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New hope for genetic disorders

Pre-implantation genetic diagnosis

Pre-implantation genetic diagnosis (PGD) represents the latest technology in genetic testing. However it also opens up an ethical minefield between the balance of scientific advances and "playing God". The purpose of this article is to provide information about the issues, preparing GPs and primary care professionals for questions from patients.

> "It is vital that GPs and other health professionals know more about genetic testing and genetic services in New Zealand so they can better facilitate informed consent, know when to refer patients for testing and be able to offer some degree of genetic counselling if required." *Professor Mark Henaghan, Human Genome Research Project.*

What is pre-implantation genetic diagnosis?

Until recently the only testing option available for parents at risk of conceiving a child with a genetic disorder was prenatal diagnosis. This involves sampling foetal cells through the placenta (chorionic villus sampling) or the amniotic fluid (amniocentesis). Couples then decide whether to abort the foetus or continue with the pregnancy.

PGD is a procedure used in conjunction with in vitro fertilisation to test embryos for serious inherited genetic conditions and chromosomal abnormalities before they are transferred to the uterus. This enables parents to make a choice about the future of an affected embryo rather than an affected foetus.

Currently PGD can be used for three different abnormalities:

- Single gene defects e.g. cystic fibrosis, Huntington's disease, haemophilia
- Numerical chromosomal abnormalities (aneuploidy) e.g. Down syndrome, Turner syndrome
- Structural chromosomal abnormalities e.g. translocations

PGD can be used for couples who are carriers of a familial genetic disorder that would cause serious impairment for the child and for which there is a 25% or greater risk of an affected pregnancy.

It may also be used for couples who are having trouble conceiving due to advanced reproductive age or who have experienced recurrent implantation failure or miscarriage.

PGD involves:

1. Creation of an embryo via IVF
2. Removal of one or two cells from the embryo

3. Genetic testing of these cells for specific genetic conditions or chromosomal abnormalities
4. Transfer of unaffected embryos to the uterus

The Ministry of Health currently funds 40 cycles of IVF/PGD a year to detect serious inherited genetic diseases. There is limited availability of PGD in New Zealand (see page 7). PGD is most commonly used in New Zealand to test for Huntington's disease, cystic fibrosis and spinal muscular atrophy.

Patients considering PGD should be given relevant information, advice on alternatives and referral for genetic and psychosocial counselling from a trained genetic counsellor.

Gender selection

PGD can be used in New Zealand to select the gender of a child, if it prevents transmission of a sex-linked genetic condition such as haemophilia or Duchenne's muscular dystrophy, when a specific test is not available.

Gender selection for social reasons (e.g. family balancing) is not legal in New Zealand, although it is allowed in some other countries such as the United States. The use of PGD for any other social reasons e.g. beauty or intelligence, is not currently scientifically possible, nor would it be permitted.

Many people may perceive that gender selection for social reasons is an unimportant application for this technology. There is also concern that gender selection will result in unbalanced selection of male embryos. In the "Who gets born" report, the Bioethics Council of New Zealand found that there was insufficient cultural, ethical and spiritual reasons to prohibit the use of PGD for social reasons such as "family balancing". They have recommended that this use of PGD be re-examined in New Zealand.

> “I long for a daughter and sister for my four boys to 'balance' our family... I have thoroughly researched the new PGD technology available for sex selection, which is freely available in the US, and we are currently considering using this technology to weigh the chances of our next (and final) pregnancy being a girl. I believe I should have the right to decide whether or not to take advantage of such wonderful advancements in medical technology as PGD for sex selection. I don't believe it is up to the Government or policymakers to be able to make such personal choices on my behalf. We are a loving, hard-working family and have the resources to take care of another child; if there is a technology that allows us to increase our chances of it being a girl then we plan to take advantage of it.” *Forum, Who Gets Born.*

Saviour siblings

Saviour siblings are children who are created in order to donate mast cells to an existing sick child in the family. PGD along with human leukocyte antigen (HLA) tissue typing can be used to select genetically matched sibling embryos. In New Zealand, saviour siblings are permitted for inherited disorders e.g. beta thalassemia, under the oversight of Ethics Committee on Assisted Reproductive Technology. Approval from the Minister of Health must be sought to use cord blood on a sibling. No saviour siblings have been born in New Zealand to date.

Saviour siblings may not be used in New Zealand for general illness e.g. leukaemia. Parents may store their child's umbilical cord blood, which can be used if the child becomes sick in the future. This is permitted for autologous use only (cannot be used by a sibling). Auckland CordBank, offers cord blood storage for an initial fee of $2500 plus $200 per year of storage.

The Human Genome Research Project group, sponsored by the New Zealand Law Foundation has recommended that the use of saviour siblings should be extended to include any serious or life threatening condition. They also recommend that the use of tissue, blood and bone marrow should be permitted. The donor child should have an appropriately qualified advocate and ethical considerations include addressing potential feelings of the saviour sibling as a "spare parts factory".

> "The question over screening siblings' compatibility for medical procedures is the hardest one for me. Where does one child's right to life take precedence over another child's right to be left alone, when they can't make their own decisions legally?" *Forum, Who Gets Born.*

Considerations for PGD treatment

- Although PGD is diagnostically reliable, patients must still undergo prenatal diagnosis to ensure that PGD has been accurate and to screen for other abnormalities.
- The live birth rate for PGD is 20–30% per IVF cycle which is the same rate as for IVF in general.
- There is a lack of consistent evidence to show that PGD for aneuploidy screening (e.g. Down syndrome) improves the live birth rate of couples having fertility problems.
- Long term health risks of children born as a result of PGD are unknown. An advisory group has been established to examine long term health risks of assisted reproductive technology.
- PGD is expensive and may be inaccessible to many families. In New Zealand PGD costs around $11 000.
- There is a long waiting list for PGD with delays of a year or more.

Some suggest that PGD discriminates against people with disabilities and promotes the view that birth of children with disability should be prevented.

> "In applying and advancing scientific knowledge, medical practice and associated technologies, human vulnerability should be taken into account. Individuals and groups of special vulnerability should be protected and the personal integrity of such individuals respected." *Article 8 of the Universal Declaration on Bioethics and Human Rights 2005*

Who gets born?

The following discussion occurred during a public consultation forum for the Bioethics Council of New Zealand "Who Gets Born" report about pre-birth testing in New Zealand. This feedback provides insight into some of the ethical and social issues that PGD raises.

> "It comes down to your moral viewpoint on, where does life begin? Is it equally repugnant to you to destroy an eight-cell embryo as an eight week old foetus or as an eight month pregnancy? You probably draw the line somewhere along that spectrum. But where? And why?"

> "There is a shift in paradigm from pregnancy being a gift or fate, to the idea of a tentative pregnancy... where we have all the tests before deciding whether to continue with it."

> "As a carrier of cystic fibrosis and having witnessed what it can do to someone, I have no problem with testing for it. The guilt I would feel if I brought a child into this world with a death sentence attached is just not worth it (especially when I have the opportunity to avoid it)."

> "People need to know that it was shattering having this Down syndrome baby, but it passed; we love him and wouldn't be without him. He has every right to be here and while his life is more difficult in some ways, he's still having a great time. Every time we hear that a baby with Down syndrome has been terminated we feel sorry for the people (and the baby of course) because they don't know what they have missed out on."

> "Pre-birth testing raises many ethical challenges, and everyone has an opinion based on their own personal experience. Someone who was born with a genetic condition and raised in a loving family will argue vehemently against pre-birth testing. Someone who was born with the same level of disability but was not raised in a loving family – was

> in fact mistreated and abused – will wish that pre-birth testing had been available before he/she was born.”

> “Imagine you are the parent of a child who has inherited a lethal genetic condition. Imagine the fear we feel going into a subsequent pregnancy, knowing that we have a 25%, or even 50% chance of conceiving a baby with the same genetic illness, and with the same outcome. Imagine living with that fear for 40 long, terrifying weeks if there is no diagnostic tool. Imagine trying to fight for your baby's life, knowing the second time that child will die. Now imagine there exists the medical technology to know for a fact whether or not that subsequent baby carries the genetic condition that will kill him or her. Imagine that you could spare a child that pain.”

Fertility clinics offering PGD

In New Zealand PGD is currently offered by Fertility Associates based in Auckland, Hamilton and Wellington, Fertility Plus in Auckland and Repromed in Christchurch. Egg collection, IVF and embryo culture are performed in New Zealand then the embryos are biopsied and cells sent to Australia for most tests. Results are received within one to two days allowing embryos to be selected and transferred.

PGD for serious genetic conditions with a 25% chance of inheritance or greater may be publicly funded, with couples being offered up to two cycles of treatment. Women need to be aged 39 years or younger and meet some other criteria related to the chance of success with IVF for public funding.

Genetic counselling

Genetic services in New Zealand are limited and are based in Wellington and Auckland, with clinics held in some other centres. GPs may refer patients to these services.

Northern Regional Genetic Services
Private Bag 92024
Auckland Hospital Site
Grafton
Auckland
Ph (09) 307 4949 extn 5530
Toll free 0800 476 123
Fax (09) 307 4978
Email gensec@ashsl.co.nz

Central Regional Genetic Services
Wellington Hospital
Private Bag 7902
Wellington
Ph (04) 385 5310
Toll free 0508 364 436
Fax (04) 385 5822

Central Regional Genetic Services
Christchurch Hospital
Christchurch
Ph (03) 379 1898 or (03) 364 0640 extn 89777
Toll free 0508 364 436 (South Island callers)
Fax (03) 379 1343

Further reading

National Ethics Committee on Assisted Human Reproduction. Guidelines on preimplantation genetic diagnosis. March 2005.

Available from: http://www.acart.health.govt.nz/moh.nsf/indexcm/acart-resources-guidelines-preimplantation

Bioethics Council. Who gets born? A report on the cultural, ethical and spiritual issues raised by pre-birth testing. June 2008. Available from http://www.bioethics.org.nz/publications/who-gets-born-jun08/index.html

National Human Genome Research Institute. Frequently asked questions about genetic testing.

Available from: http://www.genome.gov/19516567