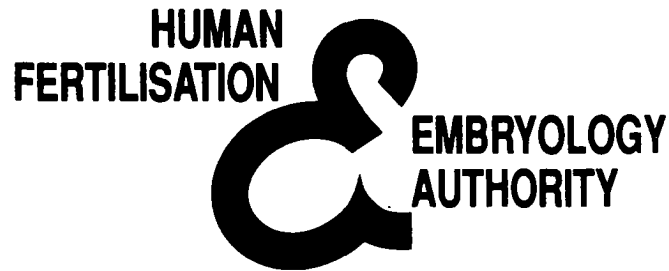




**DONATED OVARIAN TISSUE IN
EMBRYO RESEARCH &
ASSISTED CONCEPTION
PUBLIC CONSULTATION DOCUMENT**



**DONATED OVARIAN TISSUE IN
EMBRYO RESEARCH &
ASSISTED CONCEPTION
PUBLIC CONSULTATION DOCUMENT**

Human Fertilisation & Embryology Authority
Paxton House, 30 Artillery Lane
London E1 7LS

Telephone: 071 377 5077
Fax: 071 377 1871

HUMAN FERTILISATION AND EMBRYOLOGY AUTHORITY

PUBLIC CONSULTATION DOCUMENT

DONATED OVARIAN TISSUE IN EMBRYO RESEARCH AND ASSISTED CONCEPTION

INTRODUCTION

The purpose of this document

1. Ovarian tissue is obtained from the ovary of a woman. The ovary produces the hormones and eggs required for reproduction. This document looks at the issues surrounding the use in research and treatment of ovarian tissue obtained from mature women, from girls or women who have died (cadaveric tissue), or from aborted fetuses. It discusses the reasons for wishing to use ovarian tissue from these sources and some of the surrounding legal, scientific, social, ethical and moral issues and implications.

2. In preparing this consultation document the Human Fertilisation and Embryology Authority (HFEA) has considered these issues and implications and it hopes that the document will prompt a wide range of responses which it will be able to take into account in deciding whether to license embryo research or treatment using this donated material. In reaching conclusions, the HFEA will take account of the interests of all those involved, of donors, patients, children, next-of-kin, scientists, doctors and the wider public.

The Role of the HFEA

3. In 1990 Parliament passed the Human Fertilisation and Embryology Act (the HFE Act) which is concerned with regulating the provision of certain fertility treatments and any research involving human embryos. The HFEA was set up by the Act primarily to regulate, by means of a licensing system, all centres in the UK carrying out:

- a. fertility treatment which involves the use of donated eggs or sperm (eg donor insemination), or of embryos created outside the body (in vitro fertilisation or IVF),
- b. storage of eggs, sperm and embryos, and
- c. research using human embryos.

The Authority is also required to maintain a Code of Practice giving guidance about the proper conduct of the licensed activities. The Code is concerned with areas of practice which raise fundamental social and ethical issues.

4. The HFEA recognises that the emergence of new techniques to alleviate infertility often causes controversy, partly because news of them tends to be broken unexpectedly, sometimes sensationally, to a public unprepared for the issues. Concern is sometimes expressed that scientific and medical research runs ahead of consideration of the ethical and social issues involved, and that the views of the general public are not taken into account at an early stage. The purpose of this document is to stimulate public debate about a particular area of research which is still in the very early stages of development but which may lead to techniques for future medical treatments.

5. There is a valid aim for scientists to discover as much as possible about biological systems. However, science must have an ethical context. The drive to attain knowledge must be weighed against the legal, moral and ethical considerations of society at large. It is also subjected by scientists themselves to consideration of whether or not relevant research should be undertaken, and of how the results of the research are to be applied in practice, for example, in medical treatment.

6. The subject of this consultation is a matter of considerable sensitivity and raises fundamental and complex issues. The HFEA is aware that while the public is generally willing to accept organ donation and the use of fetal tissue for therapeutic purposes generally, it may feel an instinctive repugnance to the use of ovarian tissue from these sources for research or fertility treatment. The HFE Act has resolved the earlier debate on research on human embryos, but the public may still be alarmed that the frontiers of medical science are being pushed forward too far and too fast. The Authority has a role in informing the public about these issues in a balanced way.

7. In the UK, research on fetal and cadaveric tissue has been carried out for many years. This research is aimed at understanding, treating and preventing disease and congenital disorders, (for example, juvenile-onset diabetes, Parkinson's disease and cancer). Widespread benefits could accrue from this research which is carried out under guidelines adopted by the Department of Health. Issues concerned with this type of research lie outside the jurisdiction of the HFEA and are not considered in this document. This document invites views about whether the use of ovarian tissue from adults, cadavers or fetuses may be considered necessary or desirable in the context of licensed fertility treatment or embryo research in the UK.

BACKGROUND

Why are donated eggs needed?

8. For treatment - IVF and some other treatments help women who cannot have a child because they cannot produce normal eggs. Some couples are infertile because the woman is unable to produce eggs at all. This may occur because her ovaries have never developed properly, because of ovarian failure (premature menopause), or because surgery or chemotherapy has made her sterile. Some women who can produce eggs are carriers of inherited disorders which are passed on through the mother's egg, for example, Duchenne's muscular dystrophy or haemophilia. These women can often be helped by receiving donated eggs. Some women who do not respond to the drugs used to produce eggs or who produce possibly abnormal eggs may also benefit from egg donation. At present there is a shortage of donated eggs in the UK and women who need them often face a very long wait for treatment.

9. For research - Under the HFE Act donated eggs can be used to create embryos for research with one or more of the following purposes:

- a. promoting advances in the treatment of infertility,
- b. increasing knowledge about the causes of congenital disease,
- c. increasing knowledge about the causes of miscarriages,
- d. developing more effective techniques of contraception, or
- e. developing methods for detecting the presence of gene or chromosome abnormalities in embryos before implantation.

The shortage of donated eggs is a constraint on this scientific and medical research.

Sources of eggs for donation

10. The current methods of obtaining mature eggs involve adult women in intrusive and uncomfortable medical procedures which are not without risk. The donor needs to take drugs to stimulate the production of several mature eggs. At present, many donors are women undergoing sterilisation who are prepared to donate eggs, or women who have surplus eggs after fertility treatment. Sometimes friends or relatives of a recipient will donate eggs but usually women donate anonymously simply because they wish to help other women who are infertile.

11. Ovarian tissue is another possible source of eggs. The tissue which can be obtained from adults, from cadavers and from aborted fetuses might be a source of:

- a. immature oocytes (eggs) which could be matured in vitro, and of
- b. ovarian tissue for grafting into a recipient woman.

12. The use of donated adult, cadaveric or fetal ovarian tissue could provide many more eggs for IVF and embryo research than are currently available. There are millions of immature eggs in fetal ovaries and thousands still remaining in the normally fertile adult woman which have the potential to ripen into mature eggs.

Actual or potential uses of immature oocytes or ovarian tissue

13. These are:

- a. immature oocytes - in the future it may be possible to mature eggs obtained from donated ovarian tissue from patients and cadavers for use in treatment or research. A South Korean group has already reported that this can be done with ovarian tissue from patients. Live births have resulted from this Korean research.¹ However, it is not yet an established clinical practice. In addition, research done on animals has reached a stage which suggests that adult human ovarian tissue or that from cadavers could become a potential source of eggs in the future;
- b. ovarian tissue grafting - grafting of functional ovarian tissue has been carried out experimentally for nearly a hundred years.² In mice, sheep and guinea pigs live young have been produced following grafting.³ Current development of this technique in humans is directed towards helping women who are likely to become sterile as a result of cancer therapy, using their own tissue which may be removed before therapy and replaced afterwards, so avoiding problems of tissue rejection. This is the female equivalent of a man in a similar position storing his own sperm. In theory donated grafted tissue could help women who are unable to produce their own eggs. The purpose of the grafting would be to allow women to produce eggs in the normal way but the eggs would be genetically the donor's. The biggest problem to be overcome would be that of rejection of the donated tissue.
- c. fetal ovarian tissue - successful transfer of ovarian tissue from mouse fetuses into recipient mice was achieved about 50 years ago resulting in live offspring.⁴ Ovarian tissue from human aborted fetuses has not been used in this way. It is not yet known whether the early female eggs from such material could develop into mature eggs or be capable of giving rise to a baby after fertilisation. Scientists believe that being able to grow and mature human eggs from fetal ovarian tissue is still some way off, as is grafting of human fetal ovarian tissue.

EXISTING CONTROLS

14. There are a number of existing controls operating broadly in this area. These include the following.

The Human Fertilisation and Embryology Act 1990

15. The HFE Act states that no person shall bring about the creation of an embryo outside the body, keep or use an embryo in treatment or research or use donated eggs or sperm in treatment without a licence from the HFEA. In deciding whether or not to grant a licence, the HFEA has to consider whether or not the activities to be carried out are necessary or desirable. It is a criminal offence to carry out a licensable activity without a licence from the HFEA.

The Polkinghorne Committee Code of Practice

16. Existing Department of Health (DH) guidance, known as the Polkinghorne Report⁵, currently covers the use of fetuses and fetal tissue in research and in therapeutic use. However, it does not specifically address the use of ovarian tissue. The Report recognises that the guidelines would need revision to take account of future developments. It states in its Code of Practice that "All research or therapy of an innovative character involving the fetus or fetal tissue should be described in a protocol and be examined by an ethics committee".

17. The Polkinghorne Report states that fetal tissue which has become available following miscarriage or still birth should be dealt with and regarded in the same way as tissue which is derived from abortion carried out under the Abortion Act 1967, as amended.

18. The Polkinghorne Report says that, although not required by law, the consent of the woman should be obtained for the use of aborted fetal tissue in research and treatment. This consent should be separated from the decision on abortion, and the consent should be general, ie, the woman should not be able to specify or be informed of the use, if any, to which the tissue will be put (unlike the consent required under the HFE Act for the use of donated eggs). This is to avoid women being pressurised into seeking abortions in order to provide tissue for particular purposes.

19. The Polkinghorne Report also says that the woman's identity should not be revealed, although some coding will be necessary which will enable her to be traced by those responsible for her care, should information relevant to her clinical management come to light through examination of the fetal tissue.

The Human Tissue Act 1961

20. This Act regulates the use of parts of bodies of people who have died. This use may be for therapeutic purposes or for research purposes.

SCIENTIFIC ISSUES

21. A potential difficulty might be thought to be that a generation of human development would be skipped if fetal ovarian tissue were used in infertility treatment. Ovarian tissue or eggs from an aborted fetus have not been subjected to the pressures which govern survival and normal development to adulthood. This raises questions about the degree of risk of abnormality, at present unquantifiable, in embryos produced using such tissue. This might be seen as breaking a natural law of biology.

22. A further consideration is that miscarriage is frequently due to chromosomal defects in the fetus. Unless it is possible to test a fetus which is the result of a miscarriage for such abnormalities, it may seem inadvisable to consider using ovarian tissue from miscarried fetuses for subsequent fertilisation and treatment because of the risk of transmitting genetic abnormality.

SOCIAL AND MORAL QUESTIONS

23. An important issue in considering these new sources of eggs for treatment is the psychological effect on a child of knowing that it was born from an egg derived from a cadaver or from an aborted fetus. Children born from current techniques using donated eggs or sperm, which are regulated by the HFEA may have to come to terms with the circumstances of their conception. In the case of children born from cadaveric or fetal ovarian tissue, the particular implications of finding out that their genetic mother had died before they were conceived, or was an aborted fetus, are unknown. It would be necessary to consider further how to assess the likely effects on children and their wider family relationships of knowing they were born from donated material from these sources.

24. It has been claimed that permitting the use of fetal tissue to assist conception or to further other desirable medical or scientific research could encourage abortion. On the other hand, many people think it unlikely that women would be induced to get pregnant and/or seek to abort a fetus in order to provide a supply of tissue. The Polkinghorne guidelines should be sufficient to avert the possibility of abortion being postponed until the fetal ovaries have developed.

25. The use of transplanted ovarian tissue or fetal eggs could have implications for controlling the number of children born from one donor. However:

- a. in the case of transplanted ovarian tissue, the recipient of ovarian tissue would be able to plan her family in the usual way because she would be restored to normal fertility;
- b. only a limited amount of ovarian tissue would be available from a single donor and the number of recipients would therefore be self limiting; and
- c. for immature and fetal eggs, control could be in line with the Authority's policy on gamete donors as set out in its Code of Practice, ie the use of a particular donor should cease when the number of offspring reaches 10.

26. Some people believe it is wrong to use material from an aborted fetus which has never lived in order to develop techniques to alleviate infertility, and even eventually to provide the eggs to produce children. On the other hand, it could be said that this was a positive use for material from a fetus which would otherwise be discarded.

CONSENT

27. A major issue to be considered in regard to donation is consent. Informed consent is considered an essential part of donation in current programmes. The law states that specific consent must be given by a person providing eggs or sperm for the treatment of others, for storage or for research.⁶ However, it is not clear how consent in relation to the donation of ovarian tissue or immature oocytes comes within the scope of the Act. The questions then to be considered are:

- a. is consent required?
- b. who should give consent?
- c. should consent be specific?

Is consent required?

28. The fact that consent in respect of donation of ovarian tissue or immature eggs for infertility treatment or research may not be required by law does not make it any the less desirable. The objective of the donation is the same as in the donation of mature eggs. The Authority's view at this stage is that consent should therefore always be obtained.

Who should give consent?

29. Ovarian tissue donation from adult donors is relatively straightforward in that it raises no new issues of consent or donor information (see paragraph 39). The main difference from egg donation, as regulated by the HFE Act, is the maturity of the eggs which are donated. The view of the Authority is that an adult who is willing to donate ovarian tissue and immature eggs should be treated similarly to an adult who is willing to donate mature eggs. This would mean that all adult donors should be given relevant and full information and the opportunity for counselling to enable them to give proper consent, which would specify that their reproductive material could be used in infertility treatment or embryo research.

30. Consent for the use of ovarian tissue and immature eggs from the cadavers of women and children is more complex. Adults are capable of giving consent during their lifetime, to take effect after their death, similar to those required under the HFE Act. A system of consents to use in these circumstances could therefore be introduced. However, whereas a young adult may have expressed a view on donation which might be respected, most young children would not be capable of making an informed mature decision about donation after death. In this case, the question would arise of whether the parents should have a role and what that role should be.

31. The issue of consent to the use of fetal ovarian tissue is most complex of all since a fetus cannot give consent of any kind. The Polkinghorne Report recommends that the consent of the mother should be obtained for the use of aborted fetal tissue in research and therapy. This consent should be separated from the decision on abortion, and the consent should be general.

32. The Polkinghorne Code of Practice says that "It may be desirable to consult the father since, for example, tests on fetal tissue may reveal a finding of potential significance to him, and because he may have knowledge of a transmissible or hereditary disease, but his consent shall not be a requirement nor should he have the power to forbid research or therapy making use of fetal tissue". Some people think that since the father's genetic material would also be transferred to future generations, his consent should also be obtained. Others would say that since the father has no legal say in whether or not a woman should have an abortion, he has no rights over what is done with the fetal material. In reaching a conclusion on this point it will be necessary to identify and address the interests and responsibilities of all those who might be involved:

- the people whose genetic material could be used for the treatment of others or for research,
- the people who might receive treatment using donated genetic material, and

- the child who might be born as a result of using donated genetic material.

Should consent be specific?

33. It has already been suggested that for adult donors consent comparable to that currently required under the HFE Act, should be specifically given for the use of reproductive material.

34. A particular problem in making use of ovarian tissue donations following death is that the public attitude to this might have a negative impact on other donor programmes. Donation of organs or tissue which could enhance the life of the recipient is quite a different matter from donation to create new life. Women who would be willing to donate organs or tissue for the first purpose might not necessarily donate tissue for the second.

35. In addition, with other types of donation it is usual for the hospital to ask the permission of the next-of-kin before any organs or tissue are removed, even if the donor was carrying an organ donor card. However, this potential safeguard of the donor's interests could itself lead to questions being raised about the next-of-kin's motives where they give permission for the ovarian tissue to be used in accordance with the terms of the donor's consent. For example, a donor's parents might consent in the hope that, although they have lost a daughter, they might gain access to a genetic grandchild. Guidelines to deal with such cases would be required if ovarian tissue from cadavers were to be used in the treatment of infertility.

36. The use of fetal ovarian tissue to alleviate infertility could be considered to be a special case in which the specific consent of the woman undergoing the abortion should be obtained since her genetic material would be transferred to subsequent generations. This could be dealt with by introducing the requirement that consent to use of ovarian tissue for infertility treatment should be specific.

37. The Polkinghorne Report has recommended that the woman should not be able to specify the use to which the tissue will be put, or be informed if the tissue is used at all. This is to avoid women being pressurised into having abortions in order to provide tissue for particular purposes. However, this is inconsistent with the approach to consent in the HFE Act and proposed above for other sources of donated tissue and eggs. This issue would need to be resolved if the use of fetal ovarian tissue were to proceed.

OTHER ISSUES OF CONSENT

38. The recommendations of the Polkinghorne Report could be adapted to allow a woman about to undergo an abortion to restrict consent to exclude the use of the fetal tissue for infertility treatment. However, informed consent would require a considerable degree of knowledge and understanding on the part of the woman which could be achieved only through more thorough and effective counselling.

39. If fetal ovarian tissue were to be used, there would remain the question of what information, if any, should be collected to enable any children born following the donation to find out information about their genetic background. In the case of egg donation, the HFEA collects information about donors in the interests of children born as a result of the donation. The HFEA has a legal duty under the HFE Act to tell adults who ask whether they were born as a result of treatment using donated eggs or sperm. People aged 16 or over, who ask, can be told whether they could be related to someone they want to marry. Without basic identifying information (name and age) the Authority could not establish whether or not there is a genetic (or blood) relationship between people who wish to marry. The donor information currently required to be kept under the HFE Act does not extend to the situation where donated fetal ovarian tissue is used.

LEGAL POSITION

40. Section 3(1)(a) of the HFE Act states that no person shall bring about the creation of an embryo outside the body, keep or use an embryo in treatment or research, or use donated eggs or sperm in treatment without a licence. The 1990 Act requires the HFEA to take a view on embryo research and treatment using donated eggs from whatever source. The objective of some projects to obtain eggs is ultimately to carry out embryo research and IVF and the Authority therefore has a role in commenting about the source of the material used to create the embryos. In the case of ovarian grafting, the locus of the Authority is less clearcut. Nevertheless, the issues of ethics and consent arise because the tissue will provide donated eggs.

CONCLUSIONS

41. This document seeks responses so that the Authority can establish an ethical framework within which it might consider any applications it might receive for the use of donated ovarian tissue. The applications could be for treatment or for embryo research with the purposes set out in paragraph 9. The sources of the donated ovarian tissue could be adult women, cadavers or fetuses.

42. Members of the public and interested bodies and organisations are invited to comment, giving reasons, on the following questions:

EGG DONATION

a. Should ways be sought of increasing the supply of eggs for use in research and infertility treatment? If so, what ways can be suggested?

RESEARCH

- b. Should ovarian tissue from live donors be used in research?
- c. Should eggs or ovarian tissue from cadavers be used in research?
- d. Should eggs or ovarian tissue from fetuses be used in research?

TREATMENT

- e. Should ovarian tissue from live donors be used in treatment?
- f. Should eggs or ovarian tissue from cadavers be used in treatment?
- g. Should eggs or ovarian tissue from fetuses be used in treatment?

CONSENT

h. If you think that eggs or ovarian tissue from any of these sources should be allowed to be used in treatment or research, whose consent should be required, when should it be given, and in what form? Should there be any difference in the consents required for eggs or tissue used for research, and eggs or tissue used for treatment?

43. Additional comments are invited on the following:

psychological effects;
clinical and scientific issues;
other moral and ethical issues; and
any legal issues.

44. Please send any comments by 15th July 1994 to:

Mrs Liz Baldock
HFEA
Paxton House
30 Artillery Lane
London
E1 7LS

January 1994

References

1. Cha KY, Koo JJ, Choi DH, Han SY & Yoon TK (1991). Pregnancy after in vitro fertilisation of human follicular oocyte collected from nonstimulated cycles, their culture in vitro and their transfer in a donor oocyte program. Fertility and Sterility, 55:109-113.
2. Morris RT (1895) The Ovarian Graft. New York Medical Journal, 62:436.
3. Parrott DMV (1960) The fertility of mice with orthotopic ovarian grafts derived from frozen tissue. J Reprod Fertility, 1:230-41.

Gosden RG, Baird DT, Wade JC, Webb R (1994) Restoration of fertility to oophorectomized sheep by ovarian autografts stored at -196 C. Human Reproduction, (In press).
- Castle WE, Phillips JC (1911) Successful transfer of guinea pigs ovaries introduced by genetic markers. Carnegie Institution of Washington, Publ No 144.

Eppig JJ & Schroeder AC (1989) Capacity of mouse oocytes from preantral follicles to undergo embryogenesis and development to live young after growth maturation and fertilisation in vitro. Biology of Reprod, 41:268-276
4. Russell WL & Douglass PM (1945) Offspring from unborn mothers. Proceedings of the National Academy of Sciences, USA. 31:402-404.
5. Full title: Review of the Guidance on the Research Use of Fetuses and Fetal Material 1989 Cm 762 HMSO.
6. HFE Act 1990 Schedule 3.