
بسم الله الرحمن الرحيم

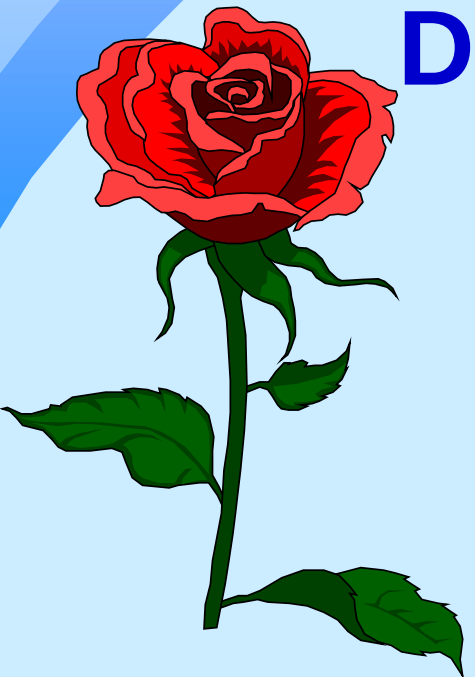
قالوا سبحانك

لا علم لنا إلا ما علمتنا

إنك أنت العليم الحكيم

سورة البقرة - الآية ٣٢

GENETIC COUNSELING



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Introduction

- **What is the genetic counseling?**
  - **Genetic counseling may be described as the process through which individuals affected by, or at risk for a problem which may be genetic or hereditary, are informed of :**
    - **The consequences of the disorder.**
    - **The probability of suffering from or of transmitting it to their offspring,**
    - **The potential means of treating or of avoiding the occurrence of the malformation or disease in question.**

Who Provide Genetic Counseling?

- Genetic counseling in common disorders is often given by the family doctor, the pediatrician or the obstetrician.
- However, with the recognition that thousands of problems have a major hereditary component, counseling is increasingly done in specialized centers which also provide the laboratory diagnostic tools which we hear so much about in our era.

Four aspects are involved in giving genetic counseling

- *1)Arriving at a specific diagnosis*: **most difficult, trying and time consuming part of the process, for the health care professionals as well as for the family. However, without a correct diagnosis, counseling is at best incomplete and imprecise.**
- *2)Estimation of risks:* **to develop the disorder and/or to transmit it to offspring.**

Four aspects are involved in giving genetic counseling

- ***3)Practical aid:*** **this includes, for example, recommending doctors for specialized examinations or health care professionals for speech or educational therapy. It often implies as well the coordination of prenatal and other diagnostic tests.**
- ***4)Supportive role:*** **Accepting and learning to live with a genetic diagnosis is particularly difficult when reproductive options are involved, and feelings of " guilt " may touch several generations.**

What types of disorders are genetic?

- *" Genetic " does not necessarily mean " hereditary ".*
  - *Genetic :means that the genetic material, on a chromosomal or a gene level, contains one or more mutations which are the cause of the disorder.*
  - *Hereditary: Once a mutation is present in a patient, it can of course be transmitted and thus becomes a hereditary disorder.*

Genetic disorders are generally of four types:

- *(1)Chromosomal disorders:*
  - *Incidence: 1/200 live-born children, and 1/500 adults.*
  - *Abnormalities :*
    - *1) Numerical abnormalities : rarely inherited, although affected individuals who reproduce may transmit the extra chromosome to their offspring.*
    - *2)Structural abnormalities, such as translocations, may cause little or no effect in carriers, but predispose to reproductive problems such as miscarriage and infertility.*

(2)Monogenic inheritance: (" Mendelian ")

- CAUSE: Mutations in single genes, at specific gene " loci.
- Incidence: 1/300 individuals will suffer from a monogenic disease manifesting within the first two decades .
- Four types of transmission :
  - a) Autosomal dominant: (one mutated gene of the pair is sufficient to produce symptoms),
  - b) Autosomal recessive :(the two alleles must be abnormal to cause the phenotype) and
  - c) X-linked, which includes:
    - 1) X-linked, recessive (theoretically, only males suffer, given that they are " hemizygous " for the X chromosome) and, less frequently.
    - 2)X-linked dominant gene mutations (males more seriously affected than females).

(3)Polygenic or " multifactorial ".

- *Polygenic implies that the association of several different genes, each one slightly modified, is necessary to produce the disorder.*
- *Multifactorial causation means that both genetic and non-genetic (environmental, either pre- or postnatal) factors are associated to produce the pathology.*
- *Some 5-10% of the population will suffer either from a malformation or from a disease in which genetic factors are major.*

(4)Mitochondrial disorders:

- *In recent years a " new " type of inheritance has been proven, that resulting from mutations in the mitochondrial genome.*
- *The incidence: of mitochondrial mutations in human disease is still unknown.*
- *In many cases the mutation is " de novo " in an affected individual, but hereditary transmission is purely maternal, since, a fertilized egg's mitochondria originate from the maternal germ cell only.*

Indication Of Genetic Counseling

Preconceptional/Prenatal Genetic Counseling

- *Mother is 35 years or older at delivery*
- *Mother's serum screening test indicates an increased risk for neural tube defects, Down syndrome, or trisomy 18*
- *Abnormal prenatal test results or abnormal prenatal ultrasound examination*
- *History of previous retarded child or family history of mental retardation*
- *Either parent carries a balanced chromosome abnormality*
- *Previous child with a neural tube defect or family history of neural tube defects (i.e. anencephaly, spina bifida).*
- *Previous child with or family history of birth defects*

Preconceptional/Prenatal Genetic Counseling

- *Either parent affected with autosomal dominant disorder such as myotonic dystrophy.*
- *Both parents carriers for an autosomal recessive disorder (e.g Cystic fibrosis and sickle cell anemia,)*
- *Mother a carrier of an X-linked recessive disorder (i.e. hemophilia, Duchenne muscular dystrophy)*
- *Family history of cancer, particularly at younger ages*
- *Fetal or parental exposure to toxic or carcinogenic agents such as drugs, chemicals, radiation or infections during critical periods of fetal development*

Preconceptional/Prenatal Genetic Counseling

- *Previous unexplained stillbirth or two or more previous spontaneous abortions .*
- *Preconceptional couples with high risk factors such as advanced age, incest or a close blood relationship .*
- *Extreme parental concern or fear of having a child with a birth defect*
- *Infertility cases where either parent is suspected of having a chromosomal abnormality*
- *Mother's illness, such as schizophrenia, depression, seizures, alcoholism, diabetes, thyroid disorder and others in which fetal abnormalities may be associated with the disease or with medications prescribed for the condition*

Pediatric Genetic Counseling

- *Child with a birth defect, or suspected birth defect*
- *Child with a suspected or diagnosed genetic syndrome*
- *Child with a chromosomal syndrome*
- *Child with a metabolic disorder*
- *Child with developmental delays*
- *Child with a family history of a genetic condition*

Adult Genetic Counseling

- *Adult with a genetic condition who would like periodic monitoring by a specialist*
- *Adult with a family history of a genetic condition*
- *Adult with a strong family history of common adult onset disorders such as heart disease, senility, or diabetes*
- *Adult with a strong family history of cancer*

What does a genetics work-up involve?

- *Once a family arrives in the genetic clinic, the steps to be taken, depending on whether the specific diagnosis is established, can be summarized as follows:*
  - *(1)Obtaining a detailed family history, which includes both sides of the family even if counseling has been requested for a dominant disorder affecting one parent.*

What does a genetics work-up involve?

- *(2)A review of medical and/ or pregnancy histories is especially important when the diagnosis is not yet established, but also helps geneticists to learn more about etiologies and natural histories of certain disorders.*
- *(3)A physical examination, of the affected person, and sometimes of other family members, is often needed.*

What does a genetics work-up involve?

- *(4)Medical and/or laboratory exams :*
  - *These often include chromosome study, and may necessitate DNA analysis if the identity of the gene suspected to be involved is known.*
  - *Other frequent suggestions include X-ray or ultrasound examinations, and various biochemical analyses.*
  - *Once the diagnosis is known, medical tests aimed at evaluating health risks linked to the disorder may also be established.*
- *(5)Genetic counseling can only be given at the end of this process.*

Patient, and family genetic history

History of congenital abnormalities
Neural tubedefects
Heart defects
Cleft lip or palate
Other
Chromosomal abnormalities
Down syndrome
Mental retardation (eg, fragile X risk)
Other

Patient, and family genetic history

Maternal age >34 or advanced paternal age
Inherited diseases
Hemoglobinopathy
Muscular dystrophy
Cystic fibrosis
Huntington's chorea
Hemophilia
Metabolic disorders (eg, phenylketonuria, diabetes
Kidney disease
Other

Patient, and family genetic history

Ethnicity
Eastern European Jews (Tay-Sachs, Canavan risk)
French Canadians (Tay-Sachs risk)
Mediterranean (Hemoglobinopathy risk)
Asians (Hemoglobinopathy risk)
African (Hemoglobinopathy risk)
Hispanic (Hemoglobinopathy risk)
Other
Consanguinity
Recurrent pregnancy loss or stillbirth
Maternal metabolic disorder

Uses of Genetic Testing

(1)Diagnostic testing

- *Used to identify or confirm the diagnosis of a disease or condition in a person or a family. It gives a "yes" or "no" answer in most cases.*
- *Determining the course of a disease and the choice of treatment.*
- *Examples :include chromosome studies, direct DNA studies, and biochemical genetic testing.*

(2)Predictive genetic testing

- *Determines the chances that a healthy individual with or without a family history of a certain disease might develop that disease.*
- *There is predictive testing available for some adult-onset conditions as some types of cancer, cardiovascular disease, and some single gene disorders*

(3)Presymptomatic genetic testing

- *Used to determine whether persons who have a family history of a disease, but no current symptoms, have the gene alterations associated with the disease.*

(4)Carrier testing

- *Determine whether a person carries one copy of an altered gene for a particular disease*

(5)Prenatal diagnosis

- *Used :to diagnose a genetic disease or condition in the developing fetus and includes maternal serum screening, ultrasound (sonograms), amniocentesis, chorionic villus sampling (CVS), and percutaneous umbilical blood sampling (PUBS).*

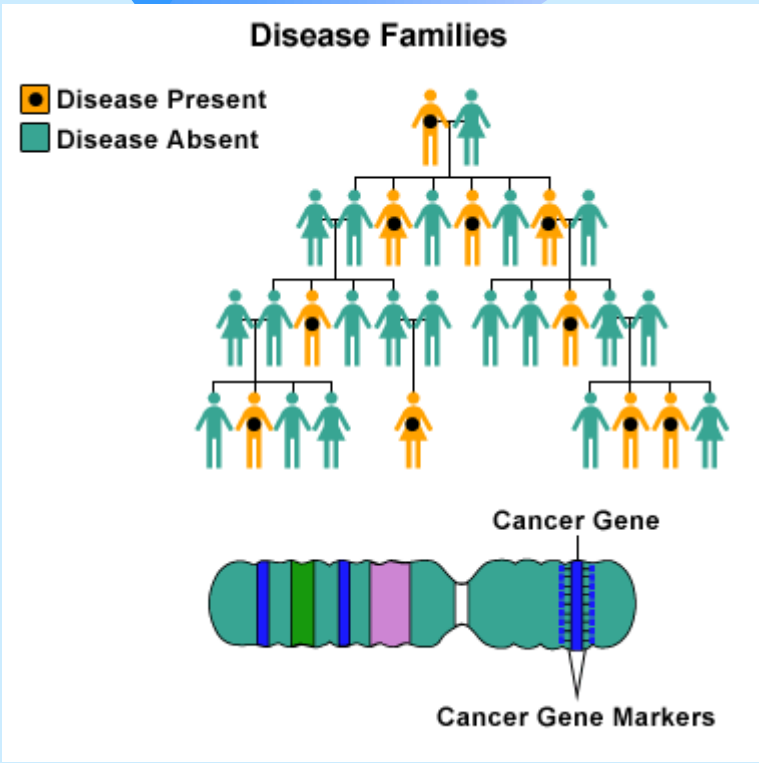
(6)Preimplantation studies

- *Used following in vitro fertilization to diagnose a genetic disease or condition in an embryo before it is implanted into the mother's uterus.*

(7)Newborn screening

- *Performed in newborns in state public health programs to detect certain genetic diseases for which early diagnosis and treatment are available.*

Types of Genetic Testing



Three main types of genetic testing:

- *1)Chromosome studies.*
- *2)DNA studies.*
- *3)Biochemical genetic studies.*

1)Chromosome studies.

- *"Cytogenetics" is a word used to describe the study of chromosomes.*
- *The chromosomes need to be stained in order to see them with a microscope.*
- *When stained, the chromosomes look like strings with light and dark "bands.*
- *" A picture (an actual photograph from one cell) of all 46 chromosomes, in their pairs, is called a "karyotype."*

1)Chromosome studies.

- *A normal female karyotype is written 46, XX, and a normal male karyotype is written 46, XY.*
- *The standard analysis of the chromosomal material evaluates both the number and structure of the chromosomes, with an accuracy of over 99.9 percent.*
- *Chromosome analyses are usually performed using a blood sample (white blood cells), prenatal specimen, skin biopsy, or other tissue sample*

2)DNA studies.

- *(A)indirect DNA studies*
  - *Involve using "markers" to find out whether a person has inherited the crucial region of the genetic code that is passing through the family with the disease.*
  - *Markers are DNA sequences located close to or even within the gene of interest.and almost always inherited together.*
  - *Because the markers are so close, to a gene, they are said to be "linked."*
  - *The accuracy of linkage studies depends on how close the markers are to the faulty gene.*

2)DNA studies.

- *(B)Direct DNA studies:*
  - *Look directly at the gene in question for an error.*
  - *Errors in the DNA may include :*
    - *Replication of the gene's DNA (duplication),*
    - *Loss of a piece of the gene's DNA (deletion),*
    - *Alteration in a single unit (called a base pair) of the gene's DNA (point mutation),*
    - *Repeated replication of a small sequence of the gene's DNA.*
  - *When a particular mutation is found in a relative with cancer, other family members should be tested for the mutation to determine the risk to develop cancers and to pass the mutation on to the next generation.*
  - *The DNA needed for direct DNA studies is usually obtained by taking a blood sample.*

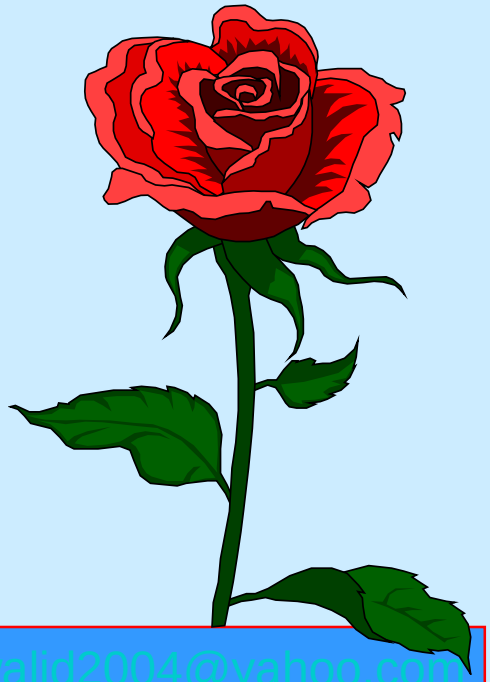
3)Biochemical genetic studies.

- Biochemical genetic testing involves:
  - (A) The study of enzymes in the body that may be abnormal in some way.
    - Sometimes, rather than studying the gene mutation which is causing the enzyme to be defective in the first place, it is easier to study the enzyme itself (the gene product)..
    - Biochemical genetic studies may be done from a blood sample, urine sample, spinal fluid, or other tissue sample, depending on the disorder.

(B) Protein truncation studies

- *Another way to look at gene products, rather than the gene itself, is through protein truncation studies. Sometimes a mutation in a gene causes it to make a protein that is truncated (shortened).*
- *Protein truncation studies can be performed on a blood sample.*
- *These types of studies are often performed for disorders in which the known mutations predominantly lead to shortened proteins.*

Thank you



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