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Genetic Counseling:
Principles and Practice

Monica Gersbach-Forrer, MD
Division of Medical Genetics
Geneva University Hospital
Genetic counseling

- Definitions
- Concept of Risk
- Steps and Tools
- A Few Principles
- Difficulties and Potential Problems
- Examples
- References
Genetic Counseling

A somewhat different patient/client – doctor relationship!

- Diagnosis
- Communication
- Information
- Decision Making
- Psychological Support
- (Treatment)
- (Recovery)
Genetic Counseling

= specialized consultation where patients and/or relatives at risk for a genetic disease are informed about:

• The causes and consequences of the disease (diagnosis, course)
• The probability of developing and/or transmitting it (genetic contribution)
• The ways by which it can be detected / prevented
• Ways for optimal adjustment, management, coping
• Possibilities concerning family planning
Genetic Counseling:
A challenging communication process where:

- Language and explanations should be easily understandable
- The available options are explored in a non directive manner
- The ethical implications
- The emotional state
- The psycho-social context and resources are addressed
- Reflection time is provided
- Psychological support if necessary
Definitions:

- **Genetic** = related to the gene constitution (not necessarily hereditary!)
- **Hereditary** = which can be passed on to the next generation
- **Sporadic / de novo** = which happens for the first time
- **Congenital** = present at birth (genetic or not! hereditary or not!)
The Concept of Risk

• Estimation of genetic risk = rarely yes or no, usually a probability, given in a percentage (odds)

• The valuation of a given risk = a very personal matter! (age, experience of life, type of personality, education, psycho-social environment,..)

• Relation of a given risk to general population risks
  – Misscarriage 12 %
  – Infertility of a couple 10 %
  – Congenital malformations (total) 3 %
  – Severe congenital malformations/mental retardation incl. 1-2 %
The Types of Risk

- **Mendelian risks** = very precise, only applicable if diagnosis and single-gene inheritance are certain!

- **Modified genetic risks** = prior risk modified by anamnestic information (Bayes calculation: probability that a Duchenne muscle Dystrophy patient’s mother is a carrier)

- **Empirical risks** = based on epidemiological studies, prenatal serum screening (PAPP-A, AFP..), prenatal nuchal fold measurement… (applicable for most malformations, chromosomal anomalies,..)

- **Estimates** (when genetic basis incompletely understood) = DNA linkage analysis (indirect, residual risk of error), causal mutation versus polymorphism, more than one gene involved (schizophrenia,..)…
Steps and Tools

• Assess patient/client expectations
• Preliminary gathering and study of the medical documents → correct diagnosis
• Family history / family tree
  – Appropriate symbols
  – Always document both sides of family
  – Ask for consanguinity, parental age, miscarriages, stillbirths, mental handicap, congenital malformations, potentially genetic pathologies
• Medical + reproductive history of counselee
• Clinical examination, by specialist if necessary
• Organize genetic tests (karyotype, DNA) when indicated to confirm/infirm a clinical diagnosis, a predisposition, a carrier status
Steps and Tools (Cont’d)

• Check and update your knowledge !
  – Literature, articles, Internet : OMIM (online mendelian inherit.in man)
    Orphanet http://www.orpha.net/

• Give information regarding :
  – Causes, consequences, implications of the disorder
  – Recurrence risk / transmission : mode of inheritance : Monogenic
    (autosomic - dominant, - recessive, sex(X) - linked), mitochondrial,
    empirical risk
  – Ways of detection :
    • prenatal / postnatal
    • Presymptomatic
  – Possibilities of management

• Written report summarizing the genetic counseling in a easily
  understandable language
A few principles

• Propose a genetic counseling/consultation session, never organize one automatically
• Explain what it is, what can be expected of it

• Learn how to explain complexe facts in an easily understandable manner
• Take the necessary time, reflexion time before important decisions
• Be as non-directive as you can, respect/encourage autonomy
• Respect the « right not to know » (esp. in presymptomatic testing)
• Address potential ethical implications
• Take into account/address emotionnal status, possible guilt feelings
• Assure privacy and confidentiality

• No genetic tests in children unless direct benefit to them (therapeutic, preventive)
Potential problems

• Keep up with rapidly increasing knowledge in genetics

• Make sure counselee(s) have understood your message

• Unexpected finding: additional risk discovered through family history, unexpected finding in a test (chromosomal marker, non-paternity, …)

• Length of certain tests (weeks, months...), difficulty to find a laboratory for unfrequent tests

• Quality control
Potential problems (cont'd)

- Costs (long consultations, some tests are expensive)
- Conflict of interest between individual, family, society, public health, insurances
- Risks of genetic tests without adequate genetic counseling (proposed for lucrative interest, legal gaps)
- Lack of trained medical professionals
Examples:

• Sickle cell anaemia in previous pregnancy

• Young couple, husband’s older brother died of cystic fibrosis

• Couple with single 7 year old son affected by Duchenne Muscle Dystrophy

• Young pregnant woman, her sister’s newborn diagnosed with Down syndrome

• Young man, his father has developed a psychiatric illness, his paternal grandmother died of Chorea Huntington
Sickle cell anaemia in previous pregnancy

- Autosomal-recessive inheritance: both parents obligate carriers
- If consanguinity: Increased risk for other recessive disorders
- Implications of being a carrier (haemolysis during hypoxic stress, anaesthesia)

- Recurrence risk for new pregnancy = 25%
- Prenatal testing possible? Methods? Wished for?
- DNA analysis must be ready before prenatal diagnosis

- Family screening, haemoglobin electrophoresis (HbS band)
Young couple, husband’s older brother died of cystic fibrosis

- Medical records, molecular diagnosis of patient
- Knowledge, perception of the illness
- Monogenic autosomal-recessive inheritance

- Probability that young man is carrier = 2/3
- Probability that his non-consanguinous partner is a carrier = 1/23 (CH)
- Risk of obstructive infertility for carrier male: CBAVD (cong. bilat. absence of vas deferens)

- Recurrence risk for pregnancy of their couple
- Prenatal diagnosis or not, ethical aspects
- Type of PND, risks, possible problems
- Organize gene testing, screening of partner
Reminder of monogenic autosomal recessive inheritance

- Recurrence risk for new pregnancy of parents of affected child = 25%
- Probability that healthy sibling of patient is a carrier = 2/3

Figure: Autosomal recessive heredity of genetic traits
Couple with single 7 year old son affected by Duchenne Muscle Dystrophy

- Medical records, molecular diagnosis of patient
- Perception of how the family deals with the illness, psycho-social surroundings, support, school, …
- Other cases in the family?
- X-linked inheritance of DMD
- Probability that mother is a carrier (in theory = 2/3)
- Recurrence risk for a new pregnancy of their couple
- Ethical aspects, guilt feelings, responsibility towards son; pressure of other family members
- Prenatal diagnosis (direct, indirect molecular analysis) or not
- Type of PND, risks, possible problems
- Alternatives: preimplantation diagnosis, adoption
- Support during pregnancy, psychological support also regarding burden for affected son
Reminder of X-linked inheritance
Couple with single 7 year old son with Duchenne Muscle Dystrophy
Young pregnant woman, her sister’s newborn diagnosed with Down syndrome

Points to discuss:

- **Diagnosis**: clinical or based on karyotype
- **Natural history of Down syndrome**
- **Type of trisomy**: classical free trisomy or parental translocation
  Explain mechanism
- **Recurrence risk**
- **Prenatal diagnosis**: indicated? what type, when?
- **Ethical implications**: autonomous choice, do both partners agree, reflection time
- **Guidelines for best care of affected child**
- **Education material, support groups**
Young pregnant woman, her sister’s newborn diagnosed with Down syndrome

Free trisomy 21 (95%)

In 3-4 % cases: Translocation trisomy 21: recurrence risk!
One parent translocation carrier:
Trisomy 21 (Down syndrome)

3 main types:

1. **Approx. 95 % = extra chromosome 21 (47). Majority by meiosis I non-disjunction (>> meiosis II, early mitosis non-disj.)**

2. **Translocation (3-4 %) = the extra 21 chromosome is attached or translocated on to another chromosome, usually on chrom. 14, 21 or 22. Examine the parents' chromosomes: in at least 1/3 cases a parent carries the translocation → risk for relatives**

3. **Mosaicism (approx. 1 %) = Some cells have 47 chromosomes, others 46 chromosomes by error in cell division early after conception.**
Young man, his father has developed a psychiatric illness, his paternal grandmother died of Chorea Huntington

- Medical records, molecular diagnosis of patients
- Perception of how the family deals with the illness
- Family history
- Natural history of disease, usual course and management
- Autosomal-dominant inheritance, nearly full penetrance
- Recurrence risk for the young man (25-50%), age of onset
- Option « Right not to know »
- Option of presymptomatic testing: adapted setting, pluridisciplinary consultation over various amount of time
- Recurrence risk for a pregnancy of his couple
- Ethical aspects, responsibility towards partner, towards children to come, pressure of other family members, …
References


• OMIM www.ncbi.nlm.nih.gov/Omim/
• Medline www.ncbi.nlm.nih.gov/pubmed
• Orphanet www.orpha.net
References (cont’d)

• Ethical guidelines on the internet