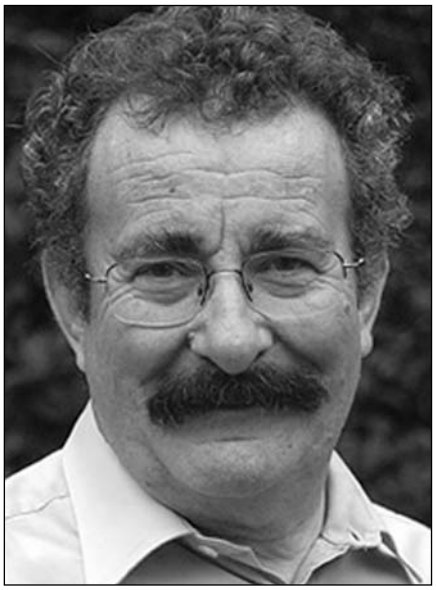
MEETING OF THE PARLIAMENTARY AND SCIENTIFIC COMMITTEE ON MONDAY 19TH JUNE 2006

The Human Fertilisation and Embryology Authority (HFEA) has recently been criticised for the imposition of unnecessary and bureaucratic restrictions on the development of scientific advances in human reproductive technologies in the UK while at the same time failing to provide effective regulation of some of the more commercial aspects of the business of aided human reproduction. Hence the question has arisen as to whether there is still need for regulation of this branch of medical practice by the HFEA in the UK and if so how this should be modified to respond to the need to encourage and promote scientific advances in the future while managing the negative aspects better. For example, about half of the multiple pregnancies in Britain, with all the related additional financial and healthcare burdens borne mainly by the NHS, are attributable to the work of fertility clinics that are still able to generate twin births unrestricted by the HFEA.

Regulation by the Human Fertilisation and Embryology Authority isn't Working



The Lord Winston, House of Lords

There is one area that Peter Braude and I agree about, but otherwise I wish to suggest to you that the mechanism for regulation in the UK is totally unsatisfactory. In my view the Human Fertilisation and Embryology Authority (HFEA) that regulates clinical work and research in this country is unnecessary and is inhibiting work. This has reached the stage where many of the advantages, had we not had a regulatory authority, have passed us by. I should emphasise that I have never been a member of the HFEA and neither would I have chosen it had I been asked.

There are two areas that the HFEA is responsible for, the first is clinical work involving gametes which are donated or stored, and embryos which are for use by in vitro fertilisation (IVF). It is not for infertility, which is mostly unregulated; that is the first anomaly. It is perfectly possible in this country to transfer any number of eggs to the fallopian tube by means of GIFT (Gamete IntraFallopian Transfer) and enjoy multiple pregnancies thereafter. That is not regulated. So is it justifiable to single out one branch of medical practice for regulation? I think there is possibly no justification. There are many other areas which may damage small, or as yet unborn children which are not regulated and no particular suffering results in consequence. This is true of neonatal paediatrics and obstetrics practice and other areas of medicine where there is equal risk of damage to babies and children. So why single out the embryo for special regulation in clinical practice?

The second issue is how practice is actually regulated. That was one area where I think Peter Braude and I undoubtedly agree. He will show you figures that support his view and I agree with them. About half the multiple pregnancies in Britain are generated through IVF techniques. They are a colossal burden on the patients, on the babies, and on the health service. There does need to be some mechanism by which we can prevent multiple births which must mean avoidance of multiple embryo transfer. But beyond that I cannot think of any other regulatory justification for this Authority. What has happened in consequence of this special regulation is that IVF is seen to be disreputable, dangerous, outside medicine in general. That has certainly damaged it. It is not funded in general through the NHS, because it is seen to be disreputable treatment, and in consequence out of the 30,000 women who will be treated this year, perhaps only 5,000 will get treatment under the NHS. Every excuse is constantly used not to include this treatment in the NHS. If it were, of course, then we would have a totally different mechanism of governance. At the present time it is subject to all sorts of curious practices which

are dubious, and impossible to control. For example, the HFEA has hardly managed to control private practice at all. There is gross exploitation of patients, an example is seen with overcharging. Where things cannot be done by approval by the HFEA, there is clear evidence that patients are going overseas; moreover, they are often going overseas not merely with the blessing of a clinic but actually by arrangement by that clinic. There are a number of practitioners in London who have monetary arrangements with clinics overseas. Some of you who read The Observer will remember the story of Svetlana in Kiev who was hyperstimulated five times, who received only US$300, while patients paid £3,000 a treatment for her eggs. Some of those patients were almost certainly British.

The practice of pre-implantation genetic diagnosis is an example where the HFEA has gone to great lengths to regulate. It is a curious situation whereby every mutation which is being tested for has to have approval by the HFEA. Yet, patients can get a termination for pregnancy in this country perfectly legally and without controversy for any serious or life-threatening mutation without regulatory recourse. Abortion is clearly a much more grave decision, but pre-implantation diagnosis cannot be done without lengthy regulatory approval to select the embryos which are genuinely believed to be free of serious health defect.

There are numerous examples of where the HFEA has taken a thoroughly bad decision. Let us take one example, such as the area of egg donation where payment of donors is not allowed. On reflection it might be better if it was. What, of course, the HFEA does allow actually is the payment of egg donors. It allows up to £3,000 of payment in kind by the process of egg sharing. A woman who cannot pay for her treatment can go to a private clinic and can get IVF as she effectively pays for it by giving some of her eggs. She may not get pregnant from her own treatment but the other patient who has received her eggs does. Now with the loss of anonymity of donors, there is this shocking scenario which means that, in eighteen years time, a woman who never got pregnant as a result of her own treatment may find that she has a child tracing her who she never knew that she had as a result of egg sharing. Oddly, the HFEA has connived at this process.

On the clinical side, let me mention two other matters, one is the use of league tables. I find it astounding that just in the last few weeks the HFEA has again published league tables showing one clinic getting a 54% pregnancy rate, and with another one getting about 48%, and some other clinics getting about 20% pregnancy rates. Now what a regulatory authority should be doing surely if it is going to have any clout at all is to ask the question "Why is this clinic so much more successful than everyone else?" The evidence is that some of the clinics that are very successful are doing all sorts of things with the mechanism of recording which actually gives a false impression of their success. For example, sometimes treatment is recorded as a drug trial and the results subsequently excluded when patients do not respond to those drugs. Alternatively patients who may not have a very good chance of a pregnancy may be referred to another clinic.

The argument for the HFEA, of course, in its present form is that it promotes public trust. The idea, of course, is that without the HFEA this treatment would be seen as being more damaging and dangerous and not in the public interest. But the social science research to demonstrate whether this opinion is true has never been done. In fact one of the problems with the HFEA is that it has never in its consultation process got things right. Does it really do effective consultation with the public? It just set up a website, and it could well be that regulatory authorities like this actually increase public distrust, not decrease it, by raising unnecessary concerns.

On the research side there is not a single justification for the HFEA. Researchers have to put through a research application to the authority having already received ethical approval. So this leads to a doubling up of the research approvals process. It delays research. In my most recent application to do stem cell research on testicular cells, by the time I had got the licence for the work that I wanted to do, it had already been published in Nature by another group.

The HFEA still maintain that they are a model for the Universe, that they are the ideal paradigm which other countries follow, but I think I am right in saying that of the larger countries only Canada has followed this model. No other country has done so and no European country has done so. And they are right not to do so because it isn't a sensible way of regulating research. Take the issue of embryonic stem cells, for example, the great pride of our biological science. A search through PubMed reveals that there are several hundred papers published on embryonic stem cells from the United States of America where, of course, President Bush has banned public funding for embryonic stem cell research. In Britain at my last count, from the 14 clinics licensed in the United Kingdom, there were a total of 17 peer reviewed publications in the literature, of which 13 come from just two units, Cambridge and Newcastle.

So far from promoting research, the evidence is that the HFEA is actually inhibiting it and delaying it and it is a serious worry at a time when academic medicine is so much under threat that we have this arcane and archaic method of regulation of research. There is no question that people cannot do illegal experiments. Cloning is a criminal offence. There are a number of issues which are clearly defined in the Statute Books, which do not need the HFEA to regulate. So my proposition is that if we are going to review the Act of Parliament, we need to review it very thoroughly indeed and consider whether or not this method of regulation is sensible.

Do we still require regulation and what still needs regulating?

Professor Peter Braude,
Head of Department of Women's Health, King's College London.

Four key reasons for establishing the Human Fertilisation and Embryology Authority were:

- to protect patients and their offspring by monitoring the safety and efficacy of a new therapeutic technique
- to allay public concerns about the creation and manipulation of human embryos by erecting barriers and having visible regulation
- to protect scientific freedom by reassuring the public that the work was subject to monitoring and proper control, and
- to protect those working in the field from criticism and claims of unethical behaviour.

On balance the HFEA is and has been a successful regulator that has fostered confidence from the public that clinics are being monitored and embryo research is being policed. There is less confidence from the profession where some aspects of practice have been made turgid by having to comply with obsolete requirements of an inflexible Act. Although the Act has served well for the past 15 years, it is timely that it is being revised.

What no longer needs regulating

Confidentiality: To the public and the profession, IVF has become mainstream fertility therapy, and the draconian provisions to protect information (even from other doctors as it was initially constructed) is no longer appropriate. Such confidentiality has been destructive in that it has prevented the linking of information through other medical databases, such that epidemiological information and safety of IVF cannot be examined. Substantial effort is wasted by clinics in trying to deal with this requirement, and significant time is apportioned during inspection processes to examine compliance. Adverse incident reporting that arises from defaulting the process is unnecessarily bureaucratic.

"Welfare of the Child" provisions: Concern for any child, even for those not yet born, is part of good medical practice. Specific legislation is unnecessary and simply frustrates clinics. The application as part of good practice should be extended to all parts of fertility treatment, where concerns should be acted upon. The requirement has promoted the inclusion of counsellors into IVF practice, but their need is wider than the law requires.

Anomalies

Training in embryo manipulation techniques: The strict terms for protection of the embryo – treatment, storage and research licences – means that there can be no training in how to biopsy (remove a cell for testing) outside of a licensed research project. Licences for embryo biopsy are not granted until a certain number of procedures have been undertaken. Where clinics do not perform research but may be good at therapy, there is no means by which practitioners can learn the skills of biopsy to satisfy the regulations needed to become a licensed practitioner.

Length of cryostorage and research: Embryos may be stored frozen for 5 years, and that may be extended for a further 5 years if there is clinical need. The 5-year initial restriction has created problems; it can only be extended if there are reasonable grounds to expect the patient's reproductive ability to be permanently impaired. In practice it is rare for this not to be able to be argued and hence it is simply an additional bureaucratic step. In addition, should the 5 years be up, the law as stands does not allow extension of storage if the embryos are to be donated and stored subsequently for research. This restricts the use of a valuable resource for stem cell research amongst others.

Blunt instrument for sanctions: The only recourse that the HFEA has to non-compliance is removal of a treatment licence, or referral to the DPP if the law has been breached significantly. These extraordinary measures have only been used a couple of times, and if implemented have significant implications for patients in, or waiting for treatment at, that clinic. Simpler strong medicine which would have direct effects on the owners or practitioners in the clinic (fines, suspension, name and shame) is required for repeated or serious misdemeanours.

Future Challenges – The continuing need for regulation

Dealing robustly to ensure patient safety: Multiple pregnancy is a significant problem in assisted reproduction. Triplets were a constant feature of IVF treatment in UK until early 2000, whereupon the HFEA encouraged practitioners to replace no more than two embryos at a time. Although many complied, the financial imperative and competitive drive for commercial clinics to have the highest pregnancy rates meant that a number continued with a high triplet rate. The imposition of mandatory regulations of two only has halved the triplet rate in this country and saved many damaged children and saved considerable money in the NHS. However the problem of twins still needs addressing. Although the residual triplet rate will include those that result from natural forces, the rest derive from other unregulated forms of fertility treatment. Absence of regulation with teeth will simply allow the problem to persist.

Stem cells: The process of developing stem cells from the ***in vitro*** cultured human embryo requires extended culture in the laboratory. Although in most cases the tissue destined to become placenta is separated from the ***in vitro*** embryo at an early stage (5-6 days) rendering it incapable of implantation and thus strictly no longer an embryo, it has been reported in the literature that day 4 or day 5 embryos cultured whole, may be more reliable for stem cell generation. Although the structure of these embryos changes during the culture, such that we believe they are incapable of further development in a womb, they may have to be cultured for more than two weeks before they show the clear appearance of stem cell formation. Would this be in breach of the HFE Act 14-day rule despite non-appearance of the "primitive streak" or semblance of normal embryonic formation? Clarity in this area of the Act may be required.

Therapeutic and reproductive cloning: It is clear that one possible way forward in the pursuit of stem cells useful in therapy and research would be to develop embryos from eggs that have had their genetic material removed and replaced by a nucleus from a somatic cell from a specific individual in order to produce a "tailor made" stem cell line. Although the process may be viewed as similar to reproductive cloning, the intention of the process is entirely different. But relevant law does not include purpose. We now have legislation to forbid the process for reproductive purposes, but for patients with inherited mitochondrial disease, in whom the defect resides in the cytosol of the egg, the only way forward to avoid the disorder being inherited in the child, would be to utilise a donated egg and have their own genetic material (nucleus) substituted – akin to reproductive cloning but for medical reasons. How will our legislation deal with this very real medical need?

Stem cells that become gametes: As in normal development of sperm and eggs from body cells, it seems increasingly possible that these gametes could be derived from stem cells. The creation of sperm or eggs in the laboratory is of real scientific interest in the study of cellular processes, but also could be used to generate a new embryo theoretically capable of implantation and development. Although fertilisation of these gametes ***in vitro*** would be covered by the Act, the use in a Gamete IntraFallopian Transfer (GIFT), a procedure where sperm and eggs are placed in the fallopian tube, is not. This anomaly demonstrates the need for a flexible approach to frequent revolutionary scientific developments. It also demonstrates the need for a regulatory body, which is conversant with, and has sufficient specialist understanding of the nuances of new developments in reproductive medicine and biology. The intention to merge the HFEA within the Human Tissue Authority in order to create a new broader Regulatory Authority for Tissues and Embryos "with a substantial lay representation", simply as a political expedient to reduce the number of NDPBs is a significant concern.

In discussion the following points were made:

An article from New Scientist was quoted where it was viewed that "an embryo in a dish has as much chance of becoming a human being as a dish of diced carrots" as its future depends on intention; if it is in a dish it is not going anywhere, if it is in a uterus, that is a different story. Discussion about the faith view centres on when the soul enters the fertilised egg. The possibility of generating two cleaving embryos in the laboratory by splitting an earlier stage (eg an eight-cell embryo into two four-cell embryos) begs the question as to whether two individuals have been created with two souls. If this is then followed by their subsequent recombination into a single embryo as has been demonstrated in some mammals, does this individual, now have one soul and what happens to the additional soul thereby created? So the location of soul is where you want it to be, and there is no consensus on this between different faiths. Furthermore, a common sense view recognises that the majority of eggs, both fertilised and unfertilised in normal circumstances are simply flushed down the toilet without ceremony or undue concern by anyone.

One of the most important medical problems impinging directly on the NHS is the current generation of about fifty per cent of all twin births arising from IVF due to the simultaneous implantation of two embryos. An unacceptably high proportion of the twin births thus created have serious medical problems giving rise to unnecessary pain and suffering for the children and expense for the general taxpayer which is a vitally important matter for the HFEA to consider and respond to.