

Genetic Counseling

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I-Introduction

More than 2000 hereditary (genetic) diseases have been documented and 0,7% of newborns have an unbalanced chromosomal anomaly. Miscarriages or sterility in couples can also be related to a genetic defect. Overall 4% of live births show an anomaly that may or may not be due to a genetic defect.

II-Motives for seeking genetic advice

II-1. Couple before reproduction

history of genetic disease in one of the future spouses or in their family;
consanguinity.

exposure to a suspected physical or chemical mutagen, toxic or therapeutic agent.

II-2. Couple at risk

sterility investigation (search for a chromosomal anomaly).

spontaneous miscarriages: a foetal loss occurs in 15 % of pregnancies; a karyotype is indicated for couples after two (or more) unexplained miscarriages.

exposure to a teratogen (rubella, toxoplasmosis...) during pregnancy

history of a handicapped child in the family (stillbirth, neonatal death, . . malformed newborn or child in whom a genetic related anomaly or hereditary metabolic disorder was later detected).

advanced maternal age.

medical information that later came to the couple attention about a degenerative disorder.

III- Genetic counseling consultation

III-1. Climate of anxiety

Feeling of permanent commitment for the future.

Delicate interview on familial medical 'handicaps' with occasional blame from distant relatives.

Transmission of secrets (adultery, incest) leading occasionally to erroneous information.

The consultation must include a thorough analysis of the family tree and a precise diagnosis of the disease thus permitting to establish its mode of inheritance and repercussions.

III-2. Pedigree

The family tree must be complete and include the deceased individuals, the pregnancy losses, and the causes of death.

III-3. Diagnosis of the disease

A careful physical examination must be carried and the necessary biological tests completed.

The normal heterozygote carriers must be identified, and if possible the obligate heterozygotes as well.

A detailed examination of aborted fetuses and stillbirths must be carried including: a detailed morphological description, photographs, skeleton radiological examinations, biological specimens, a cardiac blood sample or other tissue for karyotype, and a detailed autopsy authorized by the parents.

it is essential to conclude as precisely as possible on the nature of the diagnosis since several similar diseases can have a different mode of transmission.

IV- The counseling will be based on:

the risk of recurrence (mode of transmission, penetrance, expressivity, coefficient of inbreeding, gene frequency in the population).

the seriousness of the disease and the availability of treatment taking into consideration the genetic family history (number of affected individuals, number of normal children).

for a severe disease, with a high recurrence risk, without efficient treatment and non available prenatal diagnosis.

(or if parents refuse this last option), they should be alerted to the high risk of having abnormal children and should remain in contact with the geneticist since constant developments occur in this field.

the genetic counseling session requires time and disponibility (often partners must be seen in consultation separately if one suspects erroneous registered information, or undisclosed secrets).

a sound psychological approach.

a good knowledge of genetic diseases.

V- Risk evaluation

V-1. Autosomal dominant inheritance

an affected individual has a 50% risk of having an affected child

in a given family a normal individual has almost no risk (excluding a spontaneous mutation) of having an affected child.

however if there is incomplete penetrance or variable expressivity the above eventualities do not hold.

an isolated case is due to illegitimacy, a spontaneous mutation or incomplete penetrance. In the second case only the risk of recurrence is null.

V-2. Autosomal recessive inheritance

parents are normal

an isolate case is not a rare event in a family

the risk of recurrence, if the parents are normal, is $\frac{1}{4}$.

the siblings (brothers and sisters) of an affected individual have a $\frac{2}{3}$ risk of being heterozygous

an affected individual a has probability $pq=q$ (mutant gene frequency) of having and affected child

consanguinity in a family increases the probability of being affected measure the consanguinity coefficient)

a spontaneous mutation or an illegitimate mating may occur

V-3. X-linked recessive inheritance in the family

half the children of a carrier mother will be affected

often, a male affected individual is identified in the family

a spontaneous mutation is possible; an illegitimate mating has no influence on the risk of recurrence

V-4. Multifactorial inheritance

statistical data on a disease in a given population allows the drawing of a preliminary risk of recurrence

this risk will increase 1) if several individuals are affected in a family 2) if the disease is severe 3) according to the degree of consanguinity between the affected individuals

the risk is expressed as a frequency of recurrence or according to the number of times the risk of the general population

V-5. Chromosomal diseases

Most often due to a parental meiotic non disjunction: low risk of recurrence but not null (1 to 2 % of cases of a standard trisomy 21).

Occasionally due to an abnormal segregation secondary to a parental rearrangement: the risk of recurrence is not easily established (due to the type of the rearrangement, the size and the nature of the segment involved, the sex of the carrier).

V-6. Consanguinity

Increases the risk of occurrence of an autosomal, recessive or multifactorial disease. Measure the consanguinity coefficient. Notable risk in the case of a known familial disease.

V-7. Exposure to mutagens

Low risk but a prenatal diagnosis can be offered to reassure the couple if one of them has undergone anticancerous treatment during the months preceding the pregnancy. A prenatal evaluation must be proposed, if feasible, in future pregnancies, for any of the above situations.

VI- Adult onset of hereditary diseases

The treatment of hereditary metabolic diseases during childhood and the transfer of those pediatric patients after the adolescence have contributed to the development of adult genetic medicine. Late onset disorders like Huntington disease and several others diagnosed at a later age are now often cared for by those clinics.

VII- Speciality clinics

VII-1. Speciality clinics

. Adequate genetic counseling is more than often offered in speciality clinics particularly for blood dyscrasias, mucoviscidosis, renal diseases, hearing deficits and more frequently now in breast, ovaries and colon cancer clinics.

. Individuals seeking genetic counseling may be guided towards one of those clinics .

VII-2. Role of genetic units

The role of genetic units in relation to speciality clinics is to insure coordination of teaching and the medical care of the patients. The genetic unit is often responsible for the diagnostic tests as part of global evaluation and it must make sure that the pertinent information is transmitted to all individuals at risk.

VIII- Associations, parents groups

VIII-1. Associations

Individuals suffering from a chromosomal or monogenic disease are often invited to join an association. The muscular dystrophy and mucoviscidosis associations were among the first to be known to the public. For instance short stature individuals will gain by sharing their views on how to improve their daily activities such as access to public services and also be able to contact organizations or para-medical clinics that may diminish the burden of their handicap.

VIII-2. Parents groups

Parents of individuals affected with a genetic disease will share, during those informal meetings, information that may not have been given to them during the counseling sessions: for instance details on nurseries, stimulation groups, nursing homes, specialized schools, summer camps and on the expected course of development and the handicaps specific to the diseases.

IX- Corollaries to genetic counseling

IX-1. Treatment

The genetic counseling must also offer to individuals and families information and advice on the treatment of genetic diseases that is by offering a follow up or else by directing them towards para-medical services like dietetics, speech therapy, physiotherapy or others who can help those patients.

IX-2. Contact with patients

Genetic counseling implies the transmission and interpretation of data.

The geneticist will guide the individual and family members and support them in their actions if they face a risk of transmitting or developing a genetic disease. The genetic counseling is not limited to a session of information and it is appropriate to plan a visit to make sure that the information has been understood correctly, to update the medical history and quite often to inform individuals of the recent findings in diagnostic facilities and treatment.

IX-3. Contact with families

The diagnosis and counseling must be complemented by the follow up of families. It is frequent in genetic clinics to insure the follow up of several members of the same family particularly in familial chromosomal aberrations, monogenic dominant or X-linked diseases like for instance hemophilia .

IX-4. Patients charts and registries

Nominal information confidentiality must be applied according to local rules. Consent forms specific to clinical interventions are part of the dossier. We recommend to patients to inform the genetics clinic of their new residence especially if a follow up is indicated.

IX-5. Disclosure of results

It is frequent during the course of familial investigations that one or more individuals will accept to undergo a diagnostic test but refuse to be informed of the results. This situation is frequent in the susceptibility tests or during the screening for degenerative diseases for which there is no treatment. All information referring to the risk of reproduction must be given to the individuals concerned.

X- Screening programs.

X-1 Newborn

All screening tests for a genetic disease to identify affected individuals or normal carriers must include an informed consent and foresee appropriate genetic counseling. A newborn screening program for the detection of a metabolic disease will include a follow up if the screening test is abnormal or a control is requested.

X-2. Children and adults

A systematic screening program may be justified when there is a high incidence of hereditary diseases for instance blood dyscrasias in Mediterranean countries or Tay Sachs disease among Ashkenasic Jews.

A screening program must be complemented by the publication of information in the interest of the population under study and offer an individual and confidential approach if results are positive.

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