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SEX SELECTION

The recent development of more reliable techniques offers prospective parents a better chance of influencing whether they have a girl or a boy. This has brought a new focus to the issues around sex selection. The Human Fertilisation and Embryology Authority (HFEA) will publish the findings of a wide-ranging review of sex selection regulation and technology, and advise government on whether new legislation is required, later this year. This briefing focuses on the regulatory options for sperm sorting and pre-implantation genetic diagnosis (PGD).

Background

Under normal circumstances, the chance of any child being a particular sex is around 50%; typically 102-106 boys are born for every 100 girls.[1] Motivations for attempting sex selection can be broadly divided into two categories: medical and non-medical.

Medical reasons for carrying out sex selection

There are several hundred known genetic diseases that affect only males – e.g. haemophilia and Duchenne's muscular dystrophy. In families that have a history of such disease, parents may wish to reduce the chance of their child suffering serious illness by having a girl.

Non-medical reasons for carrying out sex selection

- to have a family that includes children of both sexes (known as 'family balancing')
- to rebuild a family after the death of a child with another of the same sex (see box opposite)
- to fulfil a general preference for children of one sex over another. This could be related to economic, cultural or social reasons.

Methods of sex selection

The consumption of particular foods, the use of various vaginal douches and the timing of intercourse in relation to ovulation are some of the many methods believed to influence whether a girl or a boy is conceived. There is little evidence that these methods significantly alter the ratio of male to female births. This briefing will focus on more reliable techniques:

Sperm sorting. Sperm carry either an X chromosome or a Y chromosome; all eggs carry an X chromosome. If an egg is fertilised by an X-bearing sperm, the child will be female, while a Y-bearing sperm will produce a male. Sperm sorting aims to produce a sample with a higher proportion of X- or Y-bearing sperm; this increases the chance of conceiving a child of the preferred sex (see box on page 2). Sperm sorting is not regulated in the UK and is offered by three private clinics.

Pre-implantation genetic diagnosis (PGD). The sex of embryos created by in vitro fertilisation (IVF) can be determined using PGD (see box on page 2). In the UK, PGD may be used for medical reasons only and is available on the NHS. This means that female embryos may be selected where there is a known risk of sons being affected by serious genetic disease.

The Masterton case

Alan and Louise Masterton from Monifieth near Dundee lost their youngest child, three year old daughter Nicole, in 1999. The Mastertons, who have four sons, campaigned for the right to rebuild their family with a daughter.

Louise Masterton had been sterilised after the birth of Nicole and so sperm sorting followed by artificial insemination, which is available and unregulated in the UK, was not an option. The Mastertons wanted the Human Fertilisation and Embryology Authority (HFEA) to allow them to undergo IVF treatment and select a female embryo using pre-implantation genetic diagnosis (PGD). They argued that their family had a psychological need for a daughter. However, the HFEA will only consider an issue if a clinic applies to them for a licence. The Mastertons could not find a UK clinic that was prepared to take up the case on their behalf and so sought treatment in Italy instead. However, only one male embryo was produced, which was donated to an infertile couple.

Selective abortion. The sex of a foetus can be determined by ultrasound examination from around 14 weeks after conception. It is then possible to abort foetuses of the unwanted sex. In the UK, abortion can be carried out for medical reasons but is not permitted on the grounds of sex alone.

Infanticide. Parents can influence whether a child of the unwanted gender survives, either through active infanticide or through neglect, which may lead indirectly to death. This is illegal.

Sperm sorting

The Ericsson technique

The Ericsson technique was developed in the 1970s. A sample of sperm is allowed to swim through a column of albumin with sperm being separated on the basis of their swimming ability. Depending on whether a girl or boy is desired, a different fraction of the sperm is recovered and used to artificially inseminate the woman. Those seeking a girl are also treated with clomiphene citrate; this drug induces ovulation and on its own increases the chance of producing a girl to ~55%. There are limited data available on the pregnancy rate although individual clinics claim that most women become pregnant within three to six attempts.

The technique is licensed to clinics by a US based company, Gametrics. In the UK, a network of three clinics in Birmingham, London and Glasgow have offered the Ericsson technique since 1995 and some 150-200 couples seek treatment each year at a cost of £4000 each; this price includes four attempts at conception. Charges at US clinics are considerably lower: for example $600 (~£360) for each sort and insemination attempt. On the basis of 2,328 births, Gametrics report that 70-75% of couples have a baby of the desired sex. Most are selected for family balancing reasons. However, the technique has attracted controversy as it is not clear how it works and attempts to replicate the results have not always been successful.

MicroSort

MicroSort has been available since 1995 and is currently undergoing clinical trials in the US. The technique uses a fluorescent dye, which is added to the sperm sample and binds to chromosomal DNA. X-bearing sperm contain 2.8% more DNA than Y-bearing sperm so they take up more dye and on this basis the sperm can be sorted. An X- or Y-enriched sperm sample is used for artificial insemination (again women seeking a girl are offered clomiphene citrate) or to create embryos for IVF. The pregnancy rate per treatment cycle is 16% following artificial insemination and 33% following IVF (this compares well with normal IVF).

Only two US laboratories are currently licensed to use MicroSort. They offer a 'mail order' service in collaboration with other clinics; frozen sperm samples are sent to the laboratory and then returned after sorting for use in artificial insemination or IVF. Laboratory charges for sperm sorting start from $2,300 (~£1,400). Within the US, the company permits the technique to be used only for medical or family balancing reasons. 90% of couples seek treatment for family balancing reasons and 80% of those want girls. Of 376 pregnancies the success rate has been 91% for those seeking girls and 76% for boys. Concerns have been expressed that the fluorescent dye may damage the sperm's DNA although, for the births that have taken place with MicroSort so far, the incidence of abnormalities is similar to the general population. Many more births will need to be followed up for statistically significant data on both safety and reliability to be collected.

Regulation

Licensed clinics

Any clinic that offers IVF, PGD, or sperm storage or donation must be licensed by the Human Fertilisation and Embryology Authority (HFEA) and is expected to follow the HFEA code of practice. This code can be used to control licensed clinics' use of techniques that do not themselves require a licence: for example, sperm sorting. The code specifies that PGD should not be used to select the sex of embryos for non-medical reasons, and that sperm sorting should not be used for sex selection at all. The ruling on sperm sorting followed a 1993 public consultation on sex selection; it reflects concerns over the ethics of sex selection and the reliability of sperm sorting.

Unlicensed clinics

Clinics that do not offer any of the techniques that require licensing by the HFEA are freely able to provide sperm sorting services; the Ericsson technique is offered in the UK by unlicensed, and hence unmonitored, clinics. The development of the MicroSort technique has raised concerns at the Department of Health (DH) that more people will be tempted to use sperm sorting. As a result, in 2001 DH asked HFEA to carry out a review of sex selection. The HFEA is considering both technical and ethical issues, and has carried out a public consultation.[2]

Future regulatory options

HFEA will advise DH on the circumstances under which sex selection should be permitted and whether any new legal provisions are needed, later this year. There is no set timetable for a response or action from DH.

Pre-implantation Genetic Diagnosis (PGD)

PGD involves the removal of one cell from an embryo and analysis of the chromosomes and DNA. This is done three days after fertilisation when the embryo has about eight cells and does not appear to affect development. Only embryos with the required genetic characteristics are placed in the woman's uterus. This could mean choosing embryos that are of the desired sex or are known not to be affected by a particular genetic disease. The pregnancy rate per PGD cycle is typically less than 20% (slightly lower than for IVF).

Nine UK clinics are licensed by the HFEA to offer PGD where there is a risk of a serious inherited genetic disease, including sex-linked diseases that affect only males. Clinics must apply to the HFEA each time they want to test for a new genetic disorder. Two clinics are licensed to use PGD to screen for chromosomal abnormalities. These do not run in families but certain groups of parents (for example, women over 35 or with a history of recurrent miscarriages) are known to be at greater risk. PGD is not permitted to be used for sex selection for non-medical reasons. Research evidence has emerged recently showing that IVF babies have a slightly increased risk of being affected by some rare diseases. Insufficient numbers of PGD births have taken place to know if this technique carries additional risks.

One UK clinic, which offers sex selection using PGD by offering part of the treatment through a clinic in Spain, has treated 49 couples over a 3 year period at a cost of £6,000-7,000 each. For many of the couples, the ability to screen for chromosomal diseases was a significant factor in choosing PGD. 60% were seeking sons; this suggests that they were not using sex selection for medical reasons.

Most Council of Europe member states are signatories to (although many have yet to ratify) the Convention on Human Rights and Biomedicine, which states that sex selection should be used only to avoid serious hereditary sex-related disease.[3] Although the UK has not signed this treaty, current UK regulation of sex selection by PGD and selective abortion is in line with it.[4] HFEA reviewed its guidance on PGD in 1999 and is unlikely to propose any change in response to the sex selection consultation.

HFEA is therefore focusing on the options for regulating sperm sorting and on whether sex selection for non-medical reasons should be permitted. It is likely to recommend that regulation is necessary to ensure, as a minimum, the safety and quality of sperm sorting technology and services. A decision would then be needed on when to permit the use of sperm sorting and on whether there is any reason for regulation to be different from PGD. A brief comparison of PGD and sperm sorting technology is given in the table below. Sperm sorting is cheaper, less invasive and more ethically acceptable than PGD, but less reliable. The main options for regulation are:

- **Ban the use of sperm sorting for sex selection**.
- **Permit sperm sorting to be used for sex selection for medical reasons only.** This would bring regulation of sperm sorting in line with that of PGD.
- **Permit sperm sorting to be used for sex selection for medical reasons and for family balancing.** In its consultation, HFEA presented family balancing as the most acceptable form of non-medical sex selection and proposed a model whereby a family with at least two children of one sex and none of the other would be permitted to use sex selection.
- **Permit sperm sorting to be used for any purpose.** The role of regulation would be to protect the public while allowing individuals to make private decisions when planning their family.

However, most ethical and social issues apply to any method of sex selection as discussed below.

PGD vs sperm sorting

	PGD	Sperm sorting
Invasiveness	Highly invasive - requires women to undergo IVF treatment involving intensive hormone treatment and extraction of eggs.	Requires only the collection of a sperm sample from the man, followed by artificial insemination.
Ethical issues	Ethical issues arise over the fate of unneeded embryos.	Only sperm are manipulated in the laboratory.
Pregnancy rate	~20% per cycle.	~16-25% per cycle.
Reliability	Nearly all pregnancies are with a child of the desired sex.	A child of the desired sex is produced in 70-90% of pregnancies.
Safety	Insufficient number of births to draw statistically significant conclusions on safety.	Insufficient number of births to draw statistically significant conclusions on safety.
Cost	From £4000.	UK clinics charge £4000. Fees in the US are much lower – starting from ~£360.

Access to treatment

Sex selection for medical reasons using PGD is available through the NHS. However, funding is limited. Applications for PGD are assessed against common principles with the intention of providing equality of access.[5] These principles include giving greater priority to people with no living or no healthy children. A similar policy is often used to prioritise access to IVF treatment.

HFEA thinks it unlikely that NHS funding would be made available for sex selection for non-medical reasons, including family balancing. While parents can pay to have PGD treatment abroad, it is an expensive and highly invasive process – NHS commissioning guidance points out that a significant number of parents decline treatment when they realise what is involved. Sperm sorting is cheaper and less invasive, and parents may be more able and willing to pay for this service.

Ethical and social issues

Girl/boy preferences

It is not known how widely sex selection would be used in the UK were it easily available and reliable, nor whether there would be a general preference for children of one sex over another. There has long been a strong cultural preference for boys in many Asian countries. Until recently, this has not had a significant impact on the numbers of males and females in the population. However the increasing availability of technology, particularly the use of ultrasound to determine the sex of a foetus, now allows parents to put their preferences into practice (see box on page 4).

There is often an assumption made that this preference for boys applies across cultures. However, it is interesting that 80% of parents approaching MicroSort clinics in the US want a girl (see box on page 2). The reasons for this preference for girls have not been explored but some clinics suggest that it is linked to the improved status of women in US society and a belief that girls are easier to raise.

Impact on the population

There is a chance that the widespread use of sex selection could lead to a skewed population where one sex outnumbered the other. The effects of such an imbalance in the sexes are difficult to predict. Discussion tends to focus on cultures where there is a strong preference for sons. Academics have attempted to model the impact of demographic change and have, for example, suggested that simple social adjustments in India, such as an increase in the remarriage of widows, could rectify an imbalance.

If sex selection were used only for family balancing there would be no overall effect on the balance of the sexes in the population. However, the widespread application of family balancing could lead to a smaller average family size and therefore a reduction in overall births. In the UK, women with two children of the same sex (two girls or two boys) are more likely to have a third child than those with a son and a daughter. Similarly, in India

some families will continue to produce children until they have a son. Studies in India have found that sex selective abortion is progressively more likely to be used the more daughters that a family already has.

Welfare of the child

Where sex selection is used for medical reasons there is a clear intention to benefit the health of a prospective child. However, there is concern from disability and religious groups that sex selection technology will be used to select against progressively milder conditions (an extreme example of this would be colour blindness). The definition of 'serious' disease is not an issue specific to sex selection but applies to any medical intervention that aims to avoid the birth of people with disabilities.

Where sex selection is used for non-medical reasons other issues arise. Clinics offering sex selection say that couples who choose to use their service do not do so lightly: they have planned their family carefully and are therefore well placed to provide a loving home for any child. For them, the decision to use sex selection is a personal one that the state has no role in regulating. Further, some people believe that children benefit from being raised in a family that includes both sons and daughters.

However, sperm sorting at its best leaves a 1 in 10 chance that a child of the 'wrong' sex will be produced. The HFEA consultation reflected widely expressed concerns that the relationship between these children and their parents would be damaged. Similar concerns are expressed even where a child of the preferred sex is produced, based on a belief that parents might have stereotypical expectations of how their child will behave.

Such concerns will not be applicable in all families and a child of the 'right' sex may indeed benefit from a better relationship with its parents. Nevertheless, there is a general feeling that sex selection for non-medical reasons is primarily for the benefit of the parents rather than the child. The question then is, if no-one, including the child, is harmed through the use of sex selection, can the state reasonably prevent parents from using this technology.

Slippery slope

There is considerable debate in the media about 'designer' babies, predicting that developments in genetics will allow parents to specify the type of child that they want. Many groups, including religious groups, regard sex selection to be the first (unacceptable) step along this pathway. Sex selection technology does not enable parents to 'mix and match' the genetic characteristics of their child but it does allow them to make a choice between potential children.

Sex selection in India and China

Chinese census data show that 20 years ago there were 108 boys under the age of 5 for every 100 girls, and that by 2000 this ratio had shifted to 117 boys to 100 girls. This ratio varied across the country with some regions showing a normal 102-106 boys to every 100 girls and other, more prosperous, regions showing ratios of up to 135 boys for every 100 girls. These figures probably exaggerate the true situation because parents may be less likely to register the birth of a daughter so that they can then try for a son; under Chinese law parents have the right to only one child, although since 2002 they have been able to apply to have a second under rules laid down on a regional basis.

However, a similar trend has been reported in India, and again higher levels of education and affluence are directly associated with a greater imbalance in the boy:girl ratio. It appears that in both China and India there is easy access to ultrasound scanning for parents who can afford to pay and that female foetuses are being selectively aborted. A study carried out at a hospital in Punjab, India found that the only girls born following sex determination by ultrasound had been incorrectly identified as male or had a male twin.

The use of ultrasound and abortion for sex selection has been banned since 1994 in India and 1995 in China. In neither case has the legislation been enforced. While some observers argue that effective enforcement of the ban is essential, others believe that this would drive the practice underground where it would be unregulated and potentially unsafe. Instead, they believe that the priority should be to change attitudes so that parents no longer have a preference for sons. Such cultural change is likely to take a long time.

Overview

PGD and sperm sorting are the two sex selection techniques most likely to be used in the UK. PGD is already closely regulated by the HFEA and is permitted for medical reasons only. Sperm sorting is unregulated. The key decisions are therefore whether to introduce regulation of sperm sorting, whether to license it for use under the current level of knowledge and, if so, under what circumstances to permit its use. The debate is likely to focus on how legislation could be used to avoid risks to health and to ensure the welfare of the child. Whether to permit sperm sorting to be used for non-medical reasons such as family balancing is likely to be a particular issue of debate.

Endnotes

1 The reason why slightly greater numbers of boys than girls are born is not known.
2 *Sex selection: choice and responsibility in human reproduction*. HFEA. 2002. The consultation closed on 22 January, 2003. Available via www.hfea.gov.uk.
3 *Article 14: Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on human rights and biomedicine*. ETS no. 164. Opened for signature 1997. Available via www.coe.int
4 Article 18 of the Convention prohibits the creation of human embryos for research purposes. This is permitted in UK law.
5 *Preimplantation genetic diagnosis – guiding principles for commissioners of NHS services*. Department of Health, 2002. Available via www.doh.gov.uk

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