Briefing paper on the need to protect the possibility of conducting research on serious diseases, stem cell biology and cellular reprogramming by relying on the generation and use of human admixed embryos.

Prepared by

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Context:

Human Fertilisation and Embryology Bill: Part 1-Amendments of the Human Fertilisation and Embryology Act 1990

Summary:

A dire shortage of human egg cells is inhibiting progress in stem cell research. This shortage could be overcome by using the eggs of non-human animals as an envelope in which human genetic material can be developed. Such 'human admixed embryos' as they are called in the Bill are extremely valuable research tools. Their creation and use is strictly regulated by the Bill and will be overseen by the HFEA. Despite recent scare stories the creation of live "human-animal chimeras" will be strictly prohibited, the cells may not be kept in culture beyond 14 days and such embryos will only be used for research. Implanting such embryos into a woman's uterus will be forbidden in the Act.

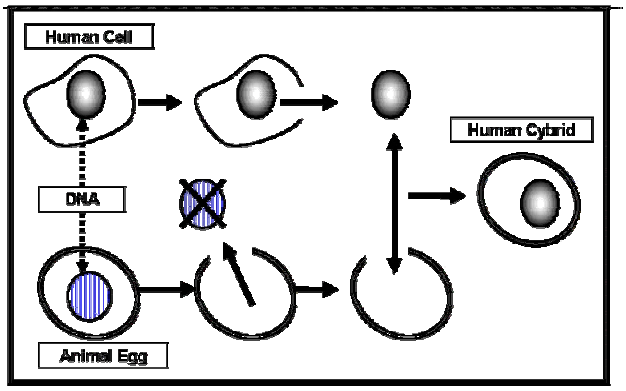
The Bill in its current form contains sufficient safeguards in establishing a system of stringent regulatory oversight that addresses public concerns without banning this important research outright.

Contents – 5 pages:

(2) Scientific Background

Current research involves removing the genetic material from a non human mammalian egg (usually a cow or rabbit) and inserting a whole cell derived from a human patient.

Typically researchers would aim to use human skin cells (fibroblasts) because they are easy to obtain from small skin biopsies. The resulting structure can be induced to begin embryonic development to create a 'cybrid' – a human-admixed embryo that is genetically 99% human. The only genetic material that is left from the animal is provided by the mitochondria – tiny, energy producing structures that linger in the cell plasma. It is not fully clear how long these structures remain until they are replaced by human mitochondria.



This work is potentially useful in at least three ways:

1) The creation of cell lines to study specific diseases

For stem cell research to move forward, it is crucial that cells can be grown as a 'cell line' that continues to grow in the laboratory. It would be very valuable to be able to generate stem cell lines with established genetic mutations known to cause human diseases such as Alzheimer's. These lines would provide an invaluable model for study of the diseases in the Petri dish. However, a great number of eggs are required to produce an embryonic stem cell line.

2) The use of cells in tissue therapy

Embryonic stem cells are potentially useful because they can be differentiated into most of the cell types found in the adult body so in theory at least they could be used as a source of cells to replace disease damaged tissues. To prevent immune rejection of these cells, it would be necessary to make their source genetically identical to the patient – the only way this can be done so far is by nuclear transfer (sometimes known as therapeutic cloning) which involves taking the egg of a donor and inserting the patients DNA. Since Dolly, we know that the process works in animals, but also that it works very differently in each species. To optimise nuclear transfer for human eggs would involve a great waste of eggs until procedures are sufficiently refined. Animal oocytes will never be used in humans directly, but the use of animal eggs allows the refinement of techniques to speed up de development of effective cures.

3) The reprogramming of adult human cells

Inside the envelope of the egg, genetic material from adult cells undergoes a remarkable transformation, regaining the power to differentiate into any cell type. If science can understand the process by which cells are reprogrammed in the egg, it may be possible to devise methods of producing embryo-like cells without having to use egg cells in the first place. This may eliminate the ethical concerns associated with the creation of embryos solely for the purpose of human embryonic stem cell derivation.

All these research leads are constrained by a common factor: A shortage of human eggs

The main source of eggs is from live human donors. It is doubtful that this can ever be relied on to provide a sufficient supply of eggs There is a real shortage of human eggs which are currently only available as surplus from fertility treatment. Human eggs are therefore very rare. As IVF techniques become technically more refined, even fewer eggs and embryos may become available for research. In contrast mammalian eggs are in plentiful supply from farming and food industries.

(3) Background to the Legislation -- Policy and ethical concerns

The 1990 Act governs research on "human embryos". The Embryology Bill as it was originally written prohibited the use of any animal material. There was no scope for further regulations in the Bill to enable such treatment to be permitted under HFEA oversight in the future. The Lords considered the issue and many peers were convinced by the arguments made at committee stage that this provision would stifle the great therapeutic and scientific potential of this research. Following three Select Committee reports which advocated that the research should be allowed, the government also decided to drop the ban in favour of regulatory oversight.

An amendment was introduced and endorsed by the Lords. The Bill currently defines a 'human admixed' embryo:

"4A Prohibitions in connection with genetic material not of human origin
(5) For the purposes of this Act a human admixed embryo is—
(a) an embryo created by replacing the nucleus of an animal egg or of an animal cell, or two animal pronuclei, with—
(i) two human pronuclei,
(ii) one nucleus of a human gamete or of any other human cell, or
(iii) one human gamete or other human cell,
(b) any other embryo created by using—
(i) human gametes and animal gametes, or
(ii) one human pronucleus and one animal pronucleus,
(c) a human embryo that has been altered by the introduction of any sequence of nuclear or mitochondrial DNA of an animal into one or more cells of the embryo,
(d) a human embryo that has been altered by the introduction of one or more animal cells, or
(e) such other thing as may be specified in regulations.

A number of **safeguards** were established:

- ✓ Research using "human admixed" embryos can only proceed if it is conducted under the supervision of the HFEA (s.4A-2).
- ✓ No "human admixed" or any other embryo or gametes that are not fully human can be implanted in a woman under any conditions (s.4A-3-1).
- ✓ No "human admixed" embryo can be implanted in an animal (s.4A-3)
- ✓ The HFEA cannot authorise the keeping or using of a human admixed embryo for longer than 14 days.

Recently, the research involved has sometimes been portrayed in a very misleading light. Some have argued that human-animal chimera would be created in this manner. It is important to debunk the emotive hyperbole and consider facts in a more balanced manner:

- The research is not about "mixing species" at all: there is nuclear DNA from only one species –the human. The non-human animal only provides the cellular envelope in which that DNA can develop and some mitochondria (see pg.2 above)
- Full hybrids have been created (albeit transiently) for years. In human sperm performance is tested by assessing the ability to penetrate the shell of hamster ova.
- The focus of this research is to gain a better understanding of disease. Under any version of the Act it is not possible that this research will ever result in an embryo that can be implanted into a woman.
- Many people have traces of animal DNA mixed into their system in medical application. Heart valves are produced from pigs. Until the 1980's insulin was extracted from the pancreas of cattle and pigs. The blood thinning agent heparin is produced from pigs. These are examples where animal DNA (other than food) actually enters the human body. The research does not aim to do even that.
- The research is not going ahead without supervision. Instead, the research is overseen and strictly audited by the HFEA. The Authority has taken considerable time to consult experts in science and ethics as well as the public on this research. After weighing the arguments, the HFEA decided to proceed under a regime of close regulatory scrutiny, rather than to stifle this promising research.

(4) Current Amendments

The provisions for human admixed embryos are comprehensively integrated in the Bill. Changes at this stage need to be carefully considered. A number of amendments have been introduced in the House of Commons to cancel or diminish the innovations recommended by the House of Lords.

The Amendments proposed by **Edward Leigh** are aimed at outlawing the research on human admixed embryos through a technical provision.

The Amendments proposed by **Mark Simmons & Andrew Lansley** are targeted at allowing research on human admixed embryos but to disallow the creation of embryos by "using human gametes and animal gametes, or one human pronucleus and one animal pronucleus". The intention here is presumably to ban research on 'true hybrids' but how this provision will be applied even to current cybrid research is far from clear. (E.g. what does 'use' of a gamete encompass?)

The Amendments proposed by **Alan Johnson** have the effect of limiting the flexibility of subsequent regulations. This risks a regulatory lock-in where the regulators may be unable to react to new scientific developments.

Since the Bill was carefully deliberated in the Lords, the issue of human admixed embryos has become subject to considerable hyperbole. In such a climate, exaggerations and oversimplifications can easily distort debates.

The Bill as it stands provides a solid basis on which to conduct research under close regulatory scrutiny and subject to a number of robust safeguards. Tampering with this framework at this sensitive stage risks curtailing scientific work in a way that may not have been fully intended by Parliament.

In the interests of medical science, we suggest the in relation to human admixed embryos, the Bill should not be further amended.

(5) Further information

This brief has aimed at presenting the perspective of scientists and clinicians on the proposed legislation in a succinct and simple manner.

We would greatly welcome a chance to explain the underlying science and the therapeutic potential in greater detail. Please do not hesitate to contact us with any further questions or comments.

The North-East England Stem Cell Institute, a collaboration between the Universities of Durham and Newcastle, the Newcastle upon Tyne Hospitals NHS Foundation Trust and other regional partners.

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