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This lecture is part of Spring 2020 – Covid-19 Pandemic – Online Education

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Prenatal Testing, Assited Reproductive Technologies, Gene Manipulation and Their Ethical Issues

Terminologies

- Prenatal diagnosis = Diagnosis before birth
- Genetic manipulation = manipulation of gene sequences to alter certain traits

Prenatal diagnosis and Gene manipulation

- Diagnosing anatomical and physiological anomalies before or at early periods of gestation
- Invasive (e.g. Amniocentesis) and Non-invasive methods (e.g. Ultrasonography, Serum screening)
- Manipulation of defective genes
- Gene therapy
- Alteration of undesirable traits

Purposes of Prenatal diagnosis

- to enable timely medical or surgical treatment of a condition before or after birth
- to give the parents the chance to abort a fetus with the diagnosed condition
- to give parents the chance to prepare psychologically, socially, financially, and medically for a baby with a health problem or disability, or for the likelihood of a stillbirth.

Prenatal testing involves a number of different types of test including;

- Genetic carrier testing
  - To provide risk information about having a child with one or more genetic conditions eg; Tay Sachs Disease
- Ultrasound
  - Common screening during pregnancy
  - 1st trimester; to determine the number of feuses
    - Nuchal ttanslucency; Down syndrome
  - 2nd trimester; congenital anomalies of various organs
- Amniocentesis
  - Chromosomal analysis
- Chorionic villus sampling (CVS)
  - Chromosomal analysis
- Preimplantation genetic diagnosis

Why is prenatal testing important?

- It promptes informed reproductive decision making
- Better when provided with pre- and post-genetic counseling
- To understand their personal risk of having a child with an inherited condition

Prenatal Genetic Screening

- Chorionic villus sampling (CVS)
  - between 10 and 12 weeks of pregnancy
  - the villus cells in the placenta have the same genetic composition as the cells in the fetus's tissues
- Other techniques looking for embryonic cells in a mother's blood and plasma
  - In development still
  - safe and relatively inexpensive cytogenetic analysis

Newborn Genetic Screening

- Small blood sample is collected from newborn infants within 24 hours of birth and tested for a panel of disorders.
- Between 3-40 tests depending on geographic region
- can save an infant's life- early diagnosis and treatment are imperative for a good outcome.
  - phenylketonuria (PKU)-unable to properly metabolize the amino acid phenylalanine
    - diet that is low in phenylalanine

What is Assisted Reproduction

- Enables the deliberate manipulation of the processes and materials of human reproduction outside of sexual intercourse

There are several reproductive technologies which are currently in use, including;

- fertility drugs,
- artificial insemination,
- in vitro fertilization (IVF),
- use of a surrogate mother,
- gamete intrafallopian transfer (GIFT),
- zygote intrafallopian transfer (ZIFT), and
- intracytoplasmic sperm injection (ICSI).

Why Assisted Reproduction is important?

- Enables subfertile heterosexual couples, single women and women in lesbian relationship to have children
- Individuals and couples who carry genetic condition may wish to use assisted reproduction in order to avoid those conditions on their children
- Important both for medical and social indications
  - Depletion in ovarian reserve
  - İnfertility
  - Endometriosis
  - Cancer treatment

Ethical Concerns about Assisted Reproduction

- Care of Multiple Embryos
- Use of Donor Eggs/Sperm
- Family Relationship
- Informed choice
- Surrogate Motherhood
- Bonding
- Gender Issues
- Embryo Status
- Financial Implications
- Access
- Genetic determination
- Commercializing Reproduction

A summary of possible combinations of gamete donors and surrogates

BIOLOGICAL SEX		SPERM	EGG	WOMB	GENETIC OUTCOME
PARTNER 1: MALE PARTNER 2: FEMALE	1	PARTNER 1	PARTNER 2	PARTNER 2	PARTNERS 1 + 2 (SPERM + EGG)
	2	DONOR	PARTNER 2	PARTNER 2	PARTNER 2 ONLY
	3	PARTNER 1	DONOR	PARTNER 2	PARTNER 1 ONLY
	4	PARTNER 1	PARTNER 2	DONOR	PARTNERS 1 + 2 (SURROGATE)
	5	DONOR	DONOR	PARTNER 2	N/A (EMBRYO ADOPTION)
	6	PARTNER 1	DONOR	DONOR	PARTNER 1 ONLY
PARTNER 1: MALE PARTNER 2: MALE	7	PARTNERS 1 + 2	N/A	DONOR	PARTNERS 1 + 2 (SPERM + SPERM)
PARTNER 1: FEMALE PARTNER 2: FEMALE	8	DONOR	PARTNER 1 OR 2	PARTNER 1 OR 2	PARTNER 1 OR 2
	9	N/A	PARTNERS 1 + 2	PARTNER 1 OR 2	PARTNERS 1 + 2 (EGG + EGG)

Table retriewed from; Beers, Breanna (2019) "The Ethics of IVF," Bioethics in Faith and Practice: Vol. 4 : No. 1 , Article 3.

Reprogenetics and Preimplantation Genetic Diagnosis (PGD)

- **Preimplantation genetic diagnosis:** a single cell, or blastomere, is removed from an embryo that has been fertilized in vitro, and this cell is tested for genetic abnormalities.

- **Reprogenetics:** the use of reproductive and genetic technologies to select and genetically modify embryos with germinal choice technology for the purpose of human enhancement

- Allows couples at risk of transmitting a genetic disease to ensure their future children are unaffected by the disease without going through the process of prenatal diagnosis (i.e., testing of fetal tissue for the presence of disease genes) and being forced to make the difficult decision regarding pregnancy termination.
- Only the embryos without genetic diseases are implanted to uterus.

Values of PGD

- Minimize the likelihood of transmitting fatal sex linked disease genes to offspring by determining sex of embryos (e.g. Duchenne muscular dystrophy affecting males)
- Single gene diagnostic testing (e.g. For Huntington's disease, BRCA mutations)
- Screening for chromosomally abnormal embryos to improve IVF efficiency

Gene manipulation in human

- Designer Baby
- Eliminate embryos with undesirable traits
- Artificial selection for desirable traits
- An outcome of Human Genome Project
- Germline modification
- Gene Therapy (T cell-based immunotherapy, stem-cell based therapy, genetic vaccines etc)
- CRISPR
- Gene Doping

Eugenics

- the study and practice of selective breeding applied to humans, with the aim of improving the species
- Eu= good or well; genes= born
- Positive eugenics encourages reproduction among the “genetically advantaged”
- Negative eugenics lowers fertility among the “genetically disadvantaged”

Benefits of Prenatal Diagnosis and Genetic Engineering in Humans

- Risk identification
- Timely disease treatment and control
- Disease elimination
- Extended Lifespan
- Improved intelligence of the race
- Better life
- Artificial selection for better traits
- Medical advancement

Proposed Ethical Guidelines for Prenatal Diagnosis

1. Equitable distribution of genetics services.
2. Prenatal diagnosis should be voluntary in nature.
3. If prenatal diagnosis is indicated, should be available regardless of couple's views.
4. Done to give information about the health of the fetus, for gender selection, is not acceptable.
5. Prenatal diagnosis solely for relief of maternal anxiety.
6. Counseling should precede prenatal diagnosis.
7. Should disclose relevant findings to the woman or couple.
8. The woman's and/or couple's choices in a pregnancy with an affected fetus should be respected and protected.

Bioethical Issues

Prenatal diagnosis and abortion

- The question of personhood is central to treatment of reproductive issues, and at the core of debates is the disagreement over when human life begins. (About 67% of fetuses with down syndrome detected are aborted in US)

PGD and selection of desirable traits

- Should people be given rights to determine the genetic makeups of their child according to their whims?

Other ethical concerns

- Morality of Eugenics?
- Selective breeding to improve human race?
- Artificial elimination of incompetent genes?
- Selection of powerful genes?
- What about failed trials?
- Unforeseen consequences
- Knowledge – power or liability?
- Discrimination against who are already living with a particular disability

- Who decides “good” and “bad” genes and on what basis?
- Are fetuses persons?
- Who draws the line?
- Danger of genetic misuse
- Techno-eugenic race
- “Genobility” (Ruling genetic class)= Inequality and discrimination?
- Financial and emotional costs
- Human gene pool- Loss of diversity
- Human cloning?
- Perfectionist expectation of parents = Conditional parenting with consumerist mentalism?

Ethical Issues in PGD

- Status of the embryo
  - – Do full human rights begin at conception?
  - – Is destruction of unsuitable embryos wrong?
- Reproductive freedom vs. social interests
  - – Does society have the right to dictate what reproductive decisions individuals should make?
- Discrimination against those with disabilities
  - – Does the use of PGD amount to a negative valuing of people living with the condition being selected against?

Ethical Issues in PGD cnt..

- Safety?
  - Long-term safety not yet demonstrated
  - More evidence required
- Resource Allocation?
  - PGD is expensive
- Psychological harm to parents and child
  - Very stressful process
  - Knowledge of procreative history: effect on future child?

Contentious applications of PGD

- Preimplantation tissue typing
  - Concerns and child welfare
- Sex Selection
  - Concerns about sex ratios and gender stereotypes
- Selecting for non-medical traits
  - Concerns about ‘slippery slopes’ and expectations on children

Conclusion

- Strong regulation
- Weighing of pros against cons
- Serious consideration about the balance
- Line between genetic manipulation for medical applications and other applications
- Transparency and participation
- Human future should be always considered

Ethical aspects of Nuclear and Mitochondrial DNA transfer

Nuclear DNA Transfer

- Cloning is a term that has been widely used in the media and in everyday language to refer in general to the production of organisms with an identical genome using laboratory techniques.
- consists of transferring the nucleus from a cell of the organism to be cloned to an enucleated oocyte, which is then stimulated to continue its biological development
- this process is called somatic cell nuclear transfer (SCNT).

Nuclear DNA Transfer

The concept of cloning, in the field of animal and biomedical research, can refer to:

- the production of DNA fragments with a sequence identical to an original DNA fragment using recombinant DNA techniques;
- the production of a cell or cell population genetically identical to another cell;
- the artificial division of early embryos; and
- the generation of an organism (biological being) genetically identical to another organism from the genetic material of a cell from the person or animal to be cloned by means of asexual reproduction

Nuclear DNA Transfer

- Depending on its purpose, SCNT can be reproductive or therapeutic, although the methodology used is the same.
- Reproductive SCNT refers to SCNT aimed at the production of an individual. This has been achieved in animals, but not in humans
- Therapeutic SCNT is aimed at the production of embryonic stem-cell lines for possible use in biomedicine.
  - cells obtained from the granular inner cell mass of the blastocyst
  - Cells of all types of tissues can be derived from these, except for extra-embryonic tissues

- it goes against the dignity of the human individual produced;
- it infringes personal individuality by producing genetically identical human beings;
- it is contrary to the right to ignorance of the child produced;
- there are negative side effects in children born using this technique;
- it goes against the dignity of the egg donor; and
- there are human embryos lost as a consequence of the still low efficacy of the technique.

mtDNA Transfer

- Nucleic acids from the mitochondria, instead of the cell nucleus, can also be transferred.
- This is the case in mitochondrial transfer or mitochondrial replacement.
- Prevention of mitochondrial disease transmission
- also known as “3-person IVF” is a form of inheritable human genetic modification

- What are the likely policy consequences of permitting nuclear genome transfer?
- If it is allowed inheritable genetic modification for preventing the transmission of mitochondrial diseases, won't it increase pressure to allow it for other diseases?
- If a new line is to be drawn, where would it be?
- Or will people simply design their children as they wish as soon as technology allows?
- If so, how could a "genetics arms-race," leading to new and increasing social disparities, be prevented?
- How will women affected by mitochondrial disease be informed of alternative options for having healthy children, which include IVF with genetic screening to choose a healthy embryo, prenatal genetic testing, using third-party eggs with IVF, and adoption?

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