PRE-IMPLANTATION GENETIC DIAGNOSIS

INTRODUCTION

This ***Headline Bioethics*** study guide contains background information and structured activities based around online video clips to enable busy lecturers and school teachers to address the science and ethical implications of new developments in biology and biomedicine. The availability of online news archives and clips from other programmes, make it relatively straightforward to incorporate streamed media of this kind into Biology, RE and/or General Studies lessons. The **FAQs** section of this guide presents a series of question and answers regarding pre-implantation genetic diagnosis including background information about the science, history and ethical arguments. In addition, **'off the shelf'** worksheets have been produced for use in conjunction with the selected video clips.

All of the recommended video clips are currently being streamed on the BBC website (www.bbc.co.uk).

VIDEO LINKS

Below are links to three recommended video clips that illustrate the science and ethical issues that surround the topic of pre-implantation genetic diagnosis (PGD).

The first video illustrates how PGD is used to diagnose genetic disease and follows the family of Jean Gillard who has mitochondrial disease.

'Genetic advance raises health hopes' – BBC News, 26th Aug 2009 (2min19)
http://tinyurl.com/pgdvideo1

The second video is about using PGD to create a tissue matched sibling. It contains an interview with the Whitaker family 5 years after the creation of a son, Jamie as a 'Saviour sibling' for Charlie. In the clip, the family welcomes the vote to allow the creation of 'saviour siblings'.

'Couple welcome MPs' vote' – BBC News, 20th May 2008 (3min10)
http://tinyurl.com/pgdvideo2

The third clip concerns the use of PGD for diagnosing late onset diseases such as cancer. The video features a short interview with Paul Serhal, a fertility expert, who talks about the first baby born free of the breast cancer gene in the UK as well as the scientific background to procedure.

'Breast cancer gene-free baby' – BBC News, 9th Jan 2009 (1min55) http://tinyurl.com/pgdvid3

STUDENT WORKSHEET

'Genetic advance raises health hopes'
BBC News, 26th Aug 2009 (2min19)
http://tinyurl.com/pgdvideo1

From the Video

1. What disorder does Jean Gillard have?
2. How is the disorder passed down through the generations?
3. Briefly explain how a genetic egg transplant is carried out?

Thinking Deeper

Think of THREE reasons why people may object to using PGD to screen for mitochondrial disease?

Who should decide which disease can be screened and why?

Bioethics BYTES

STUDENT WORKSHEET

'Couple welcome MPs' vote'
BBC News, 20th May 2008 (3min10)
http://tinyurl.com/pgdvideo2

From the Video

1. To which country did the Whitaker family travel to undergo PGD?
2. When Jamie was born, what was taken from him in order to help Charlie?

Thinking Deeper

1. The Whitakers have been accused of having a 'designer baby'. Do you think this is a valid criticism? Why or why not?

2. Give TWO arguments for and TWO arguments against 'saviour siblings'

3. After the Human Fertilisation and Embryology Authority (HFEA) banned the Whitakers from having pre-implantation genetic diagnosis in the UK, they chose 'fertility tourism' and travelled overseas to get the treatment they required for Charlie. Give TWO arguments for and TWO arguments against 'fertility tourism'

STUDENT WORKSHEET

'Breast cancer gene free baby'
BBC News, 9th Jan 2009 (1min55)
http://tinyurl.com/pgdvid3

From the Video

1. Briefly explain the science of genetic egg transplantation.
2. Why did the baby's parents decide to screen embryos for the breast cancer gene?
3. How do critics see this technology?

Thinking Deeper

1. Imagine someone is seeking to have pre-implantation genetic diagnosis for a disease that will affect their baby from birth. Would you recommend that they are allowed to do this? Why or why not?

2. Breast cancer caused by known genes has 'incomplete penetrance' (i.e. not everyone with those genes will actually suffer the disease.) It is also unlikely to affect the woman until she is 40 or older. Does this differ from the situation in question 1? Why or why not?

ONLINE RESOURCES

- A good place to start is the **Bioethics Briefing** on Pre-Implantation Genetic Diagnosis which contains background information on the scientific techniques and the ethical considerations http://tinyurl.com/pgdbriefing

- The **Nuffield Council on Bioethics** are an independent body who examine and report on the ethical issues within biology and medicine. A past project on genetic screening published a report in 1993 titled 'Genetic screening ethical issues.' http://tinyurl.com/pgdnuffield

- The **Human Fertilisation and Embryology Authority (HFEA)** have a question and answer page dedicated to PGD http://tinyurl.com/pgdhfea

TEACHERS NOTES – PRE-IMPLANTATION GENETIC DIAGNOSIS FAQS

What is PGD?

- Pre-implantation genetic diagnosis is a set of procedures that can be carried out on embryos prior to fertilisation
- It is a method used to determine whether the embryos are at risk of developing a genetic condition that could possibly lead to disease

What is the difference between genetic screening and pre-implantation genetic diagnosis?

- Genetic screening is the general term given to all tests for genetic disorders
- Screening is broadly divided into four groups
    - Adults
    - Newborn
    - Antenatal
    - PGD

When was PGD first used?

- 1989 to determine the gender of an embryo
- Region of Y chromosome amplified using PCR (polymerase chain reaction) to select against the male embryos due to their susceptibility to 'sex-linked' illnesses

How are the embryos prepared?

- PGD cannot be used for natural conceptions and therefore begins with in vitro fertilisation (IVF)
- Embryos are usually screened 3 days after fertilisation, when they consist of 8 cells
- A hole is made in the jelly layer surrounding the embryo and one or two cells, known as blastomeres, and are removed using a fine pipette

What are the methods for analysis?

- The nature of the problem depends on the test that is carried out on the embryo
- For problems at one specific gene, Polymerase Chain Reaction (PCR) based methods are used
    - Creation of millions of copies of a specific section of DNA (amplification) without having to create new cells
- For checking whether an embryo has the correct number of chromosomes or testing the gender of an embryo, Fluorescence In Situ Hybridisation (FISH) or Comparative Genome Hybridisation (CGH) is used

What are some examples of diseases can PGD can be used?

- Cystic fibrosis, sickle cell anaemia, haemophilia
- Beta-thalassemia, spinal muscular atrophy
- Huntington's disease
- X-linked diseases such as fragile X syndrome, and Duchenne Muscular Dystrophy

What are other uses of PGD?

- Sex Selection
    - This involves selecting the gender of a child for non-medical reasons
    - It is currently illegal under HFEA in the UK however is carried out in the United States

    - Cases include the Masterton family, who already had 4 sons and a daughter who died. They wished to have another daughter and were not allowed to do so in the UK even though it was self-funded
- Aneuploidy
    - Aneuploidy – possessing an abnormal number of chromosomes
    - Extra or missing chromosomes are a common cause of genetic diseases

PGD for the diagnosis of genetic diseases

- Video **'Genetic advance raises health hopes' – BBC News, 26th Aug 2009 (2min19)**

What are mitochondrial diseases?

- Mitochondrial disease is a neuromuscular disease which is caused by damage to the mitochondria in the cells
- Mitochondria are responsible for producing energy or ATP and as such are the 'power packs' of the cell
- If the cell does not receive enough energy it does not function correctly
- Symptoms of the disease vary and depend upon the number and location of cells that are damaged
- The most common part of the body that is affected are usually those with the highest demand for energy such as the brain, muscles, liver, heart and kidneys
- They are rare, very hard to distinguish and no treatments are currently available

The Gillard family – background

- Jean Gillard suffers from mitochondrial disease, an inherited condition passed down maternally – i.e. from the mother
- Although it is too late for her family, the success of egg transplants in genetically modified monkeys in America could eliminate genetic diseases

PGD and the creation of a tissue matched sibling – the Whitakers

- Video **'Couple welcome MPs' vote' – BBC News, 20th May 2008 (3min10)**

What is a 'Saviour Sibling'?

- The term 'Saviour Sibling' is used to describe a child who is born to provide stem cells and/or organ transplants to a sibling who suffers from a disease.

Who are the Whitaker family?

- Charlie Whitaker suffered from Diamond Blackfan Anaemia (DBA)
- The best possible chance for Charlie to live a relatively normal life was to perform a transplant from a tissue-matched donor
- The family wished to screen their embryos to select a tissue match for Charlie. At the time, however the HFEA would not allow the procedure as they believed that there would be no benefit and potential harm for the new child
- The family therefore travelled to America to carry out the procedure – they became an early example of the phenomenon known as 'fertility tourism'

- As a result, Jamie was born – a tissue type match for Charlie
- Stem cells were harvested from Jamie's umbilical cord and successfully used in a bone marrow transplant for Charlie

What is Diamond Blackfan Anaemia?

- A disorder that gives a low red blood cell count
- Usually treated with corticosteroids and blood transfusions
- Bone marrow transplants
- Thought to be spontaneous rather than an inherited condition
- It is characterized by genetic heterogeneity where by a number of different genes may be involved
- Currently impossible to screen embryos for the disease

What is the current law surrounding tissue matched siblings?

- UK law currently allows PGD for tissue-matched siblings on a case by case basis
- Some of the criteria includes whether the condition is life threatening
- Only cord blood should be used to decrease any suffering for the donor baby
- However, PGD procedures are still allowed in other countries, and as such, fertility tourism is still likely to occur

Are there any other cases where PGD for tissue matched sibling has been allowed in the UK?

- Zain Hashmi suffers from thalassaemia – an inherited blood disorder
- The HFEA initially gave permission to Zain's family to produce a saviour sibling
- After pro-life campaigners sought to ban the treatment, the case was taken to the High Court who found in favour of the family
- The HFEA argued that the procedure would benefit both Zain and the new child
- As of yet however the Hashmi family have been unsuccessful in producing a suitable donor embryo

PGD for diagnosing late onset diseases – Breast Cancer

- Some diseases do not develop until much later in life
- They include Alzheimer's, Huntington's, heart disease and some cancers
- Complex situation as they have both genetic and environmental influences
- Genetic tests can show whether a person may be susceptible to these diseases

Breast Cancer

- 40,000 cases of breast cancer are diagnosed every year in the UK
- 5-10% are thought to be caused by a mutation in the 'breast cancer genes' BRCA1 and BRCA2
- The risks of getting breast cancer increase with age and as such is a sporadic disease (i.e. a genetic disease that occurs without any family history or genetic defects from the parents – not inherited)

The use of PGD and breast cancer

- Carrying the breast cancer genes alone does not guarantee that cancer may develop

- In these cases, the disease is said to have 'incomplete penetrance' and as such the use of PGD is questioned
- First allowed by the HFEA in May 2007 to screen embryos for genes such as BRCA1 but is still permitted on a case by case basis

Background to the video

- The story relates to a baby who has been born who was the first to be screened for an altered gene which causes breast cancer
- Women in three generations of her husband's family have been diagnosed with breast cancer in their 20s
- The couple, a 27 year old and her husband, were treated by fertility expert Paul Serhal at University College Hospital London
- Wished to remain anonymous
- A daughter could have been affected by breast cancer herself if she carried the altered gene and a son could have been a carrier and passed it to any daughter he may have
- Mr Serhal, 'The objective of this exercise is not just to make sure the child doesn't have the gene but to stop the transmission from generation to generation.'
- However, not carrying an altered BRCA1 gene would not guarantee any daughter born to the couple would be unaffected by breast cancer because of other genetic and environmental causes
  Reference: http://news.bbc.co.uk/1/hi/health/7792318.stm

Ethics

What are the ethical benefits of PGD?

- Eliminate genetic disorders
- Allow 'tissue match' with older siblings in order to donate stem cells to cure another sibling
- Strongest supporters of PGD are characteristically libertarians who believe we should have the freedom to make one's own reproductive choices

What are some ethical concerns of PGD?

- Alters the relationship between parents and child so a 'gift' becomes a 'commodity'
- Fate of the embryos that are not selected
  - Some believe that life begins at conception and so it is viewed that destroying rejected embryos is morally wrong

- 'Deselecting' embryos that may have genetic disabilities is sometimes seen as taking a huge slur on individuals who already live with such conditions
  - It is argued that it is society's attitude to disability rather than the life of a 'handicapped' individual which needs to be rejected

- Eugenics
  - Use of PGD to control genetics raises spectre of eugenics, that it is the attempt to influence the genetics of the population by controlling reproduction

- Psychological concerns for the saviour sibling
  - How would they feel, knowing they were only produced to save another?

    - How would they feel if the treatment failed?
    - The donor sibling may have to go through more suffering if further procedures e.g. bone marrow transplant, were required

- Financial arguments
    - IVF and PGD are very expensive, several thousand pounds per cycle
    - Issues of justice and fairness
    - NHS resources are limited
    - Permission given to one family may cause another to lose out on this treatment

DETAILED VIDEO NOTES

Below you can find the script for each video.

'Genetic advance raises health hopes'
BBC News, 26th Aug 2009 (2min19)
http://tinyurl.com/pgdvideo1

Reporter:
"This is Meeto and Tracker, two genetically modified monkeys and their creation in the United States, could lead to the elimination of hundreds of inherited diseases forever. Jean Gillards family could be one of those to benefit.

The research could help Jean Gillard family. She is one of thousands of women that have defective eggs which increases the risk of her children developing a wide range of illnesses."

Jean:
"My mother probably had it and its come down the generations and what's going to happen to the future generations? I've got five gorgeous grandchildren."

Reporter:
"Women who have this condition pass it on to their daughters who in turn give it to theirs. But now there has been an important scientific development that could stop this disorder going from generation to generation."

(Illustration of genetic egg transplantation)
"Scientists have shown in animal experiments they can treat the condition by carrying out a genetic egg transplant. The defective eggs contain damaged genes, here shown in red. By taking out the DNA needed to make a baby and transplanting it into an empty egg with healthy DNA, shown in green, doctors believe they can overcome the problem."

"Writing in the journal Nature, scientists in the US have shown it can be done with monkeys. Doctors here believe it will soon be possible to help human patients who have the disorder mitochondrial disease."

Prof. Peter Braude:
"It has occurred against all the odds. I think it is going to create much hope for people who have mitochondrial disease and sometime in the future, their children will be free of these disorders.

Reporter:
"By making a permanent change to the DNA that continues through generations, scientists could eliminate all mitochondrial diseases from society, and by making the so called germ line genetic changes to eggs, they could completely eradicate many more inherited diseases."

Josephine Quintavale, Comment on Reproductive Ethics:
"I'm not in the business of looking for a perfect society and I certainly don't define human perfection by physical perfection. We have to be very careful."

Reporter:
"Researchers say this latest treatment could be available to families with mitochondrial disorders within the next few years."

'Couple welcome MPs' vote'
BBC News, 20th May 2008 (3min10)
http://tinyurl.com/pgdvideo2

Jayson Whitaker, Father:
(Shot in News Studio and of Whitaker family)
"We are really pleased. I was actually watching it live on the internet so the moment that we got the result we kind of knew before it was announced on the news but we were really pleased because it means that families that are going through the same situation as we were don't have to face the horrible steep hills that we had to deal with."

Reporters:
"I'm now going to ask you the most obvious question because I can see their in front of my eyes, sitting on your knee on the sofa, how is the family, how is the boys?"

Jayson Whitaker:
"The boys are doing brilliant; I mean Charlie's life is now completely normal. Jamie's life has been 100% normal from day one. It was stem cells taken from cord blood 5 minutes after he was born but it transformed Charlie's life. He went from an underweight kind of undernourished small child. He needed constant medical attention, drugs and blood; he does not need any of that now. "

Reporter:
"I wonder if I could ask Michelle, what did the treatment in America do to the family? It must have been very traumatic for you Michelle?"

Michelle Whitaker:
"It was very stressful having to travel and having to take the children to America, especially Charlie. We had to have a blood transfusion the day before we travelled and we had to be back before the next transfusion, so we were having the constant worry of him while we were in America which was very difficult."

Reporter:
"Would you say to people who are now celebrating the decision hang in there, it is worth it or did you ever think was it right to be playing God as some have accused you of doing?"

Jayson Whitaker:
"We didn't ever think we were playing God because all we were doing was stacking the odds in our favour. When they do IVF normally, they put two embryos back in because there is a chance that only one will take, so again they are putting the odds in your favour. Women will try to conceive at a particular time of month because that stacks the odds in favour so all we did was change from a 1 in 4 chance. We harvested Emily's cord blood when she was born but she wasn't a match so all we did was change it from a 1 in 4 chance to a 98% chance so there was no playing God it was just doing as much as you can to get the right result."

Reporter:
"It seems incredible; 5 years ago you were hitting headlines, now your smiling everyday must be worth it."

'Breast cancer gene-free baby'
BBC News, 9th Jan 2009 (1min55)
http://tinyurl.com/pgdvid3

Reporter:
"This is the technology that made this breakthrough possible, the moment a single cell is removed from an embryo to be tested for a gene that causes 5% of all breast cancer cases.

Paul Serhal is the man who carried out the highly sensitive screening process. The baby's parents went to him because 3 generations of their family had had breast cancer. He helped them have a little girl who's free of the gene that caused it."

Paul Serhal:
"The family is absolutely elated that a) the child will not have this genetic form of breast cancer and obviously the lasting legacy that all the future generations from this particular child will be free from this genetic abnormality."

Reporter:
"Doctors did the screening using IVF treatment. 11 embryos were created; a single cell was removed from each one for testing. 6 were found to be carrying the defective gene. 2 of the ones that were clear of it were planted back in the mother resulting in a healthy baby girl.

This type of screening is already being done to free babies of conditions like cystic fibrosis and Huntingdon's disease but this case is different because it wasn't inevitable that the baby would go on to develop breast cancer even if she had been born with particular gene.

Kelly Charles is a carrier; she knows she has an 80% chance of developing breast cancer and could pass that on if she has children."

Kelly:
"To know that a child of mine would be able to grow up without having the 50-85% chance of developing breast cancer would just be fantastic."

Reporter:
"This is controversial technology. Critics see it as another step down the road to designer babies. It doesn't eliminate only reduces the little girls risk of getting breast cancer. Even so for one family it's a technology that has made a big difference."