Postgraduate Course in Reproductive Medecine and Reproductive Biology - Geneva, March 2003

Genetics Module and Consultation

March 20 and 21, 2003

Division of Medical Genetics
Geneva University Hospital

Division of Medical Genetics, Geneva University Hospital

Who's who…

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Genetic Counseling : Principles and Practice

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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 possible 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
- Options regarding adjustment and management
- Options regarding 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 ressources are addressed
- Reflexion 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

- **Empirical risks** = based on epidemiological studies, prenatal serum screening (PAPP-A, AFP..), prenatal nuchal fold measurement…

  (applicable for most malformations, chromosomal anomalies,..)

- **Mendelian risks** = very precise, only applicable if single-gene inheritence is certain!

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

- **Estimates (when genetic basis uncompletely understood) :** DNA linkage analysis (indirect, residual risk of error), causal mutation versus polymorphism...

Steps and Tools

- Ask for 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, misscarriages, stillbirths, mental handicap, congenital malformations, potentially genetic pathologies..
- Medical + reproductive history of couselee
- 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 (www.ncbi.nlm.nih.gov/Omim/), Medline www.ncbi.nlm.nih.gov/pubmed
- Give information regarding :
  - Causes, consequences, implications of the disorder
  - Recurrence risk / transmission : mode of inheritence : 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, assure 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 : additionnal 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 developped a psychiatric illness, his paternal gdmother died of Chorea Huntington

Sickle cell anaemia in previous pregnancy

- Consanguinity?
- Autosomal-recessive inheritence
- Implications of being a carrier (haemolysis during hypoxic stress, anaesthesia)
- Recurrence risk for new pregnancy
- Family screening, haemoglobin electrophoresis (HbS band)
- Prenatal testing possible ? Methods ?
- DNA analysis must be ready before prenatal diagnosis

Young couple, his older brother died of cystic fibrosis

- Medical records, molecular diagnosis of patient
- Perception of the illness
- Monogenic autosomal-recessive inheritence
- Probability that young man is carrier = 2/3
- Probability that his non-consanguinous partner is a carrier
- Risk of infertility
- Recurrence risk for pregnancy of their couple
- Prenatal diagnosis or not, ethical aspects
- Type of PND, risks, possible problems
- Organize gene testing, screening in partner

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 inheritence of DMD
- Probability that mother is a carrier
- Recurrence risk for a new pregnancy of their couple
- Ethical aspects, guilt feelings, responsability towards son, pressure of other family members
- Prenatal diagnosis (direct, indirect molecular analysis) or not
- Type of PND, risks, possible problems
- Alternatives : adoption, preimplantation diagnosis
- Support during pregnancy, psychological support regarding burden for affected son

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 mecanism
- Recurrence risk
- Prenatal diagnosis : indicated? what type, when?
- Ethical implications, autonomous choice, do both partners agree, reflexion time
- Guidelines for best care of affected child
- Education material, support groups

Trisomy 21 (Down syndrome)

There are three main types of chromosome abnormalities in Down syndrome:

1. The vast majority of children with Down syndrome (approximately 95 percent) have an extra 21 chromosome. Instead of the normal number of 46 chromosomes in eachcell, the individual with Down syndrome has 47 chromosomes. This condition is called trisomy 21. Majority by meiosis I non-disjunction (>> meiosis II, early mitosis non-disj.)

2. The second type is called translocation since the extra 21 chromosome is attached or translocated on to another chromosome, usually on chromosome 14, 21 or 22. If translocation is found in a child with Down syndrome, it is important to examine the parents' chromosomes, since in at least one-third of the cases, a parent may be a carrier of the translocation. This form of chromosome error is found in 3 - 4 percent of the individuals with Down syndrome.

3. Another chromosome problem, called mosaicism, is noted in about 1 percent of individuals with Down syndrome. In this case, some cells have 47 chromosomes and others have 46 chromosomes. Mosaicism is thought to be the result of an error in cell division soon after conception.

Young man, his father has developped 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 inheritence, 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, pluridsciplinary consultation over various amount of time
- Recurrence risk for a pregnancy of his couple
- Ethical aspects, responsability towards partner, towards children to come, pressure of other family members, …

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