PRE BIRTH TESTING

BIOETHICS COUNCIL

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PRE BIRTH TESTING

There are many tests before birth to identify whether a child may suffer from possible illnesses, diseases or disorders. Some of these are tests for genetic conditions, but others are not. Some commonly known tests used in New Zealand are maternal blood tests, ultrasound and amniocentesis.

Genetic testing

Pre-birth genetic testing[1] is not new. For many years pregnant women have had access to tests to find out whether their unborn children have certain genetic conditions, such as Down syndrome. Tests are now available for many conditions. Some, such as Huntington's,[2] eventually result in suffering and death, while other conditions are treatable or may have more minor effects on the child.

Before the introduction of in vitro fertilisation (IVF) any testing had to be done during pregnancy. Since 1990 it has been possible to do testing before the woman becomes pregnant at the stage that the embryo is in the test tube.

Non-genetic testing

Pre-birth testing is not limited to genetic conditions. Most pregnant women have ultra sound scans which can diagnose abnormalities in the foetus[3] and blood tests can reveal conditions such as HIV.

If a test shows that there is a problem, the mother/parents must decide whether to continue the pregnancy or terminate it. The legal regulation of decisions made following testing during pregnancy is through restrictions on abortion.[4]

Preimplantation genetic diagnosis (PGD)

In the mid-1980s, research began in the United Kingdom to find out whether an embryo created through in vitro fertilisation (IVF) could be tested by using preimplantation genetic diagnosis (PGD) to diagnose a genetic condition. This is done by testing one or two cells removed from an embryo before the embryo is transferred to the mother, instead of during the pregnancy. If the mother/parents have decided that they do not want to have a child with that particular condition, an embryo free of the condition is chosen. This process avoids having to decide whether or not to abort an affected foetus once the woman is pregnant. People wanting to use PGD for inherited conditions usually already have one child or a close relative affected by the condition.

Extension of testing

The uses of pre-birth testing are widening and it is now possible to test for genes which show that there is a chance that the child will have a particular condition, or that the condition tested for may develop either during childhood or later in life. With greater possibilities will come more choices and these choices may have effects on society.

Toi te Taiao: the Bioethics Council is going to have conversations with members of the public about the present and future use of pre-birth testing. The guidelines controlling when PGD may be used are about to be reviewed.
We invite you to consider issues such as:

- How the tests might be used;
- Who should have access to them;
- Whether they should be government funded;
- Whether there should be limits on their uses; and
- Who should make the decisions in this area.

Do you think there are other issues we should discuss?

TESTING DURING PREGNANCY

Once a woman is pregnant, some of the tests carried out are for genetic conditions and some are not. Blood tests[5] and ultrasound scans are routine parts of prenatal care.

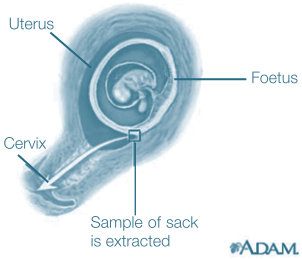


Fig 1 This is how chorionic villus sampling is done

You can find out things about the foetus such as whether parts of the body are missing or its sex. You can also discover whether there is a chance that the foetus may have Down syndrome.[6]

If these procedures indicate a possible problem, further prenatal testing may follow. This usually involves amniocentesis or chorionic villus sampling (see fig 1), to obtain tissue to test. If the test detects an abnormality, mothers/parents are faced with a decision whether or not to terminate the pregnancy. This is a private decision regulated by the existing abortion legislation.[7]

Why test during pregnancy?

Some of the reasons for testing during pregnancy are:

- Standard practice;
- The age of the mother;
- Family history of genetic disease;
- The blood tests or ultrasound show there could be a problem.

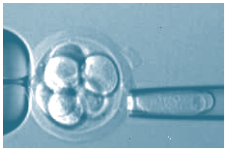
Issues and uncertainties

- Some prenatal testing has the potential to cause a miscarriage. For example, with amniocentesis around 1 in 200 procedures have some type of complication (e.g., infection, miscarriage or poking the baby with the needle).
- There is no certainty of a healthy child, as the baby may still have a condition for which it was not tested or suffer injury or illness during or after birth.
- Some women find it difficult to decide whether or not to terminate an established pregnancy.
- Some women who decide to terminate a pregnancy may have physical and psychological consequences from the abortion.

TESTING EMBRYOS

Preimplantation genetic diagnosis (PGD)

Fig. 2 Removal of a cell from an embryo



Preimplantation genetic diagnosis (PGD) is used before an embryo is transferred to the woman, to diagnose chromosomal abnormalities[8] and single gene disorders,[9] such as cystic fibrosis and muscular dystrophy.

As with using IVF for assisted reproduction, eggs are removed from a woman then fertilised in the laboratory (See fig. 3). Two to four days after fertilisation, the embryo consists of approximately eight cells. One or two cells are removed (see fig. 2) and genetic tests are done on them. PGD uses two basic techniques to analyse genetic material from the embryo:

- Chromosomal analysis to assess the number or structure of chromosomes[10] present in the cells, or
- DNA analysis to detect specific gene mutations.[11]

Embryos that do not have the defect tested for are selected to be transferred into the woman's uterus to start a pregnancy.

Why use preimplantation genetic diagnosis (PGD)?

Most people using PGD know that there is a genetic condition in their family and wish to avoid having a child with that condition. They may choose PGD rather than testing during pregnancy because:

- Only embryos that will not have the condition are transferred into the woman to start a pregnancy.
- It may be less stressful for mothers/parents to select unaffected embryos than to become pregnant naturally and then have to decide whether or not the pregnancy should be terminated.

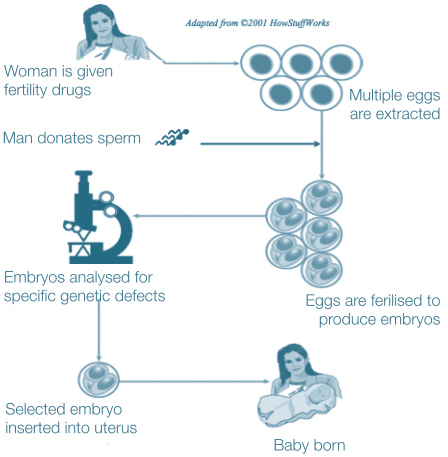


Fig 3 Preimplantation Genetic Diagnosis (PGD)

- It avoids the need to make a decision whether or not to have an abortion

Issues and uncertainties

PGD has only recently become available In New Zealand. Worldwide, since it began in 1990, more than 1,000 babies have been born after PGD. In the future, it is likely that PGD tests will become be more reliable and there will be tests for more diseases and conditions but at the present time PGD has limitations and risks:

- PGD is technically very difficult because only one or two cells are available for genetic testing.
- PGD tests are complex and the results are not always reliable, so that sometimes the embryo still has the genetic defect despite the negative result. Further testing during the pregnancy is often carried out to confirm that the child will not have the condition.
- There is no certainty that a pregnancy will occur after the embryo is transferred into the woman.
- PGD is expensive.
- There is no guarantee that the child will be healthy, as PGD only tests for a specific condition, usually one already experienced by family members.
- Some people think a pregnancy is less likely from an embryo that has been tested although there is no evidence of this.
- It is not yet known whether there are long-term effects on the people born from embryos that have had cells removed for testing. Short term, babies born following PGD are as healthy as those born using IVF.
- PGD does not appear to increase the known risks of IVF.[12]

Like IVF, PGD is ethically controversial because both may involve the destruction of embryos.[13] In addition, PGD involves screening of embryos and choosing which embryo will be used to have a child. One example is to select a female embryo to avoid a disorder that only boys get.

Most PGD is to diagnose medical conditions such as cystic fibrosis and muscular dystrophy, which develop in infants. However, it could be used for non-medical purposes. One example is that in other places, such as the United States, PGD can be used to choose a girl or a boy. Some people want to make this choice to balance their family but others just prefer a child of a particular sex.

In the United Kingdom it is possible to use PGD to diagnose conditions that may develop after infancy. These are called late onset conditions.[14] Some people are concerned about this because the person may have a good life until the disease occurs and by then a treatment may be available.

Tests for genetic susceptibility to diseases like hereditary breast cancer also cause concern because there is no guarantee that the disease will develop. This is called low penetrance.

For more information about PGD go to **www.dnapolicy.org**

THINGS TO THINK ABOUT

There are many issues that people could take into account when thinking about pre-birth testing. When considering these, think about whether you, or people you know, have other issues or views to share.

- **Who should decide?** Many people value individual choice, yet there are times when individual choices may affect or harm others or society. For example, criminal law prohibits certain actions so that people may live together in society.

  Some people say that mothers/parents are in the best position to make the decisions about pre-birth testing.

  On the other hand, these decisions may have wider implications, such as having effects on existing and future children and on disabled persons so, at some point, interference with people's reproductive freedom may be justified.

- **Carriers** Some people are carriers of inherited diseases (e.g. haemophilia) which means that even though they do not have the condition, they can pass it on to their children. Mothers/parents could use pre-birth testing to avoid having a child who is a carrier of an inherited disease. By doing this the condition could be almost eliminated from that family. Because they would not be carriers the children would not be faced with difficult decisions when they came to have their own children. Some people think this would be a good thing for their family.

  However, carrier children usually have normal health and they could choose whether or not to have children or use pre-birth testing to make sure their children do not have the disorder.

- **Quality of life** By using pre-birth testing we can find out whether a child will have a medical condition that would cause them early death or pain and suffering or reduce their enjoyment of life. Some people think that we should use pre-birth testing to give children the best chance possible to have a healthy life.

  However, many people with disabilities say they value their lives and that they make a worthwhile contribution to society.

- **Parent/child relationship** Let's repeat the difference between PGD and prenatal testing. PGD involves testing embryos and selecting an embryo to implant in the mother and prenatal testing involves testing during pregnancy.

  Some people say if parents can control the genetic make-up of their children that could affect the parent/child relationship.

  Others say that most parents want to give their children the best chance to have a good life and there are many ways that parents "shape" their children before and after birth, such as the choice of partner and the type of upbringing.

It's important to remember that:

1. Despite pre-birth testing the child could still have some medical condition for which the embryo or foetus was not tested.
2. Present scientific knowledge does not make it possible to "design" a child. Children can only inherit the genetic make-up of their parents.

- **Right to life** Some people object to all prenatal testing because it may result in the destruction of embryos or foetuses which they believe have a right to life or the same rights as a person.

  However, some people do not use pre-birth testing to prevent the birth of a child with an illness or disability. They use it to give themselves time to prepare themselves for the birth of a child with a disorder.

- **Illness or enhancement** In the future, it may be possible to enhance particular abilities, such as intelligence or athletic ability. However this is not possible at present and not likely in the foreseeable future, because many genes are involved and environment is also very important.

  Many people agree that it is acceptable to use pre-birth testing to prevent illnesses. However, there is no clear distinction between testing to prevent a child being born with a medical condition, and use of PGD for enhancement - the production of cleverer or more talented people.

  Some people point out that parents already try to influence their child's capabilities and development by things such as reading to their children, providing music lessons, coaching them in particular sports and organising extra maths classes. What is different about these attempts to produce more able and successful children and the possible uses of PGD or prenatal testing?

- **Nature** Some people do not like the idea of reproductive technologies because they think they interfere with God's will or the natural order of things.

  Other people say using prenatal testing might alter the gene pool so that there would be less human variety.[15] However, PGD will not have an effect in the short term because only a few people will use it.

  Testing during pregnancy is common and has reduced the numbers of children born with some conditions. For example, around 60 pregnancies a year are terminated after a positive test for Down syndrome.[16]

- **Disabilities** Pre-birth testing could have impacts on the disabled community as fewer people with genetic or congenital conditions will be born. Some people think that if we have fewer people with disabilities, the things disabled people need may not be provided.

  They argue that all children bring benefits and joys and should be valued and say that disability should be accepted as being part of life.

  People have argued that parents could be under pressure to avoid having children with disabilities. This could lead to discrimination against those born with genetic or congenital conditions.

  However, others say that many disabilities occur during or after birth and so these technologies will not greatly reduce the numbers of disabled people in the community.

- **Widening range of tests** Originally, most tests were for serious health conditions, but now more tests are possible. People will soon be able to make choices about whether to have a child with a chance of a genetic condition or one that might not develop until after childhood. On the one hand, by the time the condition develops the person could have had a good life and/or by then the condition may be treatable.

  But some people argue that knowing that s/he carries the gene may unnecessarily concern the child (the "worried well") and also that the conditions tested for and the treatments are so unpleasant it is best to avoid any risk of them. Also, the treatment may not succeed.

Remember: **penetrance** is the risk that the child will actually develop the condition and **late onset** means that if it does develop it, may be many years in the future. For example, PGD can now be used to detect the genes associated with some forms of inherited cancer.[17]

SAVIOUR SIBLINGS

Some people who have a sick child needing medical treatment want to use PGD for tissue typing to have a new baby (sometimes called a "saviour sibling") who genetically matches the sick child so the baby's cord blood or bone marrow will be suitable to use to treat the sick child.

Some people think this makes the saviour sibling into a product, rather than having a child for its own sake. People wanting to do this say they will love all their children and that unless you have been in their situation you cannot understand it.

At present, PGD to have a saviour sibling must be approved by an ethics committee on a case-by-case basis. The guidelines state that:

- The sick child must suffer from a single gene disorder or familial sex-linked disorder;[18]
- The parents must only intend to use the cord blood of the saviour sibling;
- There must be no other treatment available; and
- The embryo must be a sibling of the affected child.

At present, PGD is only allowed if the sick child has an inherited condition that the new baby might also inherit and it cannot be used to produce a saviour sibling for a child with a condition that is not inherited, such as leukaemia.

WHAT ARE THE LEGAL LIMITS?

In New Zealand, the legal position is:

- Testing may be carried out during pregnancy;
- PGD may not be used for non-medical sex selection (such as parents who want to balance their families);[19]
- PGD may not be used to alter the genetic constitution of an embryo;
- PGD may not be used to select embryos with a genetic impairment seen in a parent;
- PGD may be used in the following situations:
    - A single gene disorder has been identified in the family and there is a 25% or greater risk of an affected pregnancy.
    - For sex determination if familial sex-linked disorders have been identified in the family and no test is available for the specific mutation.
    - For familial chromosomal disorders if the disorder has been identified in the family.
    - For non-familial chromosomal disorders if the woman is of advanced reproductive age, or has had recurrent implantation failure or miscarriage.

In addition, the disorder must be going to cause the child to be "seriously impaired". Serious impairment is not defined, but the fertility clinic, together with a clinical geneticist, must decide that the disorder is likely to be serious.
People have differing views about what which conditions are serious. Some people say that if this decision must be made by "experts", it interferes with the mother's/ parents' rights.

The guidelines for the use of PGD must be reviewed in 2007 by the Advisory Committee on Assisted Reproductive Technologies (ACART). You will be able to make a submission to ACART. If you wish to find out about ACART's processes visit their website: **http://www.newhealth.govt.nz/acart.**
Toi te Taiao: the Bioethics Council plans to make a submission to ACART which will be informed by what it has heard from the public.

END NOTES

1 Genetic testing identifies changes in chromosomes, genes, or proteins that are associated with conditions like Down syndrome. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person's chance of developing or passing on a genetic condition. Genetic testing during pregnancy usually involves examining DNA taken from a chorionic villus sample or from cells within the amniotic fluid (the fluid that surrounds a foetus during pregnancy) for some anomaly that flags a disease or disorder.

2 Huntington's disease (HD) results from genetically programmed degeneration of brain cells, called neurons, in certain areas of the brain. This degeneration causes uncontrolled movements, loss of intellectual faculties, and emotional disturbance. HD is a familial disease, passed from parent to child through a mutation in the normal gene. Each child of a parent with the HD gene has a 50-50 chance of inheriting the gene. If a child does not inherit the HD gene, he or she will not develop the disease and cannot pass it to subsequent generations. A person who inherits the HD gene will eventually develop the disease. The physical symptoms commonly become noticeable in a person's forties, but can occur at any age. If the age of onset is below 20 years then it is known as Juvenile HD.

3 Common examples include hydrocephalus (water on the brain), anencephaly (absence of brain), myelomeningocoele (a type of spina bifida), achondroplasia and other dwarfism, spina bifida, exomphalos (a serious eye bulge), gastroschisis (intestine protruding through a hole in the abdomen), duodenal atresia (the bowel has not developed into a tube) and foetal hydrops (rhesus factor incompatibility where the mother's body reacts against the foetus).

4 The Crimes Act s187A provides that in the case of a pregnancy of not more than 20 weeks' gestation, an abortion is unlawful unless the person doing the act believes that the continuance of the pregnancy would result in serious danger to the life, or to the physical or mental health, of the woman or girl or that there is a substantial risk that the child, if born, would be so physically or mentally abnormal as to be seriously handicapped. If the pregnancy is of more than 20 weeks' gestation, the person doing the act must believe that the miscarriage is necessary to save the life of the woman or girl or to prevent serious permanent injury to her physical or mental health.

5 For example, levels from a blood test of a protein hormone called human chorionic gonadotropin (hCG) in combination with alpha-fetoprotein (AFP) can indicate whether the baby has abnormalities in the number of chromosomes. A high level of hCG in combination with a low level of AFP suggests a chromosomal abnormality. However, this test is not yet widely available in New Zealand.

6 First trimester markers for chromosomal abnormalities, such as the absence of foetal nasal bone, or an increased foetal nuchal translucency (the area at the back of the neck) are now in common use to enable detection of Down syndrome foetuses.

7 There have been controversies about such decisions, such as in the United Kingdom over an abortion after 24 weeks gestation of a foetus with a cleft palate. Cleft palate is a condition in which the two plates of the skull that form the roof of the mouth are not completely joined. In most cases, there is also a cleft lip. A cleft lip or palate can be treated with surgery during the child's first year with highly successful results, although it may be a symptom of a more serious medical condition. Cleft lips or palates occur in somewhere between one in 600 and one in 800 births. The terms hare lip or hair lip are sometimes used colloquially to describe the condition because of the resemblance of a hare's lip. With more recent sonograph equipment, conditions such as cleft lips/ palate and congenital cardiac abnormalities may be diagnosed before birth.

8 Chromosomal disorders are abnormalities in the number or structure of the chromosomes. These disorders are often severe and may include miscarriage, developmental delay and a variety of physical deformities or even death. Examples include Down syndrome, Turner syndrome, and Klinefelter syndrome.

9 Single gene disorders are genetic conditions caused by the alteration or mutation of a specific gene in the affected person's DNA. Single gene disorders are inheritable and can run in families. Individuals with a family history of a single gene disorder may be at risk for passing the condition onto their children.

10 A chromosome is a single large molecule of DNA, and is the basic "unit" of DNA in a cell. It is a very long, continuous piece of DNA (a single DNA molecule), which contains many genes, regulatory elements and other intervening nucleotide sequences. In some circumstances "chromosome" includes this DNA and the DNA bound proteins which package and manage the DNA.

11 A gene mutation is a permanent change in the DNA sequence that makes up a gene. Mutations range in size from a single DNA building block (DNA base) to a large segment of a chromosome. Gene mutations occur in two ways: they can be inherited from a parent or acquired during a person's lifetime. Mutations that are passed from parent to child are called hereditary mutations or germline mutations (because they are present in the egg and sperm cells, which are also called germ cells). This type of mutation is present throughout a person's life in virtually every cell in the body. Mutations that occur only in an egg or sperm cell, or those that occur just after fertilisation, are called new (de novo) mutations. De novo mutations may explain genetic disorders in which an affected child has a mutation in every cell, but has no family history of the disorder.

12 Such as ovarian hyper-stimulation of the woman when her eggs are collected and possible multiple birth if more than one embryo is implanted.

13 IVF also commonly results in the destruction of embryos as a number of embryos may be created and one or two of the embryo(s) with the greatest developmental potential are selected for transfer into the uterus. Unimplanted embryos can be frozen and later thawed to give another chance of pregnancy. About 60-70% of embryos survive this procedure.

14 An example is Alzheimer's disease. There are different classes of Alzheimer's disease, depending on the genetic cause and symptoms. Onset of Alzheimer's disease before age 60 is known as early onset. Some families with inherited Alzheimer's disease develop symptoms in their 20s although this is unusual. Early onset familial Alzheimer's disease often has a single genetic cause, whereas late onset Alzheimer's is more complicated and may have multiple unknown genetic and environmental causes.

15 New genetic mutations occur all the time in families where they have not previously appeared (e.g. for haemophilia and X-linked muscular dystrophies). Everyone carries about 10-20 serious mutations although most will not result in disease because two mutated copies are usually necessary to result in a disorder.

16 About half of all pregnant women have a nuchal translucency test - an ultrasound measure of the clear space in the tissue at the back of the baby's head to screen for a risk of Down syndrome. This test is done between 11 and 13 weeks of pregnancy. The test has a high rate of false positives so almost 3000 women a year undergo amniocentesis to confirm their baby does not have Down syndrome. Amniocentesis causes spontaneous miscarriage or other complication in around 1 in 200 procedures. It is proposed to improve screening by carrying out blood tests at the same time as the nuchal translucency and again between 14 and 18 weeks of pregnancy.

17 Inherited breast and ovarian cancer caused by mutations in the BRCA 1 or 2 genes has an approximate 80% penetrance in women and 6% in men. This means that 80% of women and 6% of men with one copy of a BRCA mutation will develop breast cancer. This is called a lower penetrance condition because not everyone with it will develop the cancer.

18 If a mutant gene is part of the X chromosome (a sex chromosome; females have two X chromosomes per pair, and males have an X chromosome and a Y chromosome), the disease is sex-linked. All male offspring are affected because the Y chromosome of the XY pair does not have a compensating normal gene. Because the mutation is on the X chromosome, however, and males transmit only the Y chromosome to their sons during fertilisation, males do not transmit the disease to male offspring but only to female offspring.

19 Human Assisted Reproductive Technology Act 2004, s11.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