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LENScience Senior Biology Seminar Series
Human Aneuploidy and Related Biotechnologies

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In 2008, 64,343 children were born in New Zealand, 51% male and 49% female. All arose as a result of a successful conception, pregnancy and birth. However, pregnancy isn't always straightforward. Many conceptions do not result in live births or result in live births which bring with them challenges for both parents and child, associated with potential or actual health issues.

About 15% of all confirmed pregnancies result in miscarriage. Also, many miscarriages occur before a woman has missed her period and therefore may know that she is pregnant. **Chromosome abnormalities within the embryo are the most common cause of miscarriage in early pregnancy.**

All parents hope that their children will have a healthy life. Scientists know that a **healthy start to life** is a pre-requisite to a long and healthy life. There are many factors that determine whether a child has a healthy start to life. Some of these, such as the environment in the womb can be determined by what the mother eats and whether she uses drugs during the pregnancy. Others, such as the genes that are inherited by the embryo at conception cannot be controlled. Worldwide, 6% of infants are born with serious birth defects. Some of these conditions can be treated and controlled, some lead to an increased susceptibility to disease over a lifetime, while others cause permanent disabilities, significant pain and suffering and may lead to premature death.

An example of an inherited genetic condition is Haemophilia. In this disease the blood will not clot, leading to significant suffering and potentially uncontrolled bleeding that may result in early death. The mutation that causes this disease is found on the X-chromosome has been passed down the lineage of the Royal families of Europe for many generations. Many people who know that they carry the genes for genetic disorders that will lead to pain and suffering in an individual are troubled by the thought of giving birth to a child that will be so unwell and suffer during their lifetime. Some people in this situation make the decision not to have children to avoid this suffering. Advances in biotechnologies over the past 20 years have led to the potential for couples in this situation to use early warning systems to give them an indication of what lies ahead and make a very early decision about whether

Human Conditions Caused by Gene Mutations		**Human Conditions Caused by Chromosome Mutations**	
Cystic Fibrosis	Caused by a range of mutations in the CFTR gene on chromosome 7. Autosomal recessive inheritance pattern.	Klinefelter Syndrome	Caused by an extra X chromosome in a male XXY
Huntington Disease	Caused by a mutation in the HD gene on Chromosome 4. Autosomal dominant inheritance pattern.	Turner Syndrome	Caused by an X chromosome missing in a female XO
Breast Cancer Susceptibility	A large number of different mutations/variants found in either the BRAC1 and BRAC2 genes on Chromosomes 17 and 13 respectively are known to be associated with increase **susceptibility** to breast cancer. The inheritance pattern is autosomal dominant.	Down Syndrome	Usually caused by an extra copy of chromosome 21 (Trisomy 21). Occasionally caused by a translocation of chromosome 14 onto chromosome 21.

Table 1 Examples of Human Conditions Caused by Mutations.

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TE RAUHANGA O TE WHARETANGATA

What is Aneuploidy?

Aneuploidy is the name given to the condition where there is variation from the expected number of chromosomes within a cell. For example in a human somatic cell, it is expected that there will be 2n or 46 chromosomes. If there are 45 or 47 chromosomes, this is aneuploidy.

Aneuploidy is the most commonly identified chromosome abnormality in humans, occurring in at least 5% of all clinically recognised pregnancies (Hassold and Hunt, 2001). Because each chromosome contains a large number of genes, aneuploidy causes major disruptions, and in most cases will result in miscarriage at a very early stage in the pregnancy. However, some will survive to birth. Aneuploidy occurs in 0.3% of live births and is the most common known cause of intellectual disability in humans. Karyotpyes of common human aneuploidies, Down Syndrome, Turner Syndrome and Klinefelter Syndrome, are shown in Figure 1.

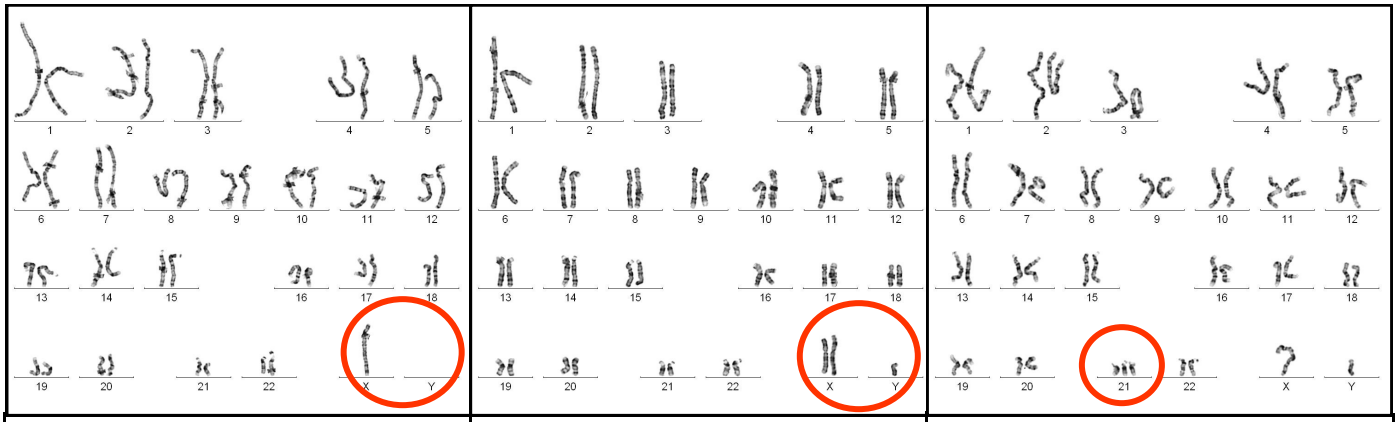


Fig 1a: Turner Syndrome (XO)

Fig 1b: Klinefelter Syndrome (XXY)

Fig 1c: Down Syndrome (Trisomy 21)

Karyotpes courtesy of Cytogenetics Laboratory, Auckland City Hospital

Aneuploidy can occur either in the autosomes or the sex chromosomes. When there is one less chromosome than normal (2n-1) the condition is known as **monosomy**. When there is one extra chromosome (2n+1) the condition is known as **trisomy**. While aneuploids usually do not survive due to the massive disruption caused to the cells, in the case of the sex chromosomes they will survive. Turner and Klinefelter Syndromes are two examples of this. In the case of Turner Syndrome (XO) it is either the second X or the Y chromosome that is missing. Because in humans only one X chromosome is active in each somatic cell, this still leads to a viable embryo, however there are some differences noted in a person with Turner Syndrome. As a result of undeveloped ovaries people with Turner Syndrome have very low levels of reproductive hormones. Secondary sexual characteristics are undeveloped and they are almost always infertile.

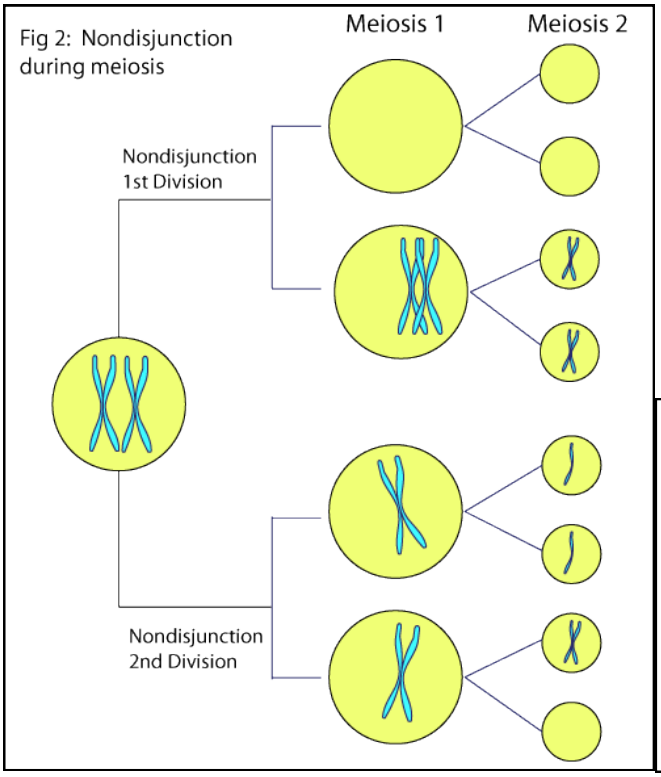


Fig 2: Nondisjunction during meiosis

What Causes Aneuploidy?

Aneuploidy is caused by the failure of chromosomes or chromatids to separate during cell division. This is called **nondisjunction** and can happen either during meiosis or mitosis.

Non-disjunction during meiosis results in gametes that are either n-1 or n+1. Fertilisation of these gametes by a normal gamete will result in an aneuploid embryo, either monosomy (2n-1) or trisomy (2n+1).

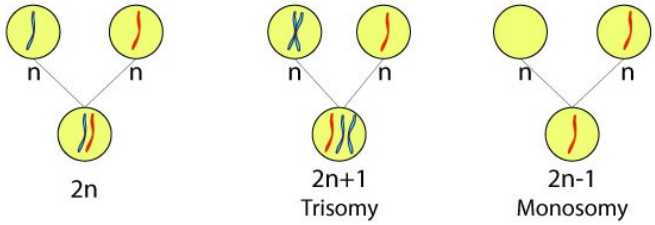
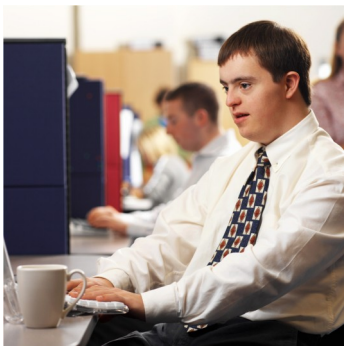


Fig 3: The effect of nondisjunction during meiosis at fertilisation

Down Syndrome (Trisomy 21)



Down Syndrome is caused by the presence of an extra copy of chromosome 21 (Fig 1c) and is the most common form of aneuploidy seen in humans. Many Down Syndrome pregnancies miscarry, so while in New Zealand Down Syndrome occurs in 1 in 400 pregnancies, it is only seen in 1 in 700 live births. The occurrence of Down Syndrome increases with increasing maternal age, rising from 1 in 1000 for 20-29 year old mothers to 1 in 90 for 40 years old mothers. There is no cure for Down Syndrome and it is not caused by any recognised environmental factor.

The extra copy of chromosome 21 causes a range of physical, intellectual and physiological phenotypic characteristics which have a life-long effect. Some of the more common physical features shared by people with Down Syndrome include flattened facial features, protruding tongue, small head, upwardly slanting eyes and unusually shaped ears. It results in a tendency for poor muscle tone, relatively short fingers and hands, short stature and slow grow. Heart and gastro-intestinal problems are also more common in people with Down Syndrome. There is usually a moderate degree of intellectual impairment associated with the condition. While some people with Down Syndrome can participate to varying degrees in school, work and social life, others have severe intellectual disabilities. Effective early education interventions assist Down Syndrome children to maximise their potential.

The extra copy of chromosome 21 found in Down Syndrome can arise in three different ways:

- **Non-disjunction during meiosis leading to Trisomy 21 (90—95% of cases)**
  The extra copy of chromosome 21 arises as a result of non-disjunction during meiosis and results in a gamete with an extra copy of chromosome 21. This is fertilised by a normal gamete (Fig 2).
- **Mosaic Trisomy 21 pattern (<3% of cases)**
  The extra copy of chromosome 21 arises as a result of non-disjunction during mitosis in the early embryo. This results in some cells that are normal and some that have the extra copy of chromosome 21. The earlier this occurs in embryonic development, the more cells are affected and the more significant the effect (Fig 4).
- **Translocation (very uncommon)**
  In this situation there are two normal copies of chromosome 21 plus an additional copy of all or part of chromosome 21 attached to another chromosome (typically chromosome 14) (Fig 5).

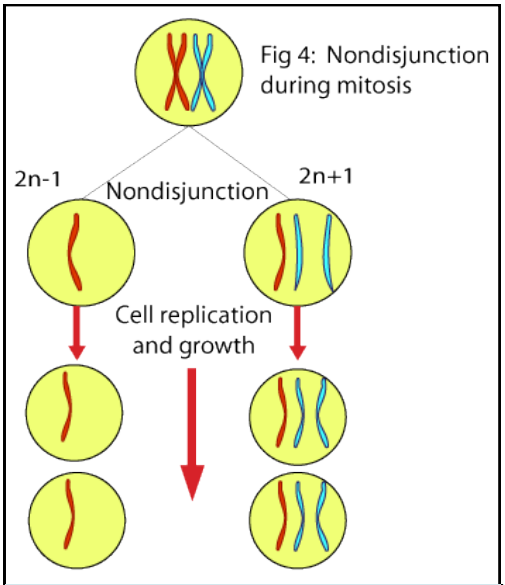


Fig 4: Nondisjunction during mitosis

Non-disjunction during mitosis in the very early stages of embryonic development can also occur and result in a mosaic pattern of affected and non-affected cells as the embryo develops. The earlier this occurs in the embryonic development, the more cells will be affected.

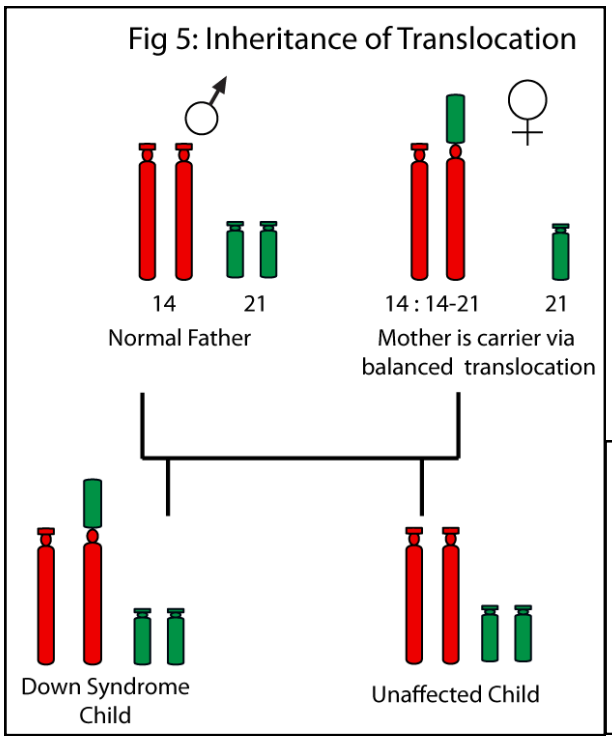


Fig 5: Inheritance of Translocation

In some cases, a translocation of genetic material can occur without the creation of additional genetic material.
This is known as a **balanced translocation** and the individual is not affected (Fig 6).
However, these unaffected individuals will create gametes that also have this translocation, and when fertilised by a normal gamete will develop into an affected child.

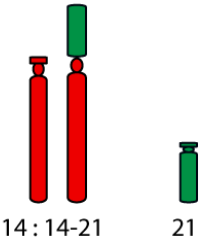


Fig 6: Balanced Translocation

The Maternal Age Effect

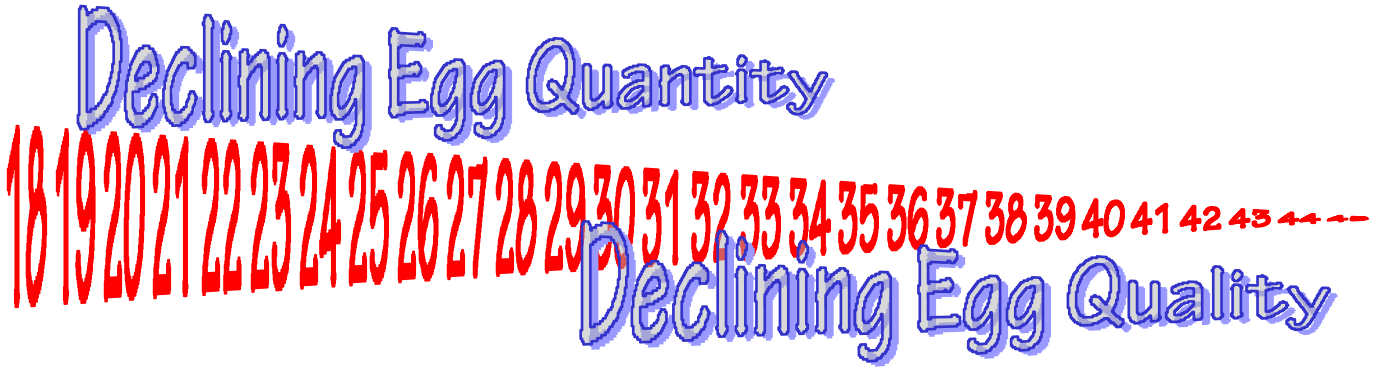
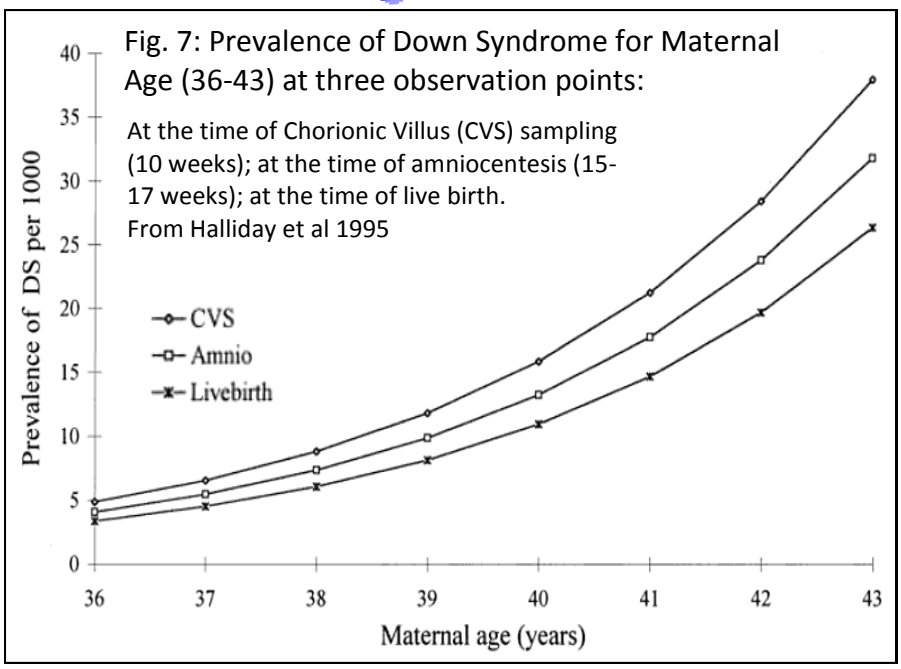


Figure 7 shows that the incidence of Down Syndrome increases significantly in older women. All of a woman's eggs are formed while she is in the womb, as many as 1-2 million. These are stored in her ovaries in a state of suspended development. Even before she is born, the number of immature eggs starts decreasing. By the time she reaches puberty only 400,000 remain. By the time she reaches her late 30's the number is down to as few as 20,000, and by the time she reaches her mid 40's there are only a few hundred left.



As well as the number of eggs reducing dramatically over this period, the quality of the eggs will also decline. This is why as women get older they are less likely to become pregnant each month and the incidence of miscarriage and chromosomal abnormality increases. The direct relationship between age and the incidence of aneuploidy suggests that the mechanism of separation (or disjoining) of the chromosomes or chromatids during meiosis is becoming less effective with increasing age of the eggs.

What about the father? The Paternal Age Effect

In contrast to women who have a limited supply of eggs, men are able to produce sperm throughout there lives. However, is sperm quality retained into old age? While it is know that most cases if Down Syndrome are a result of nondisjunction in the female gamete, 5-10% of Down Syndrome is caused by nondisjunction in the male gamete (the sperm). Yet there is no conclusive evidence that this is more common in older fathers. Aneuploidy affecting the sex chromosomes is more often caused by a faulty sperm and evidence suggests that there is around a two-fold increase in this for men over the age of 50 (Sloter E, Nath, J, Eskenazi B and Wyrobek A 2004).

It is also clear that environmental factors such as smoking (tobacco or marijuana), alcohol and excess weight in the father, all appear to be detrimental and appear to increase the risk of long term health effects for their children.

Smoking more than 10 cigarettes a day in men increases the risk of childhood cancer in their children fourfold.

Screening for Chromosomal Abnormalities During Pregnancy

In New Zealand, women can access pre-natal (before birth) screening and diagnostic tests for a number of conditions including aneuploidies such as Down Syndrome.

Screening is not the same as diagnosis.

A screening test indicates the *level of risk* that is present for a condition such as Down Syndrome. A positive result from screening suggests that there is an increased chance of a particular condition being present and a negative result means there is a decreased risk. People with positive screening results may decide to take the next step of pre-natal diagnostic testing which **will** tell them whether the condition is present or not in the fetus.
Pre-natal screening is not compulsory for anyone. Women who do choose to undergo pre-natal screening are supported throughout the process as shown in Box 1.

Women may decide to participate in pre-natal screening for a number of reasons including:

- wanting to know as much as possible about the pregnancy
- wanting to know whether or not the fetus is affected by a condition that is common in the whanau / family
- wanting the option of terminating an affected pregnancy
- wanting to know if the pregnancy is affected by a condition so that she and her partner can prepare in advance for a baby with an abnormality.

Conditions that can be tested for in New Zealand by pre-natal testing include:

- Aneuploidy (Down (Trisomy 21), Edwards (Trisomy 18) and Patau (Trisomy 13) syndromes,
- Aneuploidy affecting the sex chromosomes (Turner (XO), Klinefelter (XXY), Jacob (XYY) syndromes etc
- Physical abnormalities including neural tube defects (spina bifida), cardiac, renal and digestive abnormalities.

Box 1: The Screening Pathway

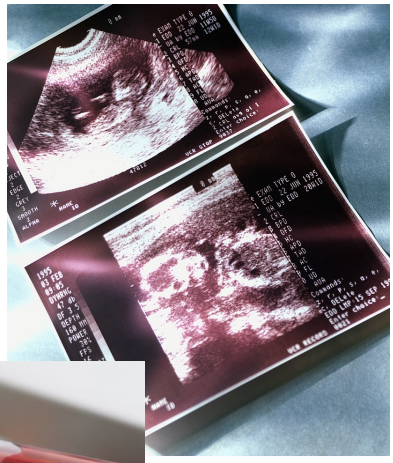
Screening is a series of steps that include:

- provision of information about the condition(s) being screened for
- provision of information about screening
- offer of screening tests
- performance of the screening tests
- offer of support and counselling to individuals with high risk results
- offer of diagnostic tests to individuals with high risk results
- performance of the diagnostic tests
- offer of support and counselling following the diagnostic test result
- intervention options

Ministry of Health (2007) *Antenatal Down Syndrome Screening Advisory Group Report.*

Prenatal Screening and Tests Available in New Zealand

1. **Maternal Age** - Pregnant women over the age of 35 are offered the opportunity to have diagnostic testing for chromosome abnormalities



2. **1st Trimester Screening** - this involves both ultrasound NT and biochemical (blood test). The blood test measures hormone and protein levels which are known to indicate an increased risk of a number of abnormalities. Many pregnant women have an ultrasound scan during the 1st trimester of the pregnancy. The Neucal Translucency (NT) test is carried out between 11 and 13 weeks. In this scan an increase in the fluid-filled area at the back of the fetal neck, is an indicator of an increased risk of Down Syndrome.

3. **2nd Trimester Maternal Serum Screening** - this uses a blood test to measure hormone levels in the mother. This information is combined with information about her age, height, weight and pregnancy dates to give an estimate of the risk of chromosomal abnormalities.

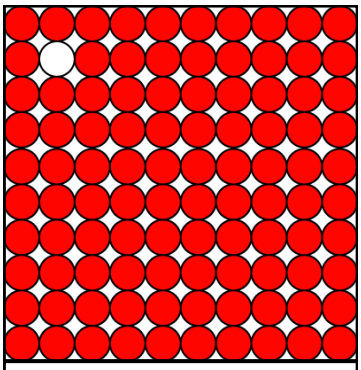
4. **2nd Trimester Ultrasound Scan**—this can detect many physical abnormalities, risk factors for chromosomal abnormalities as well as monitoring the growth of the fetus.

Prenatal Diagnostic and Tests Available in New Zealand

If the screening tests give a positive result, this does not mean YES or NO. It means that there is a higher chance of chromosomal abnormality. E.g. It may mean the woman is told that there is a 1 in 100 risk of Down Syndrome. If the screening result is positive, the opportunity to have diagnostic tests will be offered. These will give a definite result. Two methods of pre-natal diagnosis are available:

1. **Chorionic Villus Testing**—a fine needle is inserted through the woman's abdomen and cells are removed from the placenta. These cells are analysed in the laboratory to show chromosomal abnormalities. This test can be carried out at 11-13 weeks and carries a 1-3% increased risk of miscarriage.

2. **Amniocentesis**—a fine needle is inserted through the woman's abdomen and a small sample of amniotic fluid is removed. Cells from this fluid are analysed in the laboratory for chromosomal abnormalities. This test is carried out between 15 and 19 weeks and carries a 1% increased risk of miscarriage.



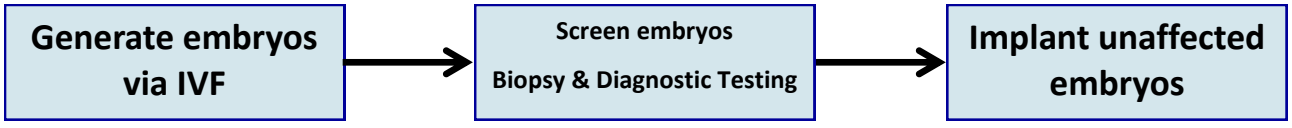
A positive screening result indicates a higher chance - not a definite result.

Pre-Implantation Genetic Diagnosis (PGD)

Pre-implantation genetic diagnosis is a technique that enables couples at risk of producing embryos with genetic abnormalities the opportunity to have their embryos checked for specific conditions before a pregnancy is established. It is an alternative to traditional prenatal diagnosis (chorionic villus sampling or amniocentesis).
PGD can be used to check for the sex of the embryo (in order to detect sex linked disorders such as muscular dystrophy) , known single gene disorders (such as cystic fibrosis), translocations, and some of the more common chromosomal abnormalities such as Down Syndrome.

The Process of PGD

In order to carry out the genetic testing, embryos must first be formed through the use of ***in Vitro*** **Fertilisation** (**IVF**: see Box 2). The diagnosis is performed on one or two cells removed from the embryo three to five days after conception via IVF, before the embryos are implanted in the woman.



Embryo Biopsy

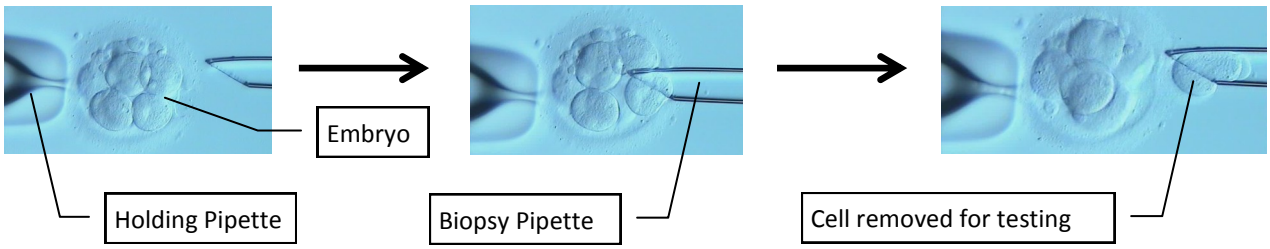


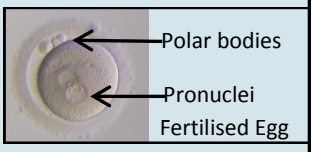
Fig 8: Embryo Biopsy

1. Early embryos are protected by an eggshell known as the *zona pellucida* (ZP). A hole around 30µm diameter is created in the zona pellucid either by dissolving it with an acidified medium released from the end of a micropipette, or more commonly by laser.
2. The embryo is held steady with a holding pipette and a finer biopsy pipette is used to remove one or two cells.
3. The embryo is returned to culture while the cell(s) that were removed are prepared for genetic diagnosis—to test for abnormalities. The embryo will continue to grow, unaffected by the removal of the cells.

Box 2 Steps in *in* Vitro Fertilisation

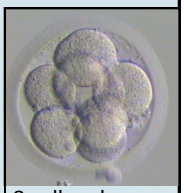
IVF is a technology which involves an egg being removed from a woman and joined with a sperm of a man in vitro—outside the body, in the lab.

1. **Ovary Stimulation** Drugs are used to stimulate the woman's ovaries to mature several eggs (oocytes) to pre-ovulation stage. Mature eggs will extrude a polar body, a product of the 1st meiotic division. This process is monitored by ultrasound scans and blood tests.
2. **Egg Collection** Before ovulation occurs, the eggs are collected from their follicles and placed into an artificial culture environment.
3. **Sperm collection and Insemination** Semen is collected from the man. The sperm and egg are brought together in culture. This is done either by the addition to several thousand free swimming sperm to the media surrounding each egg or by injection of a single sperm directly into the cytoplasm of each egg (intracytoplasmic sperm injection, ICSI).



Fertilised Egg

4. **Fertilisation** Around 16-18 hours later the eggs are checked for fertilisation. A normally fertilised egg will show equal sized pronuclei, one derived from the egg and on from the sperm, and a second polar body (a product of the second meiotic division).

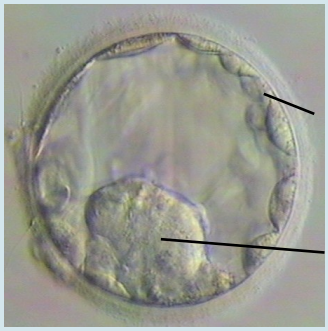

8 cell embryo

5. **Embryo Culture** Embryos are normally cultured *in vitro* for at least three days after insemination. At the end of 3 days, the embryos would normally have developed to the 8-cell stage .

If PGD is being used, at this point one or two cells can be safely removed for genetic diagnosis without affecting further embryo development. The procedure of cell removal is usually referred to as Embryo Biopsy (see Fig 8).

The embryos continue to grow in culture until the completion of the genetic diagnosis. It is possible to maintain normal growth in culture until the embryos reach the blastocyst stage, five or six days after insemination.

6. **Embryo Transfer** If PGD is not being used, the embryo will be transferred into the woman 2-5 days after insemination (usually 3 days). If PGD is being used, when diagnosis is complete, an unaffected embryo is selected and transferred into the uterus.
   Drugs to deliver extra progesterone are used to help maintain the lining of the uterus after embryo transfer.



Blastocyst, Day 5-6 after insemination

PGD for Chromosomal Abnormalities

As only one or two cells are available for analysis, the classical karyotype method of looking for chromosomal rearrangements is not an option in PGD as it is highly unlikely that the cells will be at a stage when the chromosomes are visible. The most common approaches use fragments of DNA tagged with fluorescent markers.

Fluorescence *in situ* hybridisation (FISH)

Short sequences of DNA which are chromosome specific are cloned and multiple copies made. Each specific sequence is bound to a chemical marker which will fluoresce at a specific wavelength when exposed to ultra violet light. These are commonly known as probes.

The cells obtained from the embryos are fixed onto glass slides. Fixing removes the cell cytoplasm and perforates the nuclear envelope. A solution of probes (usually limited to the eight chromosomes most commonly involved in abnormalities which can lead to failure to establish an ongoing pregnancy) is added to the slide and the mix repeatedly warmed and cooled.

When double stranded DNA is heated up to temperatures near 80^{o}C the two strands unbind into single stranded structures (DNA thermal denaturation). When slowly cooled the two strands recombine to form the double helix structure (DNA thermal renaturation). As the solutions contain thousands of copies of each DNA probe, there is a higher chance that a probe fragment will recombine with its complementary sequence on the test DNA than will the single copy of that chromosomes own DNA.

Finally the slide is thoroughly washed to remove any unbound probe and studied using a microscope equipped with an ultra violet light source. A cell with the normal complement of tested somatic chromosomes will display pairs of dots of the same colour. Trisomies will show three dots of the same colour, and monosomies only one (Figure 9).

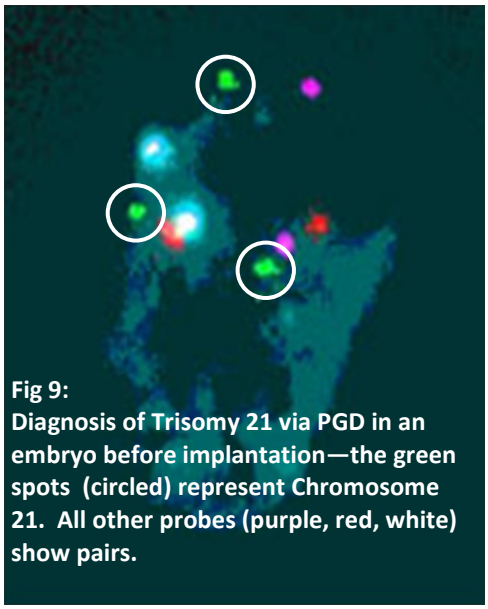


Fig 9:
Diagnosis of Trisomy 21 via PGD in an embryo before implantation—the green spots (circled) represent Chromosome 21. All other probes (purple, red, white) show pairs.

Comparative Genomic Hybridisation (CGH)

The number of chromosomes able to be analysed using FISH is limited by the number of fluorescent probes which can be discriminated by the colours available. CGH is a different test which allows us to look at all chromosomes using only two probe colours, usually red and green.

First the entire chromosomal complement of the cell to be studied is chopped into small fragments through the use of **restriction enzymes**. The fragments are copied using the **Polymerase Chain Reaction** (PCR). As with FISH, the DNA is heated until it becomes single stranded, but in a 'soup' of nucleotide elements which have been bound to a red fluorescent probe. On cooling, these labelled nucleotides **anneal** to the single strands to make new double stranded DNA. The process of **thermal denaturation** and **renaturation** is repeated many times until there are in order of one million copies of each fragment. During the cycling, a control cell (always from a normal male) undergoes the same process, but with green labelled nucleotides in the soup.

The test and control fragments are mixed then added to a slide on which a normal male karyotype has been fixed (the chromosomes are visible), and the slide is subjected to more sequences of warming and cooling. The fragments from the test and control genomes then competitively bind to their complementary sequences on the intact chromosomes.

A computer aided image analyser then scans each chromosome for the presence of red or green probe. If the test genome is normal male, there will be an equal proportion of red and green probes bound throughout all chromosomes. If the test cell has an extra chromosome, for instance, a trisomy of chromosome 21 (Downs Syndrome), there will be 50% more red labelled fragments competing for sites on chromosome 21, and the chromosome on the karyotype slide will be predominantly red. Conversely, if a chromosome is absent, a monosomy, there will be 50% more control fragments of DNA from that chromosome, so it will be predominantly green. A test cell which is normal female will have a predominantly red X chromosome (as there would be two X chromosomes against the single X from the male control) and no binding on the Y chromosome. All other somatic chromosomes will have an equal amount of red and green binding (Fig . 10)

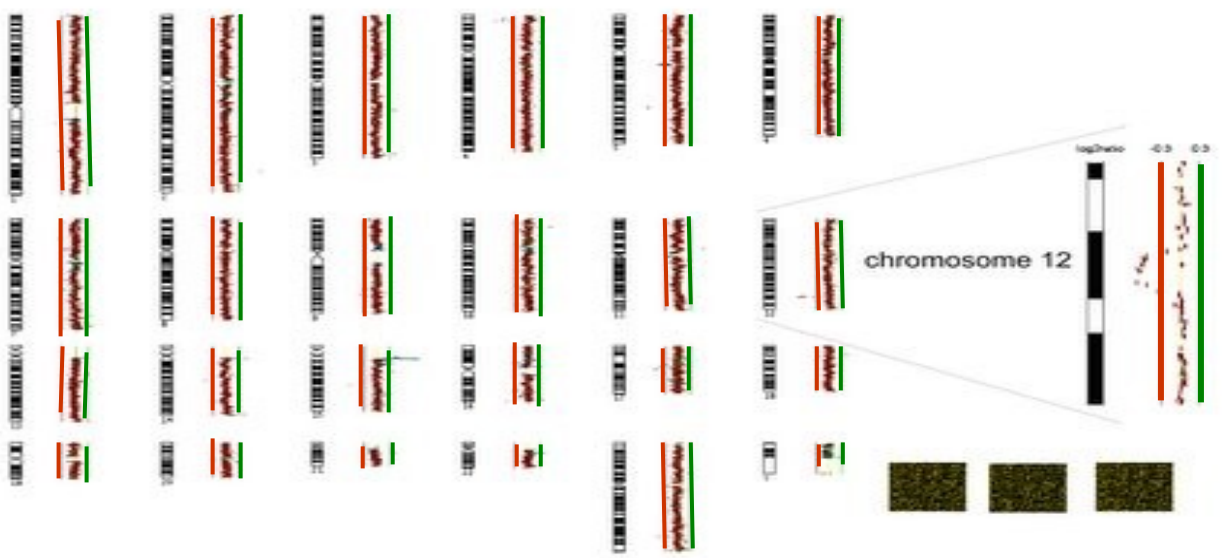


Fig. 10 Comparative Genomic Hybridisation

With CGH, it is also possible to detect chromosomal deletions (parts of chromosomes which are missing) and duplications (extra copies of entire sections of chromosomes) as within the chromosomes there will be whole sections predominantly green or red respectively.

Disadvantages of CGH are either failure of the PCR process where the test and control have significantly different numbers of fragment copies before the hybridisation against the normal karyotype, and the time it takes to amplify an entire genome (several days against FISH which takes a few hours).

As the majority of chromosomal abnormalities observed in human embryos are generated at the first and second meiotic division of the oocytes (egg), the time for analysis problem can be addressed by performing CGH on polar bodies. By performing Polar Body Biopsy (essentially the same technical procedure as embryo biopsy, but the polar bodies are removed, one before insemination / injection, and the second around 18 hours later) and looking at their chromosomal complement, an inference can be made on the number of maternal chromosomes remaining in the mature and fertilised oocyte (egg).

Using PGD for Single Gene Defects

Polymerase Chain Reaction (PCR)

This is the most common technique used to detect mutations in single genes where the coding sequence of the wild type (normal) gene is known. The normal gene can be differentiated from the mutant gene which causes the genetic disease by size (if the mutated gene has nucleotides deleted) or by electric charge (if the mutated gene has a nucleotide substituted for another). **For PCR to accurately detect the genetic inheritance of an embryo, the structures of genes of both parents must be known.**

The DNA from the test cell nucleus is digested with specific restriction enzymes which will form a fragment of DNA containing the gene of interest. As with CGH, the fragments are repeatedly warmed and cooled in the presence of basic DNA building blocks until up to one million copies of each gene are present. Drops of the highly amplified DNA are placed on lanes on a gel alongside copies of the parent DNA and other controls. An electric charge is placed across the gel. The natural charge of DNA will cause the fragments to migrate. After a few hours, the distances travelled by the various fragments can be compared, therefore identifying which genes have been inherited from which parent. Unaffected or carrier embryos can then be selected for transfer.

Pre-implantation Genetic Haplotyping (PGH)

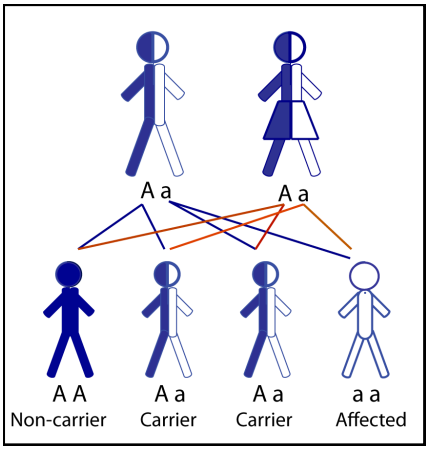
In some cases the identity of the gene which causes an inheritable disease is not known, although there is often enough evidence to narrow down its location to a chromosome or part of a chromosome. Much of each chromosome consists of non-coding DNA. As they are non-coding, these mutations are not selected against, so over generations they can become very different between individual chromosomes. There are certain regions on each chromosome which are highly polymorphic and can be used to identify which chromosome has been inherited from which parent. If the DNA of enough family members can be analysed, the chromosome bearing the otherwise unknown disease bearing gene can be identified. Rather than the test cell undergoing the PCR process to look for a gene, it undergoes PCR to identify which polymorphic markers have been inherited from each parent. The inheritance of a marker linked to the chromosome common to affected individuals is then selected against when choosing an embryo to replace.

Genetic Counselling

Genetic Counselling is a communication process that deals with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family. The process involves an attempt by one or more appropriately trained persons to help the individual or the family to:

1. Comprehend the medical facts including diagnosis, course of the disorder & available management
2. Appreciate the way heredity contributes to the disorder and the recurrence risk for specific relatives
3. Understand the options for dealing with the recurrence risk—
    - Another pregnancy +/- prenatal diagnosis
    - PGD
    - Adoption
    - Artificial insemination by donor sperm or use of a donor egg
    - Childlessness
4. Choose the course of action which seems appropriate to them in view of their risks, their family goals and act in accordance to that decision
5. Make the best possible adjustment to the disorder and/or to the recurrence risk.

(Adapted from American Society of Human Genetics, 1975).



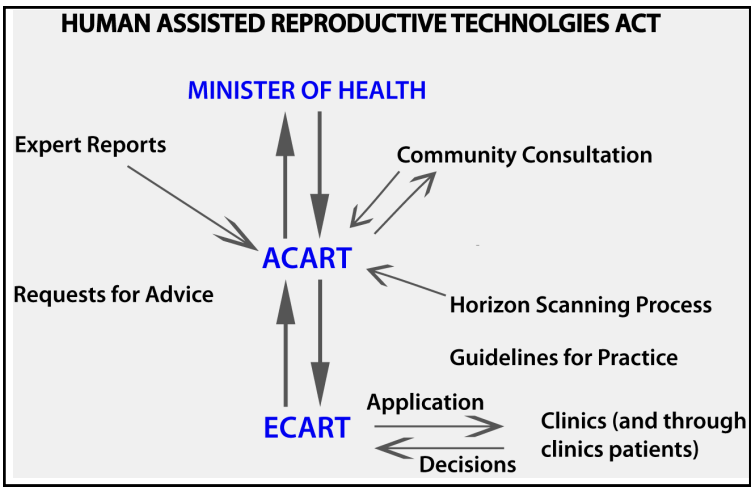
A genetic counsellor has a bachelor of science with a masters degree in genetic counselling, followed by a 2 year on-the-job training and education programme prior to registration. Currently there are only 11 genetic counsellors working in New Zealand. Common genetic referrals are from people concerned about family histories of cancer, advanced maternal age, an abnormal screening test during the pregnancy or a family history of a single gene disorder such as cystic fibrosis. Decisions that are made about the use of PDG must take in ethical considerations. **This is a complex process with many varied and relevant viewpoints.** Issues relevant to decisions about PGD include: reproductive autonomy (personal choice); autonomy of the child (under law the fetus has few rights, the moral status of the fetus is an ongoing source of debate); beneficence (doing good); non -maleficence (not doing harm) and justice (fairness, equity and the societal impact of decisions). Cultural, social and spiritual factors play a part in decision making for people, and create variation in the way people approach these decisions.

The Human Assisted Reproductive Technologies Act (2004)

The practise of Reproductive Medicine in New Zealand is regulated under the Human Assisted Reproductive Technologies Act. This Act established an Advisory committee to the Minister of Health, called the Advisory Committee on Assisted Reproductive Technologies (ACART), whose job it is to assess information about both established and emerging new treatments and to advise the Minister of Health as to how they should be further introduced, regulated, and supervised. ACART is a twelve member committee representing various community interests including Ethics, Children's rights, Māori interests and Science.

Broadly, ACART's advice to the Minister will be that a particular procedure should be an "established procedure" and that there will be no legal limitations on the use of that particular technology, or an "assisted reproductive procedure" where individual applications for use need to be made to the National Ethics Committee on Assisted Reproductive Technologies (ECART). When an application is required, ECART assess the grounds on which the request is made and give their approval or not. The applications are made by clinics on behalf of their patients and include medical, counseling and legal reports. ECART applications are most commonly about surrogacy or the use of donor gametes from certain family members (i.e. son to father, father to son, relative to relative within the same generation).

The HART Act comes as both an Act in itself and an Order in Council. The Order in Council allows continuous change in the regulations without resorting to Parliamentary debate over each and every change. The Act precludes the use of assisted reproductive technologies for the use of gender selection and bans cloning. ACART's deliberations are published on its website: http://www.ACART.health.govt.nz



Recommended Extension Reading

Bioethics Council—Issues in Focus: Pre-birth testing www.bioethics.org.nz/about-bioethics/issues-in-focus/prebirth-testing/index.html

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