Genetics Contextualised Scenario

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Learning Outcomes

Students will be able to identify, evaluate, and solve ethical dilemmas raised by current practice in genetics. Students will be able to differentiate between eugenics and genetics, and evaluate new possibilities created or envisaged by genetics.

Assessment of Learning Outcomes

Sample questions for summative assessment by means of 'Data Interpretation' Methods:

Legal

1) Question: 'All forms of human cloning are prohibited by UK legislation.' Is this statement true or false?

Answer: False

2) Question: 'UK law regards the destruction of embryos before the stage of implantation as abortive.' Is this statement true or false?

Answer: False

3) Question: 'While adult stem cell research is currently allowed by UK legislation, embryonic stem cell research is still prohibited.' Is this statement true or false?

Answer: False

Moral

4) Question: 'As prenatal diagnosis can save the life of the fetus by allowing early medical intervention, all pro-life groups have welcomed the advance of prenatal diagnosis without reservations.' Is this statement true or false? Explain why/why not.

Answer: False

Teaching Structure/Format

Format: The scenario is presented to a small group of students (seminar form)

Learning Method: Discussion
Level: Multiple moral issues
Teacher's Role: The teacher is a facilitator with expert knowledge of genetics. The teacher facilitates whole group and small group (3-4 students) discussion and explains unknown legal information. The students are normally expected to draw out the main themes for discussion and to identify why they have selected the ideas which they choose to select after reading the scenario. They are asked which principles they would choose for resolving Mark and Katie's dilemma, and asked if they could justify the decision made. The teacher provides additional ways in which decisions could be made and how these could be justified. Procedure: Students read the scenario in four distinctive chunks. Each chunk takes half an hour. Students gather in small groups of 3 or 4 students to discuss the prominent ethical issues for the first 15 minutes of each theme. This is followed by 15 minutes of whole group discussion.

Approach

A learner-centred approach is adopted

The Scenario:

The scenario is presented in four chunks of text (on overhead or powerpoint slide), around four central themes:

Theme 1: How good is it to know? (The ethics of carrier identification)

Mark's father is suffering from Huntington's disease. Mark has decided that, in spite of the fact that he knows that he has a 50% chance of being a carrier of the gene causing the disease, he prefers to live with the uncertainty. In other words, he does not want to have a test to find out if he carries the Huntington gene. (Around 80 to 90% of the population who are in a similar position share Mark's preference). His girlfriend Katie, however, feels that she would like to know whether or not Mark is a carrier.

Theme 2: The ethics of pre-implantation genetic diagnosis and of genetic engineering

Mark and Katie are now married, even though Mark has had a positive test result for Huntington's. They are now thinking of having a child. Mark and Katie consult with their GP to talk through their fear of having a child with the genetic predisposition for Huntington's. The GP acknowledges their concerns and talks about recent breakthroughs in medicine which could help them. One option is IVF followed by pre-implantation genetic diagnosis (PGD) which would enable them to select only those embryos which are free from the Huntington's gene for implantation. Another option is a trip abroad to discuss with a fertility expert elsewhere the possibility of producing a clone of Katie. Mark and Katie are inclined to choose the former option, but feel that the rationale for such a test would be the elimination of any embryos which carry the gene for Huntington's. They talk to their GP about their ethical concerns related to abortion. Their GP, however, informs Mark and Katie about the Human Fertilisation and Embryology Act 1990 which implies that eliminating embryos which have not implanted cannot legally be classified as abortive.

Theme 3: The ethics of prenatal diagnosis and of gene therapy

Katie is pregnant and decides with Mark to opt for prenatal diagnosis to check if the fetus is all right. This is because they are both carriers of beta-thalassemia trait (minor), an autosomal recessive condition. An amniocentesis is performed and they find out that the fetus has beta-thalassemia major. Prenatal treatment is advisable. As the fetal immune system has not yet developed, it will not reject foreign cells. This is preferred to bone marrow transplantation after birth as there is no need to match donor cells. A variety of sources of pluripotent haematopoietic stem cells (cells that self renew and which produce all lineages of blood cell formation) are considered for transplantation, but medical evidence points to a preference for fetal liver cells. An alternative option is fetal gene therapy, where a virus is used as a vector carrying the desired gene into the cells of the fetus. Gene therapy has been shown to have some

promise for this condition, yet research has mainly involved nonhuman animals.

Theme 4: The ethics of embryonic stem cell research

Katie has now given birth to Jason, who has not received treatment for his condition yet. Katie and Mark were not happy about the possibility of using liver cells from an aborted fetus and fear that the risks involved with gene therapy may be too great. Jason's bone marrow type appears difficult to match, and a perfect match (HLA or human lymphocyte antigens match) is required for the treatment of his condition. They now consider having another child that could be selected to match Jason's bone marrow type and act as a donor by donating either bone marrow (or perhaps even stem cells derived from its cord blood and placenta). Leaving things to chance would mean that there would only be a one in four chance that the sibling would have the required immunologic criteria for bone marrow donation. They are also looking into the possibility of creating another embryo to harvest its stem cells which could then be manipulated to grow into new bone marrow cells which could be transplanted into Jason, but fear that this may not be a practical possibility as yet.

Moral Context/Underlying Ethical Issues:

Issues related to theme 1:

1) Medical information:

For a number of late-onset diseases which are caused by single gene disorders, it is now possible to have a genetic test to find out if one is a carrier. Huntington's disease is an autosomal dominant genetic disorder. Each autosome (= a chromosome other than the sex chromosomes) is paired up with another autosome. These contain genes. A person with the genetic predisposition for Huntington's disease has one gene which causes the disease (H) and another gene (which is paired up with H) which is normal (h). Sex cells are haploid (their chromosomes are not paired up), hence 50% of them contain the H gene and 50% the h gene. This explains why only 50% of the offspring of a person carrying the gene that causes the disorder and a person without the gene will be affected.

In autosomal recessive disorders, however, the offspring have to receive two affected genes (one from each parent) in order to develop the disease. Hence, in a hypothetical family in which both parents are carriers of the gene (with neither of them being at risk of becoming ill, so both being of the Cc type) and parenting four children, statistically there will be one of the CC type, two of the Cc type, and one of the cc type. Only the child with the cc type will have the disease. The most common of these autosomal recessive disorders is cystic fibrosis.

2) Ethical issues which could be raised:

In Western health care ethics, the principle of respect for a person's autonomy (capacity to choose or right to self-determination) is of utmost importance. People in the UK are normally held to have this capacity from when they are 16. Choices are only autonomous if they are free. Yet non-maleficence (not doing harm) is also important. One could argue that Mark's desire not to know whether or not he is a carrier may cause harm to Katie (for example when she needs to decide whether or not to have children with Mark) and to the child that they might have in the future (if it would have the genetic predisposition for Huntington's). Mark might succumb to Katie's pressure, in which case his decision would not be autonomous. Would it be right for a health professional to test someone who has been forced into being tested? One could complicate things further: Would Mark's parents have had the right to take the decision to test Mark for Huntington's when he was still a child?

Issues related to theme 2:

1) Reproductive cloning

Background: The legal context: The government's ban on reproductive cloning was deemed to have no legal effect by a High Court ruling in November 2001. This relates to the definition of an embryo in section 1(1)a of the Human

Fertilisation and Embryology Act 1990 where the notion of fertilisation is crucial. One could argue that an 'embryo' created by cell nuclear replacement (cloning) has not been fertilised, but 'propagated', and that therefore the restrictions on the creation and use of embryos as defined in the 1990 Act do not apply to cloning by somatic cell nuclear transfer. To redeem this situation, emergency legislation was passed through both Houses of Parliament (on 26 November 2001, with royal assent on 4 December) resulting in the Human Reproductive Cloning Act 2001.

Some ethical issues involved: If Katie and Mark were to proceed with cloning (by somatic cell nuclear transfer), the child would only have one parent:

- Is it 'unnatural' (because this way of reproducing is different from the normal way in which people reproduce). Is it therefore also unethical?
- Are the potential psychological effects on the child unacceptable (What does it feel like to be (like) your mum?)?
- Are the dangers and the costs involved excessive? Reproductive cloning may introduce new diseases and could be perceived as a wastage of human life (given the prognosis of poor success rates, given the experiences of cloning in nonhuman animals) and as a burden on public health resources.

2) Hyperovulation

A routine procedure of in vitro fertilization (IVF) is hyperovulation. Women take drugs in order to stimulate the production of egg cells, which are then collected and fertilised. This avoids having to repeat the burdensome and invasive procedure of egg collection. The effects of these drugs on the health of women is an area of controversy.

Ethical issues: Is the treatment seen primarily in terms of meeting the mother's desire to have a healthy baby (in which case the treatment benefits her) or is the administration of a drug which may affect her health adversely done for the benefit of her future infant? If the former then it would be important to determine whether the drugs were more or less damaging than repeated egg collection. One might also ask whether one method is less likely to lead to the destruction of unwanted embryos and what moral weight should be attached to it. In either case, informed consent from the mother would be of primary concern?

3) Pre-implantation genetic diagnosis (PGD)

Background: PGD relies on in vitro fertilization. The egg cell is inseminated with a single sperm, and grown in culture until the 6-8 cell stage. At this point, one or two cells are removed from the embryo and studied in the lab. A number of single gene disorders, the sex of the embryo, and certain chromosomal abnormalities (aneuploidies) can be identified in this way. It can be defined as a technique whereby embryos created outside the body can be tested to determine whether they carry a genetic disorder before transfer to the womb is considered. It has been available since around 1990. Non-disease genes (genes which predispose for non-disease traits such as intelligence) cannot at this moment be identified through PGD, apart from those which determine the sex of the embryo. Using the technique to select the sex of your child is only allowed in the UK for those families with a history of sex linked disorders who aim to avoid passing the condition on to their progeny. Sex selection in the absence of such a history has been approved in some other countries, for example Australia. The HFEA has decided that PGD should only be offered if there is a serious risk of the embryo being affected by a serious genetic condition. More recently, it has decided that PGD followed by tissue typing (for example to create a 'perfect match' sibling) is in principle acceptable, even though applications must be considered on a case-by-case basis.

Some issues raised by PGD:

- The removal of (a) cell(s) from the embryo.
- The cells of early embryos are 'totipotent': they have the capacity to generate another human being. Doing a biopsy at this stage can thus be called 'artificial twinning' (a form of cloning). One could argue that some

embryos are in this way sacrificed ('dissected') to determine if another embryo is 'worthwhile' to be implanted into the womb. This is morally questionable for those who believe that embryos have great moral value and therefore should not be destroyed.

- What is a 'serious condition'? Do we have a duty to eliminate serious conditions?
- Should embryos with autosomal recessive conditions be replaced?
- Should embryos affected with genetic conditions be replaced (for example a congenitally deaf couple may feel that a child with normal hearing would be alienated from their normal environment which may be damaging for both the child and the couple)?
- Is there a morally relevant difference between sex selection by PGD and by other methods (e.g. sperm sorting)?
- If PGD developed into a technique which could be used to test for the predisposition of certain diseases where the likelihood of developing the disease is uncertain even if the gene is identified (e.g. the breast cancer gene BRCA1), should affected embryos be eliminated?
- If PGD developed into a technique which could identify genes which catered for non-disease traits, should only 'the best' embryos be selected?

4) Concerns about abortion/killing

Even though legally the destruction of embryos up to 14 days in their development may not be classified as abortive, Mark and Katie may still see it as a form of killing, and therefore may consider this to be immoral.

Issues related to theme 3:

1) Prenatal diagnosis

Prenatal diagnosis can be done through ultrasound scanning and the taking of blood tests. When an abnormality in the blood tests shows up, or there is a family history of a particular condition, or the pregnancy is deemed to be subject to higher than average risk (e.g. higher age), further examinations can be recommended. These can be chorionic villus sampling (CVS; usually performed around 8-12 weeks) or amniocentesis (usually performed around 16-18 weeks). The former inserts a probe to extract some cells from the placenta, while the latter extracts fluid from the amniotic sac containing fetal cells. More than 40 genetic and chromosomal abnormalities can be identified by amniocentesis. The risk for inducing a miscarriage is higher for the former than for the latter. There remains controversy surrounding the risk percentage, and some students may find that given the fact that the procedure is not risk-free, subjecting the fetus to these procedures is immoral. Others may be more positive about them.

2) Gene therapy

Gene therapy works, at present, primarily with single-gene disorders, and only with autosomal recessive disorders. One of the problems with gene therapy is that the viruses which are introduced to carry the desired gene into the chromosomes of the cells of the recipient may not work efficiently, are often not large enough to carry a full gene and may also provoke an adverse response by the immune system.

The Gene Therapy Advisory Committee, the body responsible for approving applications for trials of gene therapy in the UK, disapproves of germ line genetic alteration and genetic enhancement, but has cautiously approved of gene therapy under specified circumstances.

3) Using fetal cells?

Katie and Mark may ask the question if therapy which uses cells from an aborted fetus can be regarded as ethical.

Issues related to theme 4:

In late 2000 and early 2001, both Houses of Parliament voted in favour of amending the regulations in the 1990 Act governing research on human embryos, so as to permit the use and creation of human embryos up to 14 days old for research on the derivation and potential of human stem cells. This includes the creation of embryos by somatic cell nuclear transfer. This is called 'therapeutic cloning' and has to be differentiated from 'reproductive cloning' as the embryos are solely created for therapeutic reasons (i.e. for the use of their stem cells).

Proponents usually stress that embryonic stem cell research may yield (significant) health benefits, and that embryos may or must be sacrificed for this purpose. As embryonic stem cells are 'totipotent', meaning that they are capable of developing into all the two hundred different cell types, and potentially 'immortal' in the sense that they have the capacity to replicate themselves indefinitely, 'banks' or 'lines' of these cells could be established with the prospect of giving all those who suffer from diseases which result from the degeneration of certain cell types the chance to replace these cells with new ones. It could also lead to a better understanding of the gene locations which are responsible for congenital diseases. At present, however, only limited successes have been achieved, primarily due to a lack of understanding of how stem cells (can be manipulated to) differentiate into particular cell types.

Opponents of such research usually stress that embryos should not be used as means towards enhancing the lives of others.

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