# ETHICAL ASPECTS IN GENETIC COUNSELING

# Genetic Counseling

Genetic counselor assesses the risks for an individual or families, analyses the medical and family history, identifies the pattern of inheritable diseases and braces the society providing appropriate genetic services.

The transition from genetics to genomics, the relevance of molecular evolution fulfils the success of human genome project and supports the advancement of medical genetics.

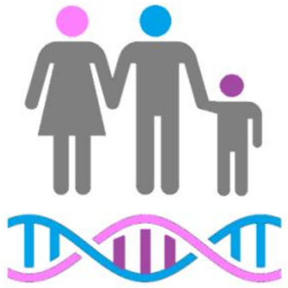
As the curve of genetic disorders is sloping high in a great significance, the urge of genetic counselling is at its field to serve the society at the earliest.

In a global scenario, visit to a genetic counsellor has almost become a routine.

Int J Hum Genet, 16(3,4): 172-180 (2016)

# Definition

- The National Society of Genetic Counselors has defined genetic counseling as a process in aiding people to comprehend and adapt to the medical, psychological and familial implications of genetic contribution to diseases .
- Recent findings conclude a vital need for genetic counseling as an important tool for the implementation of genetic disorders prevention strategies.



- Genetic counselling is a communication process which deals with human problems associated with the occurrence, or the risk of occurrence of a genetic disorder in a family.

- This process involves an attempt by one or more appropriately trained persons (genetic counsellors) to help the individual or family to

(i) comprehend the medical facts, including the diagnosis, the probable course of the disorder, and the available management,
(ii) appreciate the way heredity contributes to disorder, and the risk of recurrence in specified relatives,
(iii) understand the options for dealing with the risk of recurrence,
(iv) choose the course of action which seems appropriate to them in view of their risk and the family goals and in accordance with the decision, and
(v) make the best possible adjustment to the disorder in the affected family member and/or the risk of recurrence of that disorder

- Miglani, G. S., *Sci. Cult.*, 1986, **52**, 292–297.

- Genetic counsellors work as part of the multidisciplinary health care team providing expertise both in the science of genetics as well as facilitating the inevitable inter-generational (and often emotional) conversations from the psychological impact of the science.
- Genetic counsellor’ is an internationally recognized professional title with practitioners having specialist education, assessed competencies in genetics (and now genomics) combined with counselling skills.
- Genetic counselor’s duty is to make patients understand, adapt and adjust to the medical or psychosocial consequences of genetic contributions to disease

# Common Criteria to Refer Patient for Genetic Counseling

- A person with a known genetic condition within their family, in order to know about the risks that threatens their family and/or those of ofspring
- Parents who have children with genetic defects, referred for a possible diagnosis.
- A person with an intense family history of cancer, it is necessary to know increased risks and relevant options.
- A person with a known genetic condition willing to see an expert counselor to understand more about their condition.
- A person with potential genetic defects in the family wanting to know if a diagnosis is available, along with relevant risks and options.
- A pregnant couple with abnormal test results, wanting to know more about the abnormalities and the options which are available for them.

- Task is to help the patients understand their position biologically but then make personal decisions that they can live with in the long term.
- The decisions must be theirs, but conselors can help people to consider the various factors that may be relevant, including factors they had not thought of.

# Goals of Genetic Counseling Sevice

- Genetic counsellors facilitate knowledgeable decision making that supports patient autonomy.
- They promote meaningful informed consent based on an adequate understanding of the technical information and its implications for the individual and his or her family.
- They also foster effective adjustment to difficult situations in a manner that involves a realistic assessment of the positive and negative aspects of potential outcomes,
- Promotes individual and family competence
- Mobilises social and professional support—all consistent with the family's beliefs, values and culture.
- Promote a relationship of trust that encourages continued utilisation of their services as well as those of other health care professionals.

# Aspects of Genetic Counseling

1- Diagnosis

i) History Taking

ii) Choice of Tests

iii) Limitation of Diagnosis

2- Estimation of Risks

3- Communication and Support

# Protecting of Genetic Data

- Can be predictive of genetic predispositions for individuals
- Directly related to individual/family members/ offsipring
- May contain cultural significans for person/group/society

➢ Sensitivity on human genetic data

➢ Protection of biological datas and samples

# Ethical Aspects of Genetic Counseling

- The importance of cultural diversity and pluralism
- Human dignity, human rights and fundamental freedom
- Nondirective, culturally adapted and consistent to patients concerns

- Four principles of bioethics become inadequate to cover all aspects of ethical issues

✓Autonomy

✓Privacy

# Ethical Principles Applied to Genetic Counseling

1. Respect for persons and families regarding information.
2. Preservation of family integrity.
3. Full disclosure of all information relevant to health to individuals and family.
4. Protection of the privacy of individuals and families from unjustified intrusion.
5. Information to individuals and families about possible misuses of genetic information by institutional third parties .
6. Informing relatives about genetic risk .

7. Informing individuals about carrier status.

8. Informing people of their moral duties to disclose a genetic status that may affect public safety.

9. Unbiased presentation of information

10. Non-directive approach, except when treatment is available.

11. Children and adolescents to be involved in decisions affecting them, whenever possible.

12. Duty to recontact if appropriate and desired.

# Ethical Issues

1- The right to know/the right not to know

- The concept of the “right not to know” in genetic counseling has been heavily debated.
- It is not technically simple to secure the right not to know with WES or WGS data, or even with a multiple gene panel test, as this would require a tremendous amount of time and effort to help the P/C decide what he/she wants to know and what he/she does not want to know among the large amount of data generated

2- Coercion

True coercion involves some type of harm or the threat of harm; however, there are many other types of more subtle pressure tactics possible, including persuasion and manipulation.

3- Confidentiality

Counselors need to respect client confidentiality by not releasing any client data to a third party, including the P/C’s relatives. Ethical dilemmas can occur when the P/C does not want to share genetic test results with relatives or wants to share genetic test results with some but not all relatives.

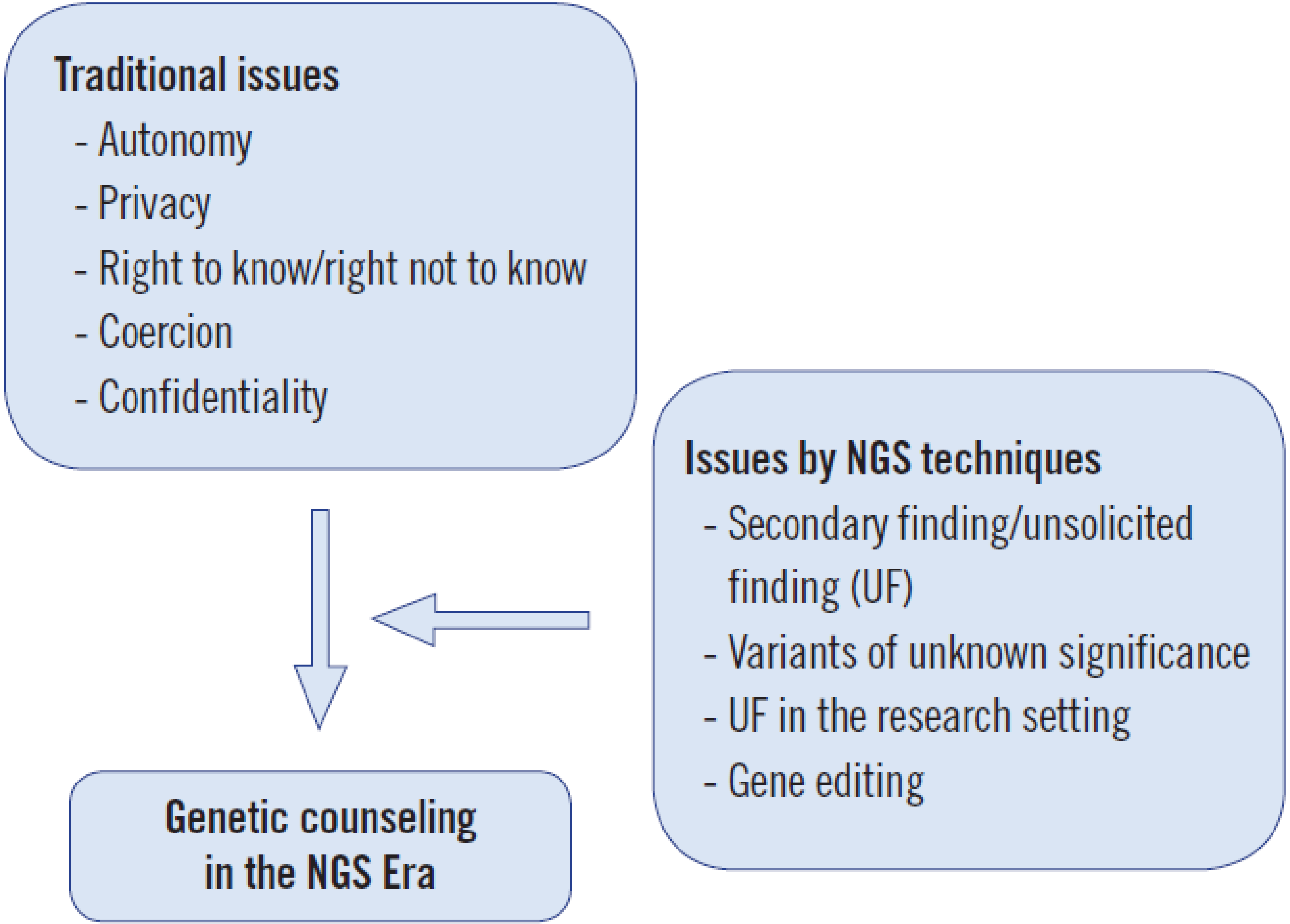
4- Testing of minors

This decision will vary on a cultural, familial, legal, and individual basis.

# GENOMIC COUNSELING

- The challenges relating to storing, interpreting and using data generated from genome sequencing are well rehearsed and remain.
- Emerging models of genomic medicine emphasize the iterative nature of variant interpretation with input from the bioinformatician, the laboratory scientist and the clinician. These multidisciplinary teams will often now include a genetic counsellor.
- The implementation of genomic medicine across the whole healthcare service has the potential to significantly increase the demand for clinically practising genetic counsellors.
- Its is essentical that the genomic counselling be included as an integral component of health care

- Traditional genetic counseling has focused on the target gene and its natural progress with respect to disease risk.
- Next-generation sequencing (NGS) can produce information on several genetic variants simultaneously, with different functions and consequences for each.
- Accordingly, determining the status of the patient or consultant and interpreting sequencing results from many genes can largely increase the complexity of genetic counseling.
- Traditionally, genetic counseling largely dealt with single-gene disorders or Mendelian diseases. However, with the progress of genomic technologies, a new era of multifactorial disease is on the horizon.




- Influence of the issues of NGS technology on traditional genetic counseling.

Yang M, et al., Genetic counseling in the NGS era, Ann Lab Med 2018;38:291-295.

- At the beginning, with genetic risk estimation,
- Decision  making about testing and conversations about consent;
- in the management and interpretation of results;
- at the point at which the result enters into the health care system and is returned to the clinician and the patient,
- at the follow up of patients in mainstream and in helping the patient to seek out and communicate the results within their family.
- In particular, application of genetic/genomic counseling should be specific for the context of the current culture of a society.

# References


- C. Patch and A. Middleton, British Medical Bulletin, 2018, Vol. 126
- EMBO *reports* vol. 3 | no. 7 | 2002
- Yang M, et al., Genetic counseling in the NGS era, Ann Lab Med 2018;38:291-295

# ETHICAL ASPECTS IN GENETIC/GENOMIC SEQUENCING

# What is a Genetic Test?

A genetic test is the analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable diseaserelated genotypes, mutations, phenotypes, or karyotypes for clinical purposes.

Task Force on Genetic Testing, 1997

# What are these clinical purposes?

- Clinical purposes include predicting the risk of disease, identifying carriers, and establishing prenatal and clinical diagnoses or prognoses.

# Predicting the Risk of Disease

- Predictive genetic tests are tests that are performed on healthy or apparently healthy individuals with the goal of identifying their risk for developing disease in the future.
- These tests are of two types:

– Presymptomatic testing

– Susceptibility testing

# Presymptomatic Tests

- Presymptomatic testing involves looking for genetic mutations that have a high penetrance (usually autosomal dominant)
- Tests need to be highly sensitive and specific (few false negatives or false positives)
- Examples include genetic testing for Huntington Disease and early-onset Alzheimer disease

# Testing Protocols

- Neurological examination
- Pretest counseling
- Informed Consent
- Results in person
- Follow-up available

# Ethical Issues in Presymptomatic Testing

1. Are we better off knowing our fate?
2. Respect for personal autonomy – Informed consent – Right “not to know”
3. Reluctance to test children
4. Psychological costs for those tested
5. Prenatal testing for late onset disorders

# Susceptibility Testing

- Susceptibility testing involves looking for genetic mutations that confer a higher risk for developing disease
- Disorders are usually multifactorial
- Tests have variable sensitivity and specificity
- Examples include testing for Apo-E4 (Alzheimer disease) and BRCA1 and BRCA2 (breast cancer)
- Test results of this type do not mean that disease will inevitably occur or remain absent; they replace an individual’s prior risk based on population data or family history with risks based on genotype.

# Ethical Issues in Susceptibility Testing

1. Education and counseling for those at risk
2. Test interpretation can be complex
3. Potential for increased monitoring and possible treatment
4. What counts as “useful information”

# Carrier Identification

- Identifies individuals who do not themselves have a particular disease but who are at risk for having a child with a particular disease/
- Carrier testing involves individuals known to be at high risk because of family history (testing a woman whose sister has a son with cystic fibrosis).
- Carrier screening involves testing individuals with no family history (testing all Caucasian women of child bearing age for cystic fibrosis).

- Examples:

»Tay Sachs disease in Ashkenazi Jewish populations (1/27)

»Sickle cell anemia in African American populations (1/13)

»Cystic fibrosis in Caucasian populations (1/25)

# Ethical Issues in Carrier Screening/Testing

1. Respect for individual's/couples' beliefs and values concerning tests taken for assisting reproductive decisions

2. Mutations for certain diseases may have a higher prevalence in certain ethnic populations raising the issue of stigmatization

3. Few choices available to those identified as carriers (refrain from childbearing, donor egg or sperm, PGD)

4. Obligation to offer education and counseling

- Prenatal Testing
- Newborn Screening

# Limitations of genetic testing

- Having positive genetic testing is not equal to developing disease.
- Risk for developing disease may not be accurate based on current research
- Most risks from GWAS data have low odds ratios for developing disease
- Does not predict when a person may show symptoms of a disease
- Does not predict severity of symptoms

# General Ethical Issues Related to Genetic Testing

- Lack of knowledge
- Direct marketing of tests to consumers
- Confidentiality issues
- Fear of discrimination
  - Insurance
  - Employment
  - Law Enforcement

# Other “risks” for genetic testing

- False positives
- Anxiety/Stress
- Harm from undergoing unnecessary tests or procedures
- False negatives:
- Ignoring a disease when genetic testing is negative
- Diseases can occur sporadically

# Case 1: “I will have PD”

57 year old woman with a family history of Parkinson’s disease who is asymptomatic

- She has a SNP associated with mildly increased risk for developing PD
- She travels from another state every year for neurological examination by a movement disorders specialist to evaluate for signs of PD
- She has planned her life to account for developing PD:
  - Early retirement
  - Bought long term care insurance
  - Moved into a single story home

**How did you counsel her?**

# Case 2: “But I can’t have PD because I don’t have the gene!”

69 year old retired lawyer with a 8 year history of parkinsonism on exam

- He does not carry any SNPs associated with PD
- Sequencing for LRKR2 mutation is negative
- He refuses the diagnosis of PD because he does not have the gene and refuses to take medications to treat the symptoms
    - He is now in a wheelchair
    - Moved into a nursing home

# ETHICAL CONCERNS ON SHARING GENOMIC DATA

# A new scientific standard: data sharing

- The idea that data sharing promotes scientific progress has been widely accepted among research communities, funding bodies, and regulatory agencies .
- Sharing clinical and genomic data promises to increase research efficiency, expedite translational efforts of research results, and ensure the traceability and transparency of published studies, while maximizing the utility of existing datasets and minimizing the burden to participants.
- Highly shared data sets include genomic research for cancer and rare diseases.
- In genomic research for cancer and rare diseases, patient family members (e.g., parents, children, siblings, or uncles/aunts) can also provide important information.

# Global sharing platforms

- International Cancer Genome Consortium (ICGC)
- The Global Alliance for Genomic Health (GA4GH)
- The International Rare Diseases Research Consortium (IRDiRC)

- While the advantage of genomic data sharing is recognized, privacy protection, security, and respecting participants’ consent remain as ethical concerns.
- Do these concerns differ between sharing only patient data and those from both them and family members?
    - there is a need to consider protection not only of the patients’ own data but also their family members’ data

# Genomic Data Sharing Policy

- Governments, scientific repositories and databases, and academic journals have established data-sharing policies to protect individual participants.
- Investigators are required to obtain informed consent from participants for future research purposes and their data-sharing plan, including whether individual-level data are shared.
- Recent data suggested that coded or “anonymized” sequenced DNA can be linked to individuals as genetic databases proliferate.

- Before obtaining informed consent from participants, researchers should explain not only general considerations for submitting and sharing their clinical and genomic data, but also how their data will be presented in databases or publications (especially regarding the relationship between family members, i.e., child, parent, sibling, aunt/uncle, etc.) and what measures will be taken to protect them.
- Informed consent should be obtained from all participants (patients and family members), without any pressures, even from enrolled family members when family-based recruitment approach is applied

- ***Initial researchers***
- ***Data submitters***
- ***Database operators***
- ***Research ethics committees / Institutional Review Boards(IRBs)***