf

10 UK Animal Procedures Committee - Report on Biotechnology , June 2001, p.18-20, http://www.apc.gov.uk/reference/biorec.pdf

11 The term 'kinds' is more commonly used in folk-taxonomy than in modern biology. Biologically, living organisms are classified into different species (that is, into groups which do not normally interbreed). For example, many believe that human beings all belong to the same 'kind': the discovery that some were, technically, of a different biological species (that is, that their population did not naturally or normally interbreed with other human populations) would be interesting, but ethically and even politically insignificant: UK Animal Procedures Committee - Report on Biotechnology , June 2001, p.18-20, http://www.apc.gov.uk/reference/biorec.pdf

12 The President's Council on Bioethics - Reproduction and Responsibility: The Regulation of New Biotechnologies - Washington, D.C., March 2004, http://bioethics.gov/reports/reproductionandresponsibility/chapter10.html

13 House of Commons Science and Technology Committee, Human Reproductive Technologies and the Law, Fifth Report of Session 2004-05, Vol.I, p 30-32. http://www.publications.parliament.uk/pa/cm200405/cmselect/cmsctech/7/702.htm

14 Jason Scott Robert ; Françoise Baylis, Crossing Species Boundaries, American Journal of Bioethics, Volume: 3 Number: 3 Page: 1-13, http://oberon.ingentaselect.com/vl=2197681/cl=54/nw=1/rpsv/cgi-bin/linker?ini=ajob&reqidx=/catchword/mitpress/15265161/v3n3/s2/p1

15 A chimera was a Greek mythological fire-breathing female monster with a lion's head, a goat's body, and a serpent's tail. The chimera was killed by the hero Bellerophon on the twin horse Pegasus, In: The Oxford English Reference Dictionary, Oxford University Press, second edition, 1996.

16 A chimera is also an embryo or fetus that consists of cells of more than one embryo, foetus or human being.

Human-human embryonic chimeras can occur naturally when non-identical twin embryos fuse in the womb a few days after conception, so that the resulting baby contains genetic material from both embryos. In addition, most twins carry at least a few cells from the sibling with whom they shared a womb, thus chimeras are not uncommon.

It is also possible to define a mosaic which is a biological organism that is made up of more than one genetically distinct population of cells, where these cells are derived from a single fertilised egg.

This happens, for example, when a person is made of a mixture of cells containing the expected two sex chromosome, such as XY, and cells in which the Y chromosome is missing. The missing Y cells are created when a Y chromosome is accidentally lost in just some of the cells of a developing embryo.

17 Canadian Assisted Human Reproduction Act 2004, http://www.canlii.org/ca/sta/a-13.4/sec3.html

18 Canadian Assisted Human Reproduction Act 2004, http://www.canlii.org/ca/sta/a-13.4/sec3.html

19 UK Animal Procedures Committee - Report on Biotechnology , June 2001, p.18-20, http://www.apc.gov.uk/reference/biorec.pdf

20 Adopted and proclaimed by United Nations General Assembly resolution 217 A (III) of 10 December 1948,

http://www.un.org/Overview/rights.html

21 Council of Europe Convention on Human Rights and Biomedicine (ETS No.: 164), http://conventions.coe.int/Treaty/en/Treaties/Word/164.doc

22 http://conventions.coe.int/Treaty/en/Treaties/Word/125.doc

23 http://assembly.coe.int/Main.asp?link=/Documents/WorkingDocs/Doc05/EDOC10716.htm

24 Canadian Assisted Human Reproduction Act 2004, http://www.canlii.org/ca/sta/a-13.4/sec3.html

25 Draft Human Chimera Prohibition Act of 2005 (S.1373) introduced in the Senate of the United States by Mr. Brownback http://www.govtrack.us/data/us/bills.text/109/s1373.pdf

26 House of Commons Science and Technology Committee, Human Reproductive Technologies and the Law, Fifth Report of Session 2004-05, Vol.I, p 30-32. http://www.publications.parliament.uk/pa/cm200405/cmselect/cmsctech/7/702.htm

27 This is possible following the ruling of R (Quintavalle) v Secretary of State for Health of the 13 March 2003. In: R (Quintavalle) v Secretary of State for Health, http://www.lawreports.co.uk/hlpcmarc0.1.htm

In this House of Lords decisions, Lord Bingham of Cornhill indicated that Parliament could not have intended to distinguish between embryos produced by, or without, fertilisation since it was unaware of the latter possibility. The reference to fertilisation was not therefore integral to the definition but was directed to the time at which an embryo should be treated as such. However, no such interpretation is automatic and the HFEA should address this issue as soon as possible in order to clarify the matter.

28 Prospects for Xenotransplantation - Scientific Aspects and Ethical Considerations (September 26, 2001), Pontifical Academy for Life, www.vatican.va/roman_curia/pontifical_academies/acdlife/documents/rc_pa_acdlife_doc_20010926_xenotrapianti_en.html

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31 Draft Human Chimera Prohibition Act of 2005 (S.1373) introduced in the Senate of the United States by Mr. Brownback http://www.govtrack.us/data/us/bills.text/109/s1373.pdf

32 Mark Greene, et al, Moral Issues of Human-Non-Human Primate Neural Grafting, Science, Vol 309, Issue 5733, 385-386 , 15 July 2005

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34 I. Kant, in Groundwork of the Metaphysics of Morals, K. Ameriks, D.M. Clarke, Eds. (Cambridge Texts in the History of Philosophy, Cambridge Univ. Press, Cambridge, UK, 1998), pp.37-38.

35 J.S. Mill, Utilitarianism (Prometheus Books, Buffalo, NY, 1987), 83pp.

36 P. Singer, Inquiry 22, 145 (1979).

37 For example, the Roman Catholic church would accept that a human embryo or a person with a sever mental disorder would still be endowed with the same moral status as that of a healthy human person even though they do not have any or very few mental capacities.

38 Jamie Shreeve, The Other Stem-Cell Debate, The New York Times, 10 April 2005

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But, as indicated under Schedule 2, Article 1. (1)(f) of this Act, a licence may authorise, in the course of providing treatment services, "mixing sperm with the egg of a hamster, or other animal specified in directions, for the purpose of testing the fertility or normality of the sperm, but only where anything which forms is destroyed when the test is complete and, in any event, not later than the two cell stage".

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