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Introduction

Loane Skene and Janna Thompson

Techniques are now available to screen fetuses for serious genetic disorders and, in the future, more and better means will be available to determine their susceptibility to disorders of lesser kinds, including those which occur later in life. It is now technically possible for parents to choose the sex of their child. In the future they may be able to choose other genetically carried or influenced characteristics of their offspring: height, body shape, and perhaps even such things as musical talent, intelligence and emotional traits. It is now technically possible to clone sheep and other animals. In the future people may have the option of cloning their offspring. All of these techniques, both existing and imagined in the future, raise concerns about the development of a 'sorting society', in which parents are able to choose the children they will – and will not – have. This possibility raises serious ethical, medical and legal issues which are discussed in turn by the authors of this book.

There is widespread support for prenatal tests which give prospective parents the opportunity to find out if their child will have a serious genetic disability, thus giving them the choice of terminating a pregnancy if the fetus is defective. Nevertheless, genetic screening has its critics. Some of these are opponents of abortion who think that even genetically defective fetuses have a right to life. Others worry more about the social implications of screening. Does a practice of detecting and eliminating 'defective' fetuses encourage a negative attitude towards people with disabilities? Is it likely to reduce the willingness of the public to provide support for disabled people and for parents who choose to have a severely disabled child? Is it likely to lead to a reduction in research to improve life prospects of severely disabled people?

However, most ethical debate centres on issues raised by existing and future possibilities for genetic manipulation. Preconception sex selection is widely criticized, especially by feminists, and some governments have banned

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it. The prospect of cloned or 'designer babies' – offspring with a genotype selected by parents – raises difficult questions about the responsibility of parents and medical practitioners, the welfare of children and the future direction of society. Some authors in this volume focus on these issues.

One of the most important ethical considerations concerns medical risk. Cloning is an imperfect and risky technique. Perfecting this technique in the case of animals would not necessarily make it less risky to clone a human being. A cloned child might be subject to serious disorders. It might suffer from premature aging, like Dolly, the first cloned sheep; or from disorders that cannot currently be foreseen or predicted, as is the case for other prospective technologies of genetic manipulation. Even if these technologies can be perfected so that they are relatively risk free, the fact remains that producing the first generations of clones or designer babies will be experiments that could go disastrously wrong. The risks have to be weighed against whatever benefits genetic manipulation is supposed to produce. In her chapter Lynn Gillam explores the advantages that might be derived from the use of cloning to avoid having children with disabilities, but concludes that the benefits do not justify the risks.

Let us assume that in the future the risks will somehow be eliminated and that technologies will be available that would enable parents not only to produce children free of minor as well as major genetic defects but also to select for desired physical, mental and emotional characteristics in their offspring. Would the use of such technologies be ethically acceptable? There are two strong reasons for answering 'yes'.

The first is the assumption that parents should be free to make decisions about having children and what kind of children to have. Genetic screening is widely accepted because it respects the exercise of reproductive freedom. As Agnes Bankier explains, an effort is made by medical practitioners to ensure that those screened have given their informed consent. What parents do about a detected abnormality in their fetus is also up to them, subject to the law. The idea that parents have a 'right' to reproductive freedom can be extended to more controversial cases. Edgar Dahl argues that this freedom should be available to people who want to choose the sex of their children. The same right could be claimed by those who want to choose other characteristics for their offspring.

The second argument for the use of genetic technology focuses on the wellbeing of children. A child with a serious genetic defect is likely to lead a short and miserable life. This seems a good enough moral reason to avoid bringing such a child into the world. In general, it is surely morally better to have healthy children with mental and physical characteristics that will make their lives go well, rather than children who have genetic disadvantages. If this is accepted then it seems that we can hardly avoid an endorsement of genetic manipulation that is much stronger in its implications than that provided by an

appeal to reproductive freedom. If it is morally better to bring a healthy rather than disabled child into the world, then parents who could make use of genetic technology to avoid having a disabled child but choose not to use it are doing something that is morally worse. Julian Savulescu provocatively argues that parents have a moral duty to have the best children that they can: children who are healthy, happy, intelligent, emotionally stable and able to make use of the opportunities that their society makes available. Good parents strive to bring about this result by upbringing and education. According to his reasoning, once a risk-free technology of genetic manipulation becomes available, it will be morally imperative for parents to use it.

This conclusion is likely to be resisted on a number of grounds. For one thing it is in tension with the idea that parents should have reproductive freedom. Those who think that something is a moral imperative are not necessarily asking for the state to enforce it. There may be good reasons for not doing so. But the state already interferes with parental prerogatives for the sake of the wellbeing of children; for example, it will not assist parents who want to use genetic screening to ensure that they have a deaf child or one with achondroplasia (dwarfism), to resemble the parents. It is not unreasonable to suppose that in an age of genetic technology the state will become increasingly involved in determining what kind of children parents are 'allowed' to have. The possibility that the state might use the technology to create a world like that described in Aldous Huxley's novel, *Brave New World*[1] (or worse) is a nightmare invoked by some critics. But even if there is little reason to think that that would happen, the costs of making the use of the technology imperative, if only to avoid genetically caused disabilities, might be considerable.

Leslie Cannold points out that reproductive therapy is intrusive and time consuming. One major reason for insisting on reproductive freedom is the role of women in reproduction. It is their bodies that are subject to risk and manipulation. It is they who have to suffer the intrusions that are imposed by reproductive technology. Even if the moral imperative to have the best possible children never becomes a legal requirement, the pressure on women to undergo the procedures and to avoid unplanned pregnancies will be difficult to resist.

Most supporters of genetic technology do not go as far as Savulescu. They prefer to defend its use as a choice that parents should be free to make. But freedom can be justifiably limited to avoid great social ills or harm to others. A number of the contributors to this volume argue that allowing parents to 'enhance' their children through genetic therapy would cause serious harm to society or to some individuals in it.

Even Dahl, who defends the freedom of parents to choose the sex of their child, allows that this freedom should not be available in circumstances where the choices of parents are likely to result in harm: for example, in those societies where parents would mostly prefer to have boys. The ability of

parents to select the characteristics of their children would open up other possibilities for harm to individuals and societies. Racial discrimination in many societies disadvantages people of minority races. To avoid these disadvantages, Black parents might choose to ensure that their children have the genetic characteristics of Whites. Cannold argues that this way of dealing with discrimination would be bad for society and especially bad for the remaining Black people because it does nothing to challenge the causes of discrimination.

Suppose that all Black parents use the technology to ensure that they have White children. Of course, this would not guarantee that their children are not subject to discrimination. Racists might continue to discriminate on the basis of ancestry, as did the Nazis. But even if parents could use genetic technology to ensure that their children would not be subject to racial discrimination, there are reasons for concern. Robert Sparrow and Mianna Lotz are worried about the way in which genetic sorting tends to identify a person with his or her genetic constitution – the very thing that is done by racists. Sparrow thinks that even existing programmes of genetic testing are problematic because they involve selecting for or against embryos on the basis of their genetic constitution. He thinks that there are morally disturbing similarities between programmes that sort fetuses according to their genetic constitution and the eugenic programmes of the past. Lotz is particularly concerned with the belief in genetic determinism which she thinks genetic technology encourages: the belief that our fate is determined by the nature of our genes.

David Neil, elaborating arguments of Habermas, maintains that programmes that allow parents to choose the characteristics of their children would undermine the very basis of a liberal democratic polity. The existence of such a polity, in his view, depends on the belief that individuals are equally worthy of respect as autonomous, self-determining beings. But if parents, or some other agent, can determine the genetic constitution of offspring, then in an important sense they cease to be self-determining. By becoming objects of manufacture they cease to be equal citizens of a democratic polity.

There is also an issue of intergenerational obligations, as Janna Thompson points out. Should parents today be restricted in their reproductive choices by reason of the effect that those choices may have on later generations? If parents are free to make whatever reproductive choices they choose, will the children born from such 'liberal genetics' ultimately be the 'best' citizens?

Most of the contributors believe that a society must put some limitation on the use of genetic technology. However, Loane Skene, in the concluding chapter, explains the difficulties in using the law to restrict the genetic tests available to parents and the circumstances in which a pregnancy may be terminated if a fetus is found to be affected. If the restricted tests are listed in legislation, the list will quickly become outdated due to the rapid development

of new tests. If tests are limited to 'serious' genetic disorders, that term may be difficult to interpret. Also, in some jurisdictions (like the state of Victoria), fetal abnormality is not in itself a ground for lawful termination of pregnancy.

The issues raised in this book are of the most fundamental and challenging kind when we are deciding the kind of society in which we want to live. Readers will not agree with many of the views presented in the book but the range of views should certainly stimulate and inform discussion.

NOTES AND REFERENCES

1. A. Huxley, *Brave New World* (Harmondsworth: Penguin, 1955).

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Genetic testing, an informed choice

Agnes Bankier and David Cram

Background

This chapter describes a range of genetic tests that are apparently available and how they offer choices to those affected. It explains some of the reasons for genetic testing and some ethical issues that have been raised concerning particular tests, especially in relation to the privacy and control of the information revealed.

Traditionally genetic counselling has aimed to be non-directive and to provide accurate information and an opportunity for discussion so that people can make informed choices for themselves. Decisions need to be based not only on scientific evidence and legal requirements but also on the personal values of the people concerned. In the context of prenatal diagnosis and predictive testing, decisions have life-long consequences for the individual and their families and need due consideration.

Gene testing is available to confirm a diagnosis in a person with symptoms of a condition and can clarify if a healthy relative or a fetus has inherited the gene in the family. Gene testing can thus provide information about the future health of the individual; this is called predictive testing. Carrier testing provides information about risk to offspring. There are screening tests, which are available to the population, for conditions of sufficient frequency that are a low known risk to individuals but can identify those who are in fact at high risk.

Prenatal testing and screening have created options for parents to find out about the health of the baby before it is born. This information can be used to prepare for the birth of the baby. In other circumstances when the baby is likely to have serious problems the parents may elect not to continue the pregnancy. Carrier and diagnostic testing is available to people who are known to be at increased risk because of their family background or on the

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basis of screening tests. Antenatal diagnosis has been widely practised for more than 20 years with a better than 80% uptake. These are invasive tests and involve some risk to the mother or the pregnancy. Pre-implantation genetic diagnosis (PGD) is an alternative reproductive option that has been available for more than ten years.

Ever since the beginning of the Human Genome Project, concerns were raised about the ethical, legal and social implications of genetic testing. Questions have been raised regarding how far we should go in applying these technologies, how far we should go in supporting parental choice regarding the type of children they choose to have. Questions have been asked about the definition of a serious birth defect and how the term disability is defined. Questions have been raised about the potential impact of prenatal diagnosis on the community's regard for people with disabilities, how they are valued and supported by the community and indeed the potential impact on our future society. If we regard prenatal diagnosis as a necessary part of reproductive autonomy, then it is important that all aspects of that choice are equally considered: that we are providing not only alternatives but real choices. Choices need to be supported. Supported choice is not only the right to a safe abortion and post-termination support but also support at every level for the care of the child who could be born with disabilities.

Population screening

Screening tests are available to a whole population, whose members individually are at a low known risk, with the aim of identifying those at increased risk. A screening test is not a diagnosis. Population screening may be undertaken during or before pregnancy (to identify problems in fetal development or carrier status in the parent) or after a child is born (newborn screening).

Pregnancy screening

Maternal serum screening

In maternal serum screening, participation is voluntary and involves a blood test. The screening programme will identify individuals who are at increased risk for Down syndrome or spina bifida. The risk for other chromosome abnormalities may be identified at the same time. The risk is determined according to agreed parameters, and women identified as having increased risk will have the option of more definitive testing to clarify their situation. They need the opportunity to understand the relevant information to enable them to make informed decisions.

Usually this information about the screening programme is offered in written form and genetic counselling is available to individuals who are found

by screening to be at increased risk. Most of those at increased risk will still have a normal result on specific testing. It is important to ensure that individuals considering screening should understand the consequences of that decision later on, that is, that it could lead to consideration of further testing and possible termination of pregnancy.

Maternal serum screening may be offered at one of two times in the course of the pregnancy. In the first trimester a blood test at 10–12 weeks' gestation, combined with nuchal translucency ultrasound measurements at 11–13 weeks' gestation, can detect 90% of babies with Down syndrome. Maternal serum screening in the second trimester involves measurements of three metabolites (triple screen: alphafetoprotein, human chorionic gonadotrophin, unconjugated oestriol) or four metabolites (quadruple screen: alphafetoprotein, free beta human chorionic gonadotrophin, unconjugated oestriol, inhibin A) in maternal blood. The risk assessment is reported, increased risk being the top 5% of the measured value. Those at increased risk may choose to have chorionic villous sampling (CVS) or amniocentesis for a definitive diagnosis.

In Victoria 70% of pregnant women now elect to have maternal serum screening in pregnancy. Since the increase in the number of women having screening tests in pregnancy, there has been a gradual decline over the past five years in the number having invasive tests of CVS and amniocentesis. Overall more older women are having babies: compare 7.8% of women over 35 years in 1985, with 22.4% in 2004 in Victoria. The proportion of babies with Down syndrome born to younger mothers less than 34 years of age (who are much less likely to have maternal serum screening) was 70.9% in 1990 and 53.5% in 2003. The live birth prevalence of Down syndrome has not decreased significantly, as a result, despite screening and testing of older women.

Ultrasound screening

The measure of nuchal translucency in the first trimester, combined with first trimester serum screening, has been a powerful screen for chromosomal abnormalities such as Down syndrome, enabling a detection rate of up to 90%.

Carrier screening in target groups

Carrier testing can be offered to identify carriers, which in turn provides choices for them. Genes come in pairs and in a single copy may not cause signs or symptoms. In a recessively inherited condition, the person who carries a single copy of the recessive gene is healthy but can have a child born with the condition if their partner is also a carrier of the gene. All individuals carry some recessively inherited gene faults. In certain populations the likelihood of being a carrier of a particular gene is increased. Once an individual is identified as a carrier they are offered genetic counselling

regarding the risks to their offspring. 'Cascade carrier testing' is then offered to the person's immediate blood relatives. That person is asked to inform family members about their potential risk and the individual is supported in doing so. One highly successful screening programme has been for Tay-Sachs disease. This worldwide initiative has virtually eliminated the condition from the Ashkenazi Jewish population, despite a carrier frequency of one in 25 in that population.

Newborn screening

Newborn screening has been established for conditions that are a significant health problem, have a known cause, a safe and reliable test, known treatment intervention and established cost-benefit. Since the late 1960s babies have been tested at a few days of age for treatable conditions in newborn screening programmes that were initially established to screen for phenylketonuria (PKU) from 1964. Testing for hypothyroidism was added in 1977 and for cystic fibrosis in 1989. In a number of centres, including all Australian states, Tandem mass spectrometry was introduced in the past decade so that some 25 additional metabolic conditions can now be screened. Screening for other disorders has been added in different centres. A blood spot, obtained by a heel prick, is tested for these conditions so that treatment can be started before the baby gets sick to prevent damage. Most of the conditions are inherited and will not be obvious at birth, even to experienced paediatricians. The blood is collected onto a special paper card, called a Guthrie card, and more recently called a newborn screening card (NBS card).

Whilst newborn screening is regarded as part of the standard of care for babies, and is clearly for the health benefit of the baby, screening is not mandated in most places and is provided as a choice to be approved by the parents. In the past decade, new genetic technologies have made it potentially possible to do gene testing on blood spots, as well as the earlier screening tests. Controversy has surrounded the storage and potential use of the blood spots for purposes other than newborn screening.

Whilst the NBS card is regarded as a health record and as such its storage and access is governed by federal and state privacy legislation, there is lack of legal clarity with respect to the status of the blood sample once it is removed from the card. The blood is no longer a health record and its use is not protected by privacy legislation or the Human Tissue Act or any other current legislation. In Victoria, access to past NBS cards is restricted by specific protocols and self-regulation. Retention of NBS card is of potential benefit to the baby, the family and to the community. Access to the blood spots is restricted to the following specific circumstances:

- **Quality assurance**: access to the blood spot is essential in case of misdiagnosis of a genetic condition. Thankfully no such case has occurred

in Victoria to date, but if it did occur it would be necessary to go back to the NBS card of all babies born on that day to ensure that there were no other undiagnosed/misdiagnosed children. Access to anonymized Guthrie cards may also be necessary when the service establishes new or improved tests such as those using tandem mass spectrometry.

- **Diagnosis**: the NBS card is a convenient way of transporting blood samples for testing interstate when a particular test is not available in Victoria (this is done with parental consent). Cards may also be used for retrospective diagnosis for the child, e.g., to establish that an infection was congenital rather than occurring some time after birth. Cards may be tested for the benefit of close blood relatives of a deceased child, e.g., to establish the genetic mutation in a child who died of muscular dystrophy in order to clarify whether a sister is a genetic carrier of the mutation.
- **Forensic identification** at the request of the Coroner's Court and by court order for identification of deceased persons.
- **Research** approved by a duly constituted Hospital Research Ethics Committee (HREC). This is permitted with parental consent if identified blood samples from the NBS card are used.
- **HREC** approval is significant for using de-identified samples, such as determining the frequency of a disease-causing mutation. In such cases, access is given only to de-identified punched out blood spots, and not the NBS card itself.

Diagnostic tests

Diagnostic tests are more specific than population screening and they can also be undertaken before birth, after birth and during a patient's lifetime.

Ultrasound diagnosis

For pregnant women, ultrasound has been used to date the pregnancy, and to establish the position of the placenta and the growth of the fetus. More sophisticated ultrasound examination performed by experts – the anatomical ultrasound examination – at the appropriate time can also identify structural birth defects. Anatomical ultrasound is most informative between 18 and 20 weeks of pregnancy. In addition, ultrasound guidance has been used for invasive tests of CVS, amniocentesis or fetal biopsy.

In one study, chromosome analysis performed after ultrasound detection of a structural abnormality led to the identification of a significant chromosome abnormality in 17.4% of a group of women and in women over 37 years of age, in 25% of them. Of the major abnormalities detected through ultrasound 61.1% were associated with increased nuchal thickening.[1]