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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 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 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

- **Mendelian risks** = *very precise, only applicable if diagnosis and single-gene inheritence 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 uncompletely 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, misscarriages, 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) www.ncbi.nlm.nih.gov/Omim/, Medline www.ncbi.nlm.nih.gov/pubmed, Orphanet http://www.orpha.net/

- **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, 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

- Autosomal-recessive inheritence: 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 inheritence

- 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

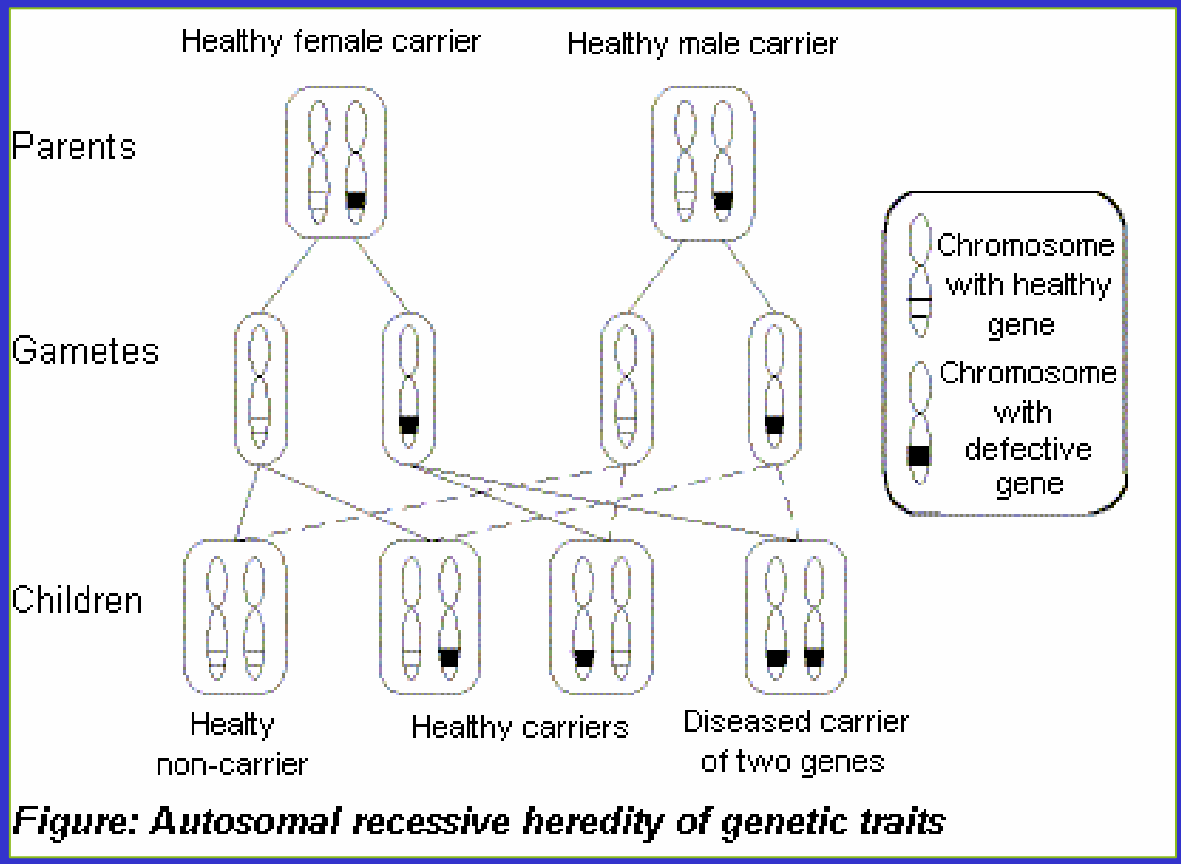


Figure: Autosomal recessive heredity of genetic traits

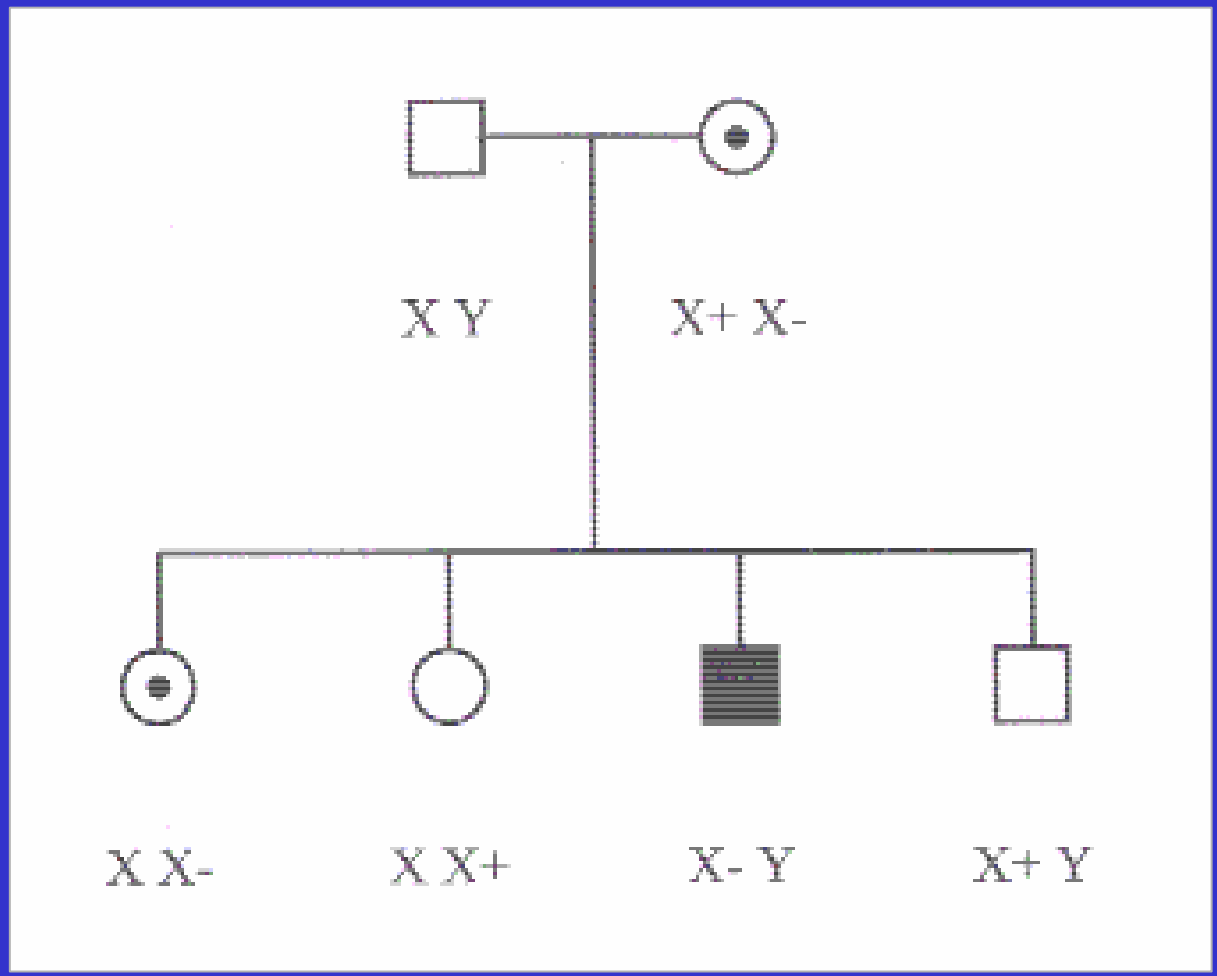
- Recurrence risk for new pregnancy of parents of affected child = 25%
- Probability that healthy sibling of patient is a carrier = 2/3

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 (in theory = 2/3)
- 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 : 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



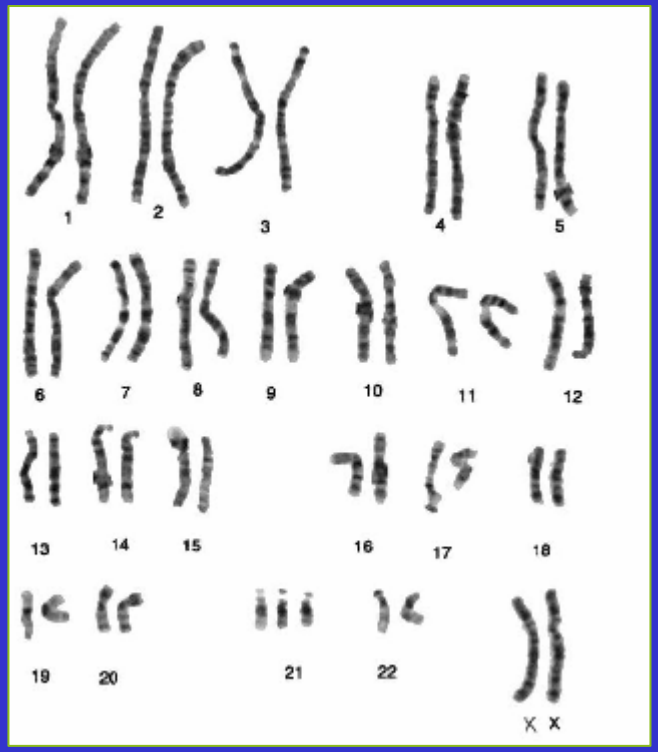
Young pregnant woman, her sister's newborn diagnosed with Down syndrome

Points to discuss:

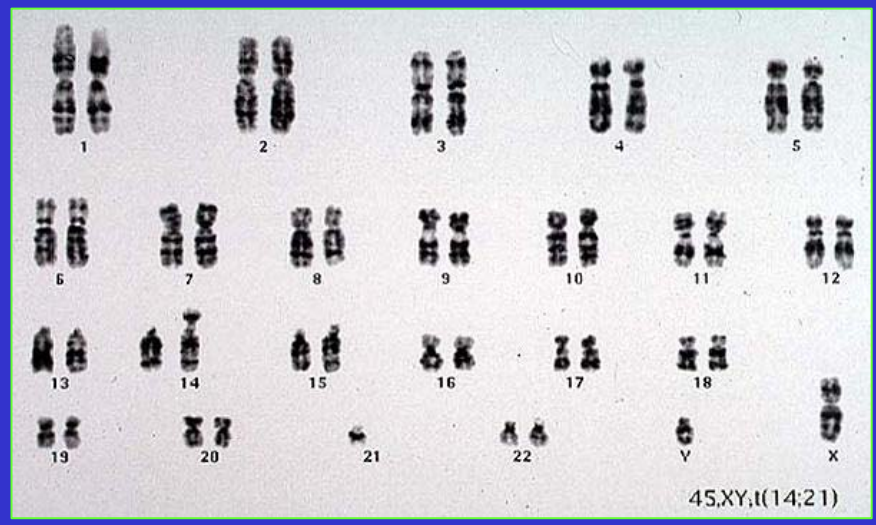
- Diagnosis : clinical or based on karyotype
- Natural history of Down syndrome
- Type of trisomy : classical free trisomy or parental translocation Explain mecanism
- Recurrence risk
- Prenatal diagnosis : indicated? what type, when?
- Ethical implications, autonomous choice, do both partners agree, reflexion time
- Guidelines for best care of affected child
- Education material, support groups

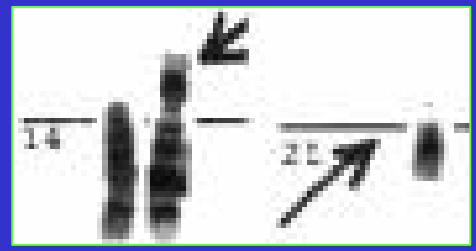
Young pregnant woman, her sister's newborn diagnosed with Down syndrome

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 $\rightarrow$ 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 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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