Genetic Counseling

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Medical Genetics: a new discipline

1 / Increase in congenital diseases v/s infectious diseases as a cause of infant morbidity and mortality.

2 / birth control → quality for small number of children.

When we say genetics

- **CARRIER HOPE**
  - *** new knowledge,**
  - *** new therapies**

- **And DESPAIR**
  - *** Today serious incurable diseases**

When we say genetics

- **TRANSMISSION to the OTHER GENERATION**

*** resemblance**

in what is common between parents and children

*** difference**

through gene flow sexual reproduction

Different types of genetic diseases

1) Chromosomal

2) Monogenic

3) Multigenic/Multifactorial

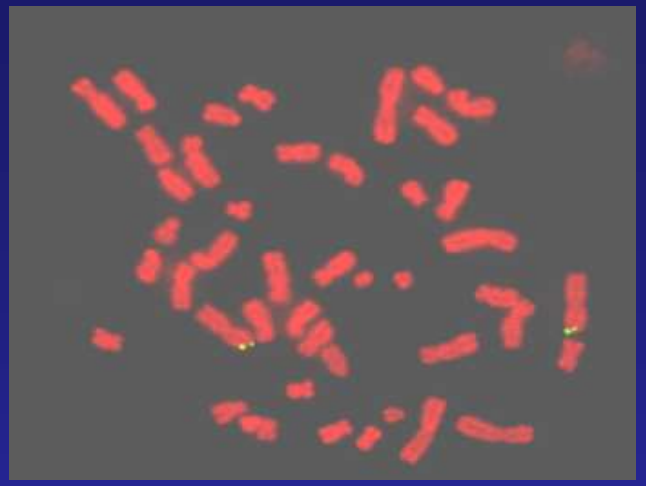
4) Mitochondrial

Chromosomal disorders (1/200)

Parder-Willi syndrome

Angelman

a



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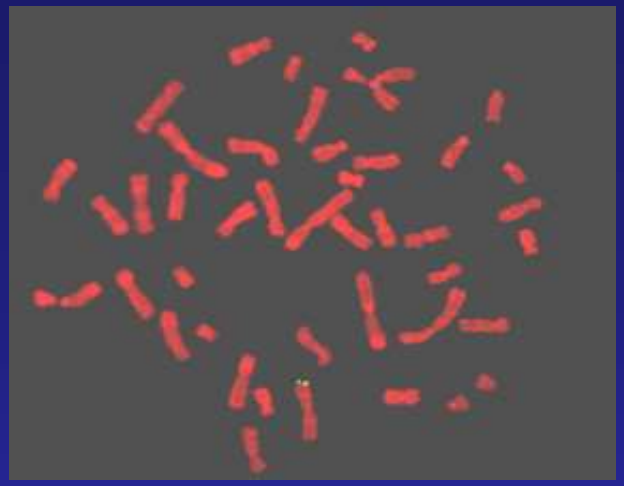

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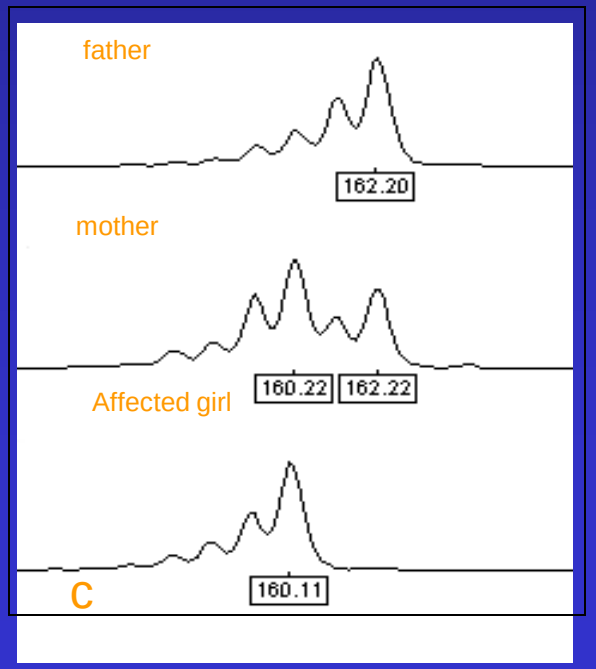
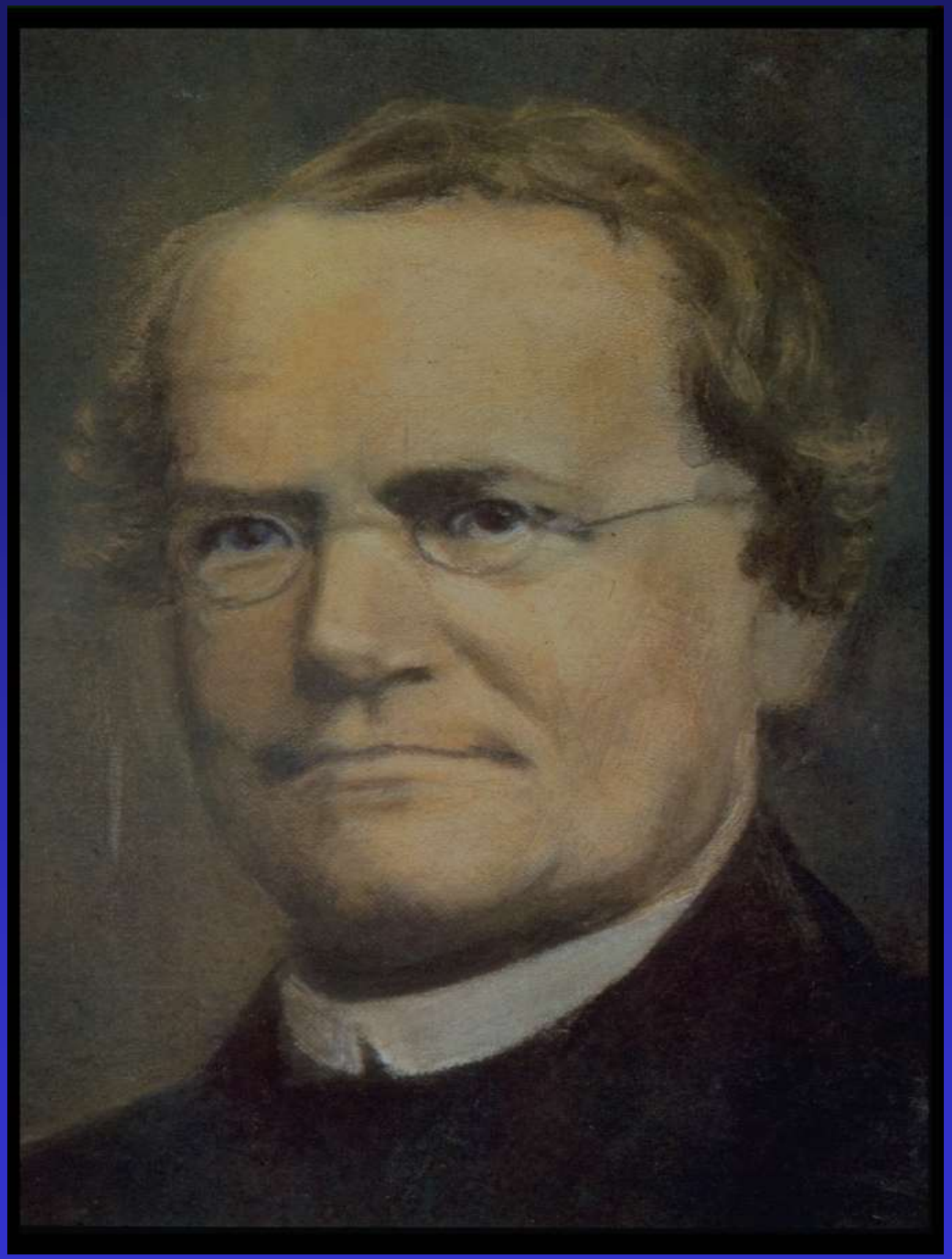
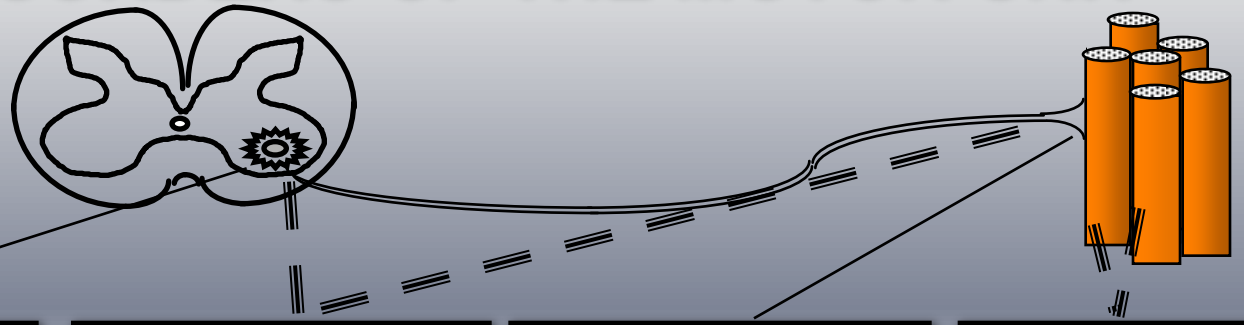


c

Mendelian inheritance/
Single gene defects (1/100)



MAIN DISORDERS OF THE MOTOR UNIT



ANTERIOR HORN	NERVE	NM JUNCTION	MUSCLE FIBER
SPINAL MUSCULAR ATROPHIES *(SMA)* Types 1-4 *(Werdnig-Hoffman) (Kugelberg-Welander)* ***A.L.S.***	**NEUROPATHIES** **H.S.M.N.** *(Charcot-Marie-Tooth, Déjerine-Sotas, others)* H.M.N. H.N.A.	**MYASTHENIAS** Myasthenia gravis Congenital myasthenic syndromes	**DYSTROPHIES** Duchenne / Becker Limb girdle (LGMD) sarcoglycanopathies Emery-Dreifuss / FSH **MYOTONIC Sd** Steinert / Thomsen **MISCELLANEOUS** Mitochondrial Congenital Metabolic Dysimmune

Autosomal Dominant (AD) - NMD

Dystrophic	LGMD 1A, 1B, 1C, 1D, 1E FSHD : Facioscapulohumeral Muscular Dystrophy AD-EDMD : AD-Emery-Dreifuss MD
Congenital	Central Core disease (CCD) Nemaline myopathy
Myotonic	Thomsen myotonia Myotonic dystrophy (DM1) P.R.O.M.M. (DM2)
Neuropathic	AD Charcot-Marie-Tooth
Miscellaneous	hereditary Inclusion Body Myopathy (h-IBM) FOP : Fibrodysplasia Ossificans Progressiva

Autosomal recessive (AR) - NMD

Dystrophic	sarcoglycanopathies (α, β,γ, δ) Calpainopathy (LGMD 2A) LGMD 2B - Miyoshi LGMD 2G, 2H, 2I Congenital Muscular Dystrophies (CMD)
Congenital	multiminicore disease selenopathy, nemaline myopathy, AR CCD
Myotonic	Becker (!) myotonia Schwartz-Jampel syndrome
Neuropathic	Spinal muscular atrophies (SMA) AR Charcot-Marie-Tooth
Miscellaneous	hereditary Inclusion Body Myopathy (h-IBM)

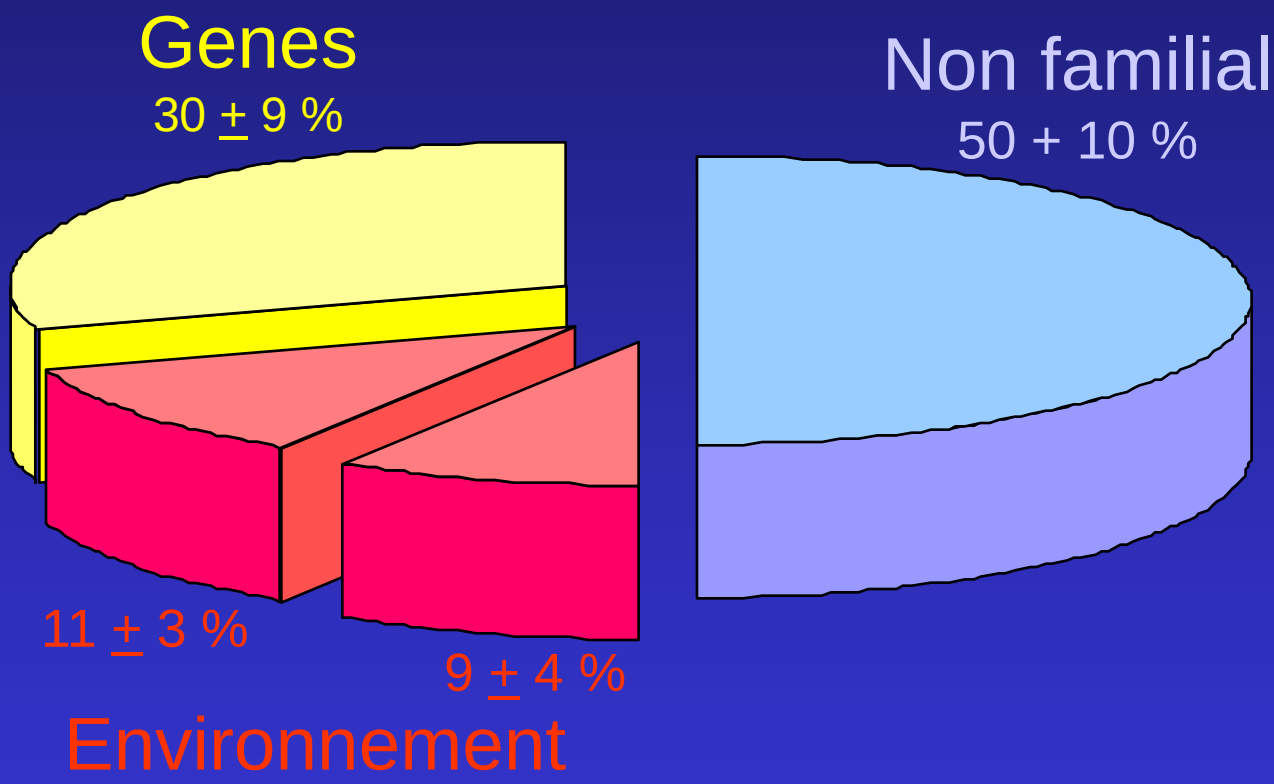
MODE OF INHERITANCE & NMD

X-linked recessive (XL)

Dystrophic	DMD : Duchenne Muscular Dystrophy BMD : Becker Muscular Dystrophy XL-EDMD : XL-Emery-Dreifuss m.d.
Congenital	Myotubular myopathy
Neuropathic	Charcot-Marie-Tooth (Cx 32) Kennedy syndrome
Miscellaneous	XMEA (myopathy + excessive autophagy)

Multifactorial diseases

Blood pressure



Mongeau et al, 1987

- **Mitochondrial (rare)**
  - **MERRF**
  - **MELAS**
  - **Kearns-Sayre**
  - **LHON……**

What is a genetic counseling

- Assess the risk for a couple to have a child with a genetic disease.

- To evaluate a person's risk of developing genetic disease.

All in reference to a family history

Genetic Counseling

- an original medical approach

It is not directed to a sick person
but:
a couple
a family
a "healthy" individual

Genetic counseling

it concerns another person

the unborn child
or
the future
(a risk of developing the disease)

Genetic counseling

- It often results in any preventive or curative treatment

- It can lead to important life choices: renunciation (not having children), decision of death (abortion), adoption

Genetic counseling

- **The circumstances that lead a couple genetic counseling are highly variable:**

  - Parents or children with hereditary disease: assessing the risk of recurrence

  - Parents who have had a stillborn child, abnormal child, disabled, without accurate diagnosis

- Parents with a child with a chromosomal abnormality or genetic disease and fear of recurrence in a subsequent pregnancy.

Genetic counseling

- Infertile couple or couples who have had repeated miscarriages
- Young couples facing a problem of inbreeding…

Bases for Genetic Counseling

1) the construction of the family tree:
- Known information
- Misinformation
- The forgotten or unknown information (strained family relationships, family conflict)
- Hidden informations (family secret; taboos around genetic disease)

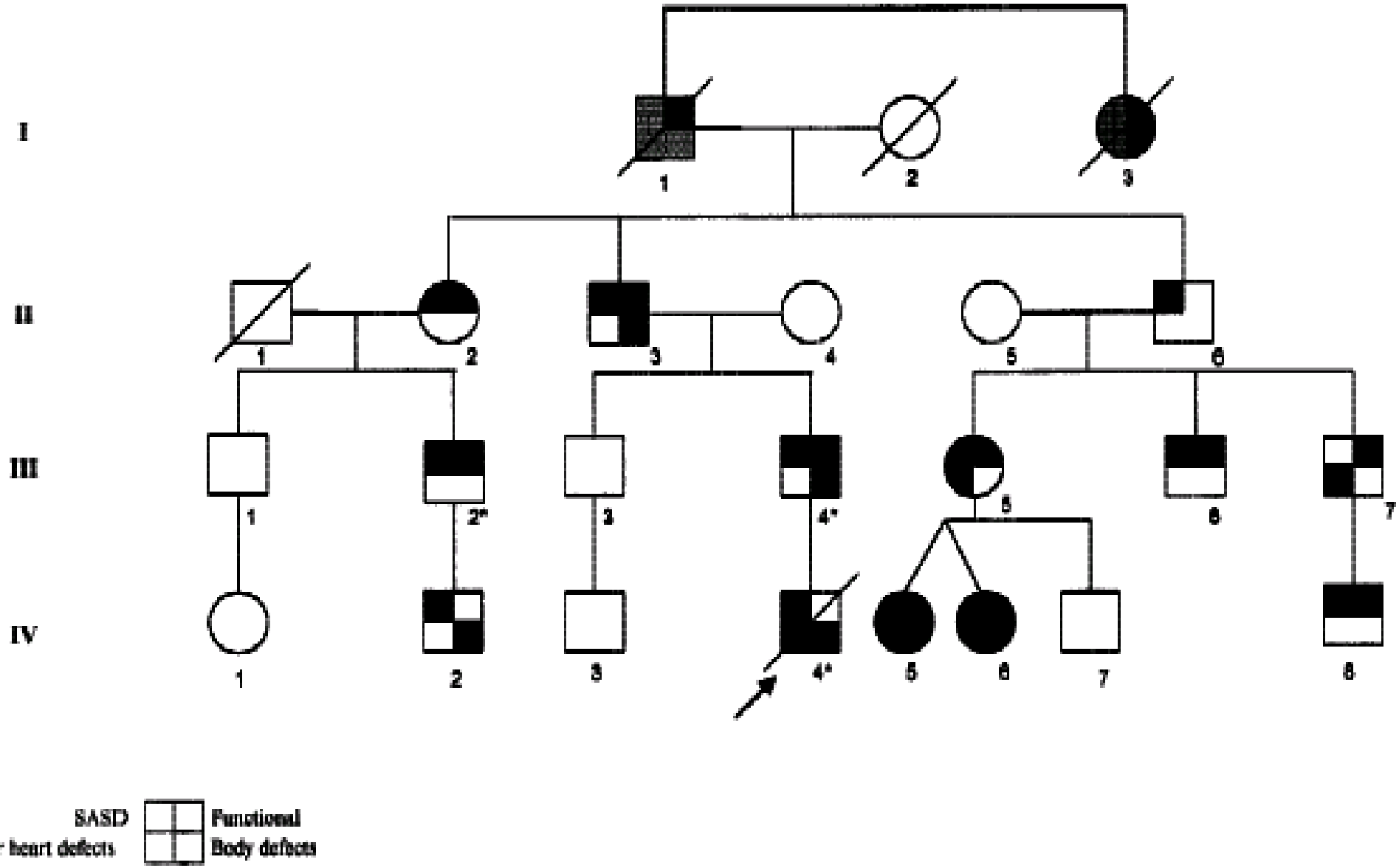
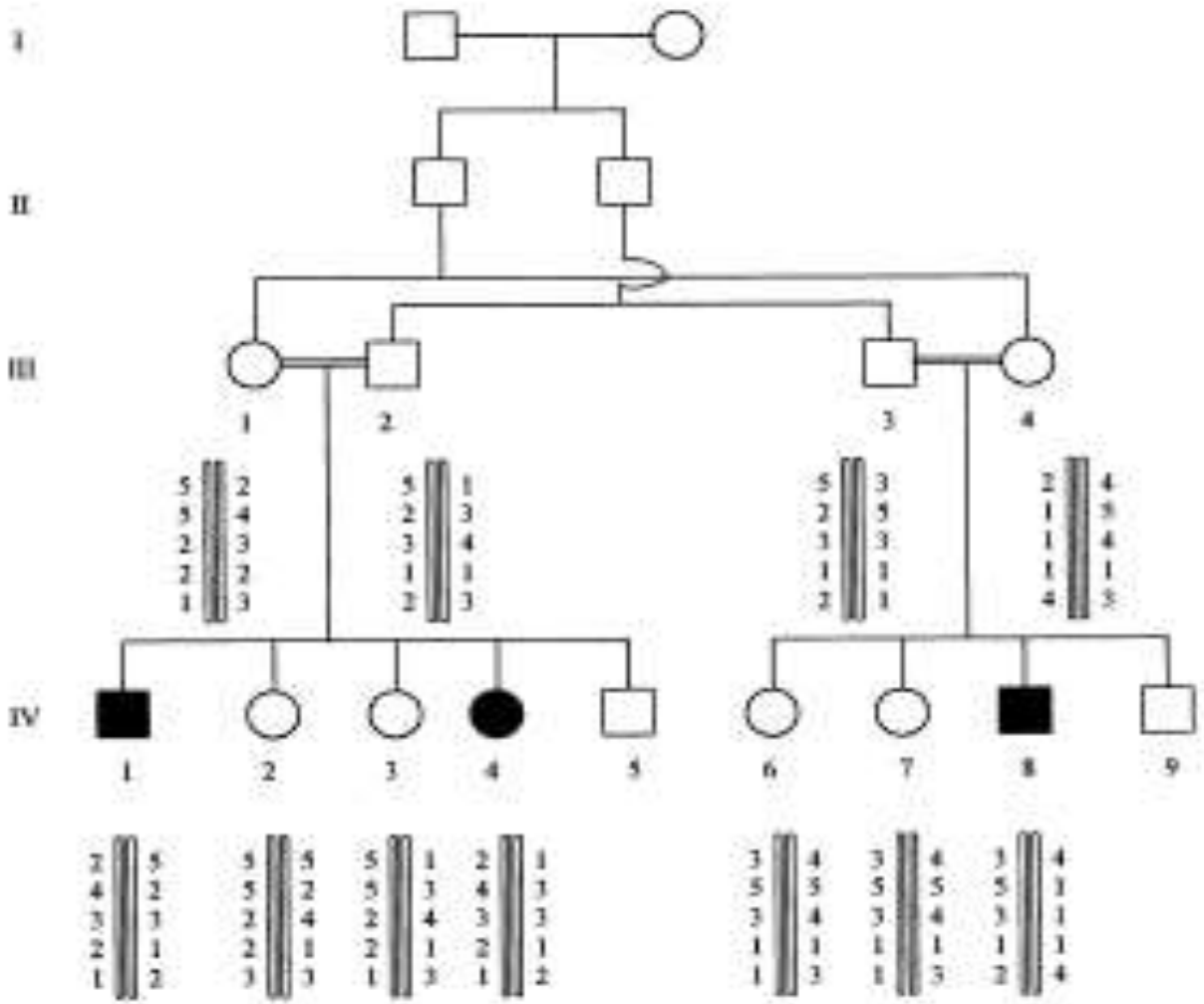


Fig. 1. Pedigree of the family. Propositus is indicated by an arrow and SASD surgically repaired by an asterisk. Various associated anomalies are represented within the four divided square or circle and detailed in the text. Dotted symbols represent nondocumented cases.

Autosomal recessive



X Linked

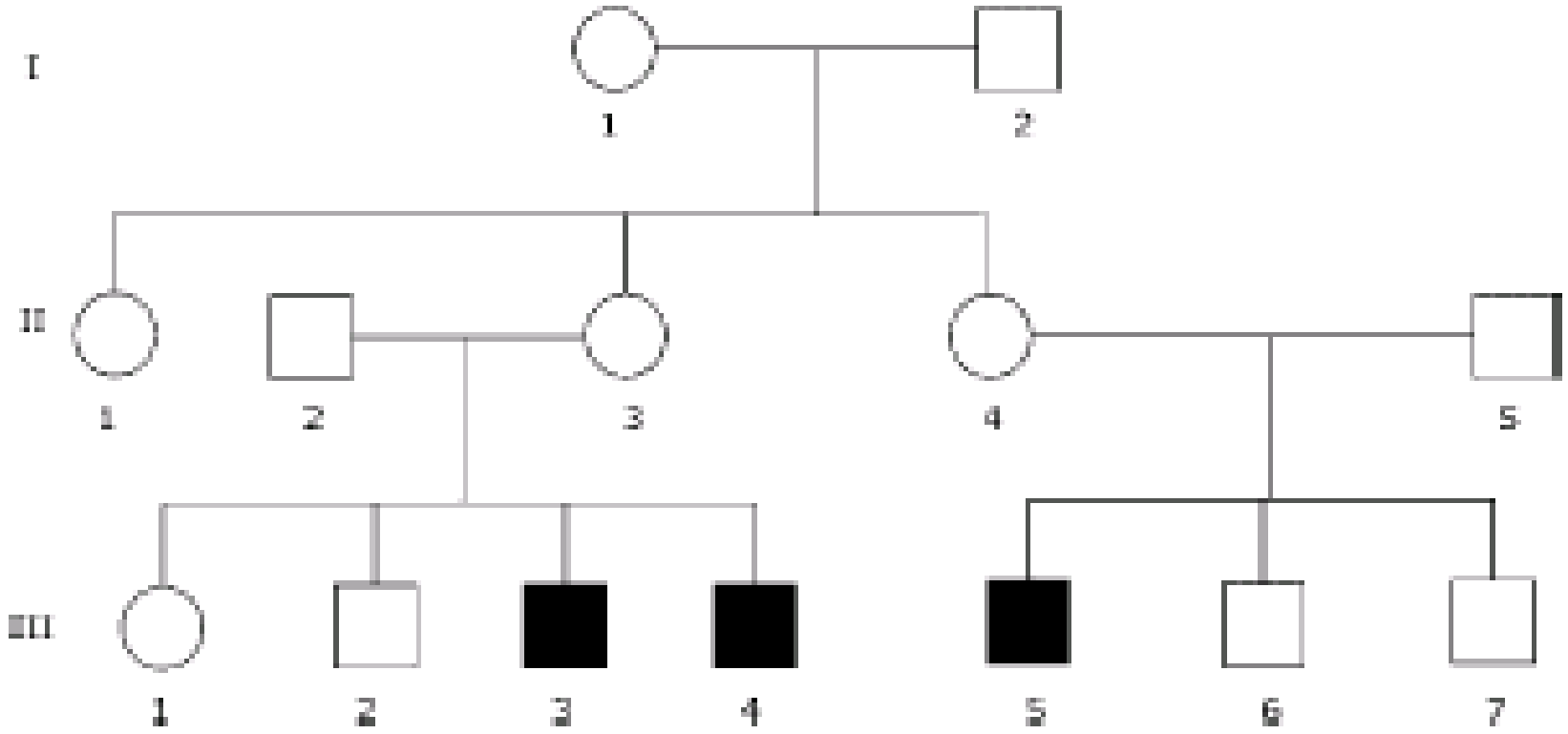
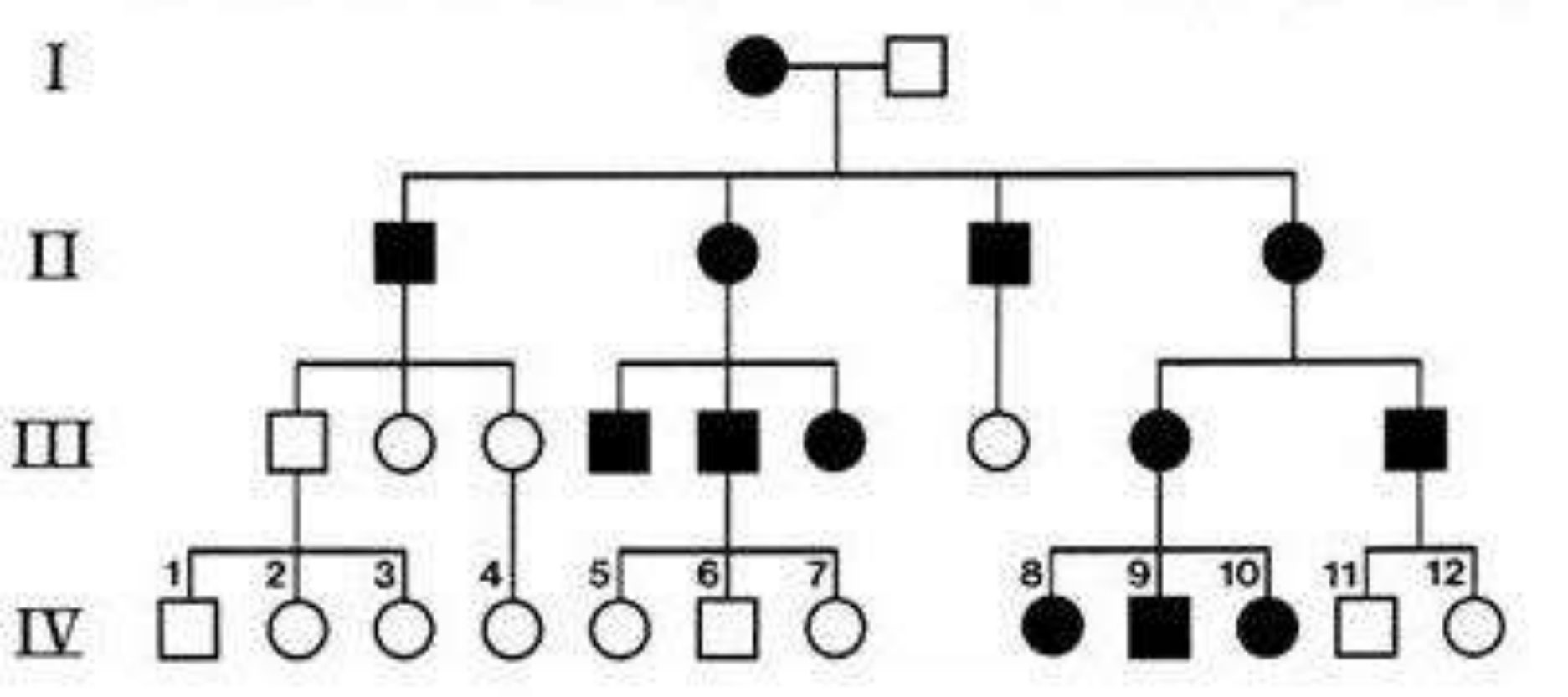


Fig. 1. Pedigree of the present family. Squares with solid dark color indicate the affected individuals.

Mitochondrial



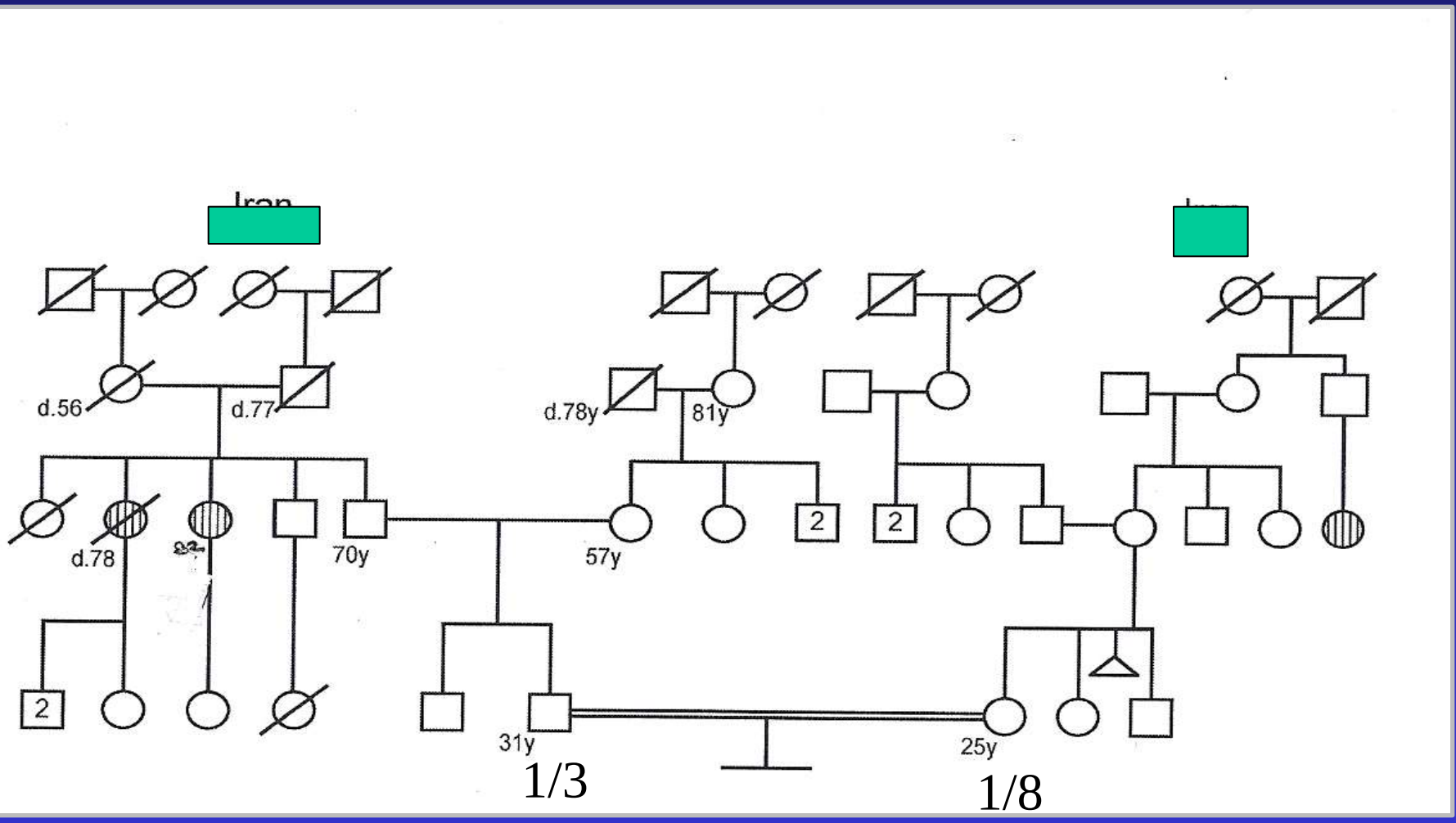
Bases for genetic counseling

- 2) risk assessment:

  expressed as a percentage (%)
  or
  in relative risk (RR)

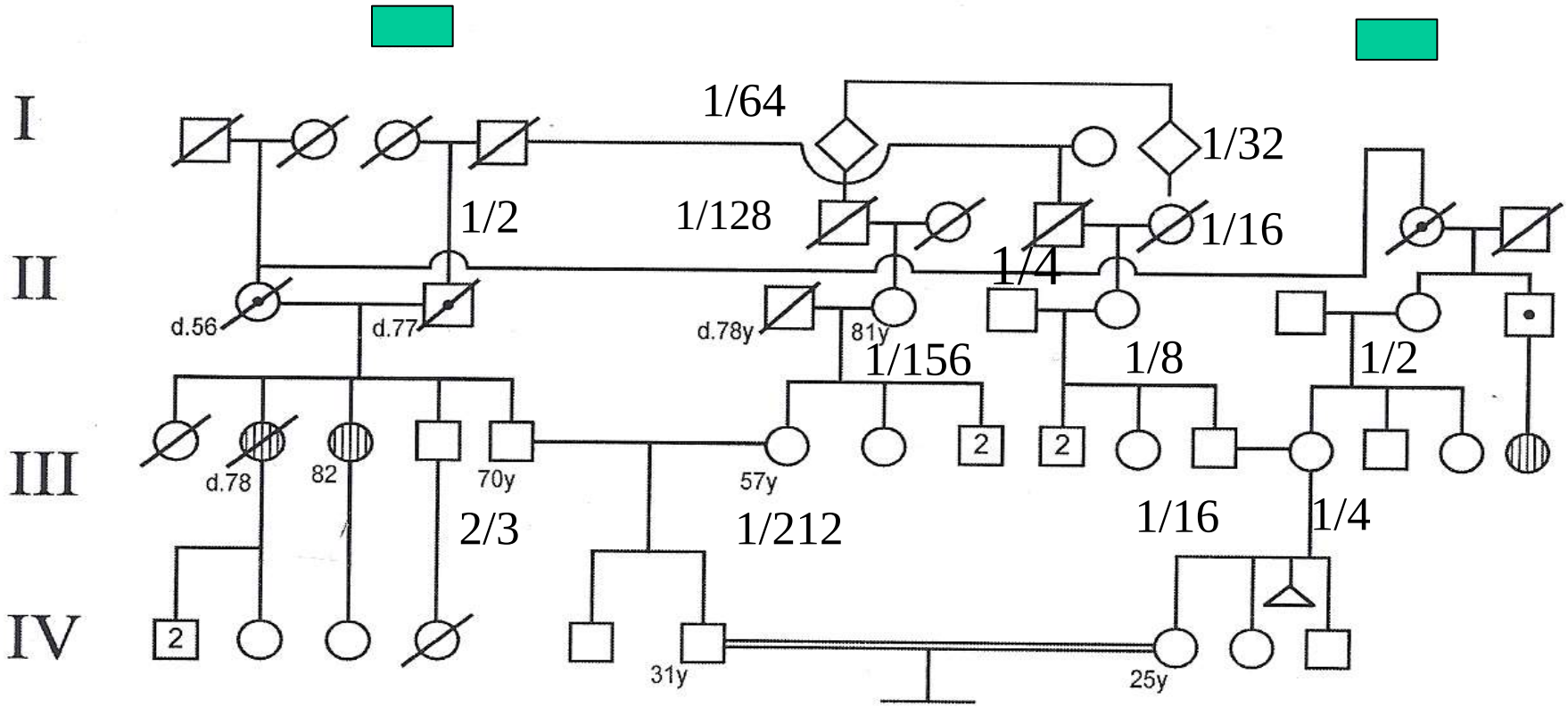
  Acceptable or unacceptable risk?

Family History Recessive Disorder



1/3 x 1/8 x ¼ = 1/96

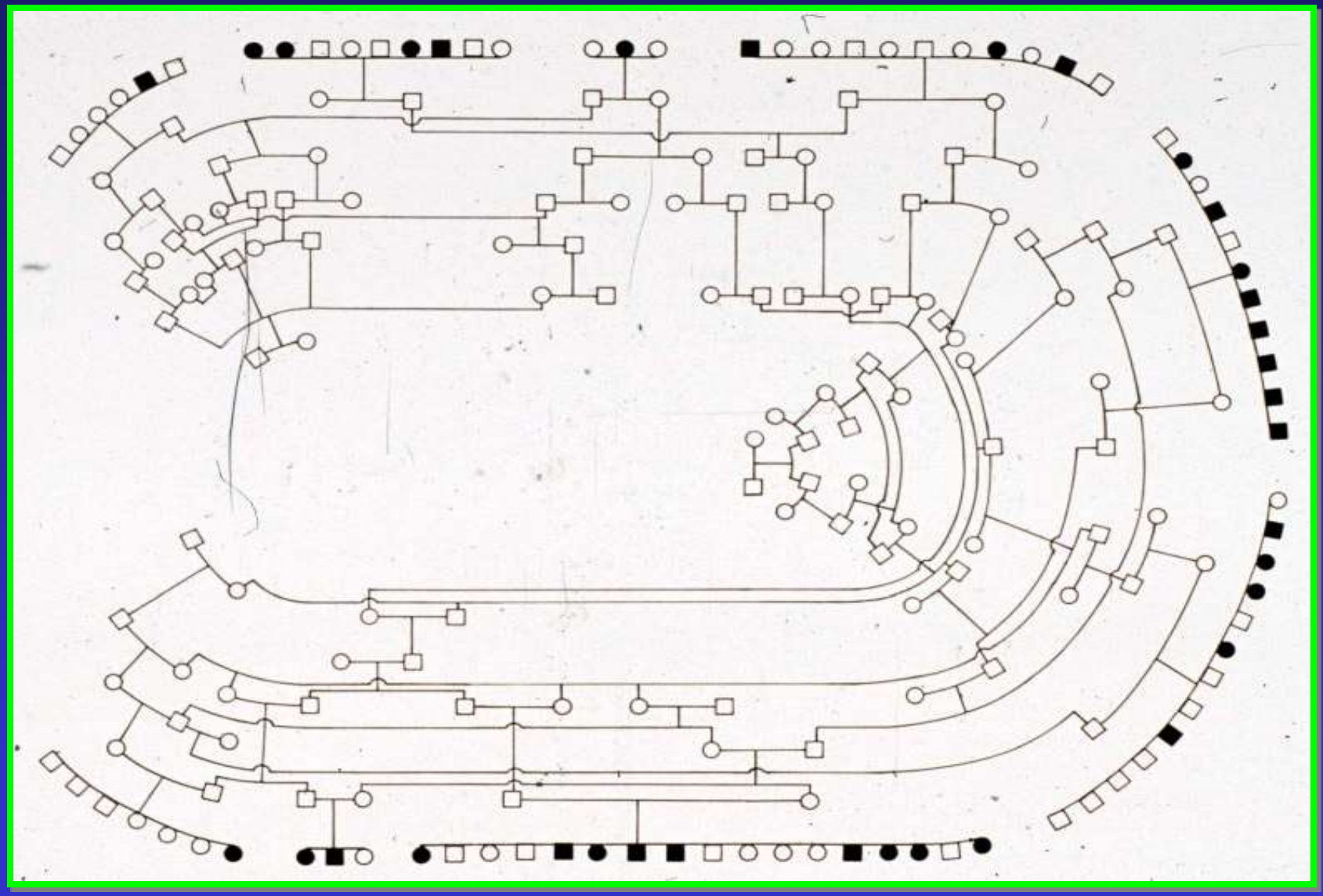
Multiple Loops of Consanguinity



(2/3 x 2) + (1/212 x 2) = 1/3 + 1/424 =~ 1/3 (1/16 x 2) + (1/4 x 1/2) = 5/32

Chance affected child:1/3 x 5/32 x ¼ = 1/77

TAKING TIME TO ESTABLISH FAMILY HISTORY AND PEDIGREE



Limb Girdle Muscular Dystrophy in the Amish Community

Bases for Genetic Counseling

- **3) the use of genetic tests:**

***Availability of genetic tests: inequality**

*** The prevalence of the disease**
the complexity of the gene in question and mutations…..
*** the scientific interest of the gene**

Genes

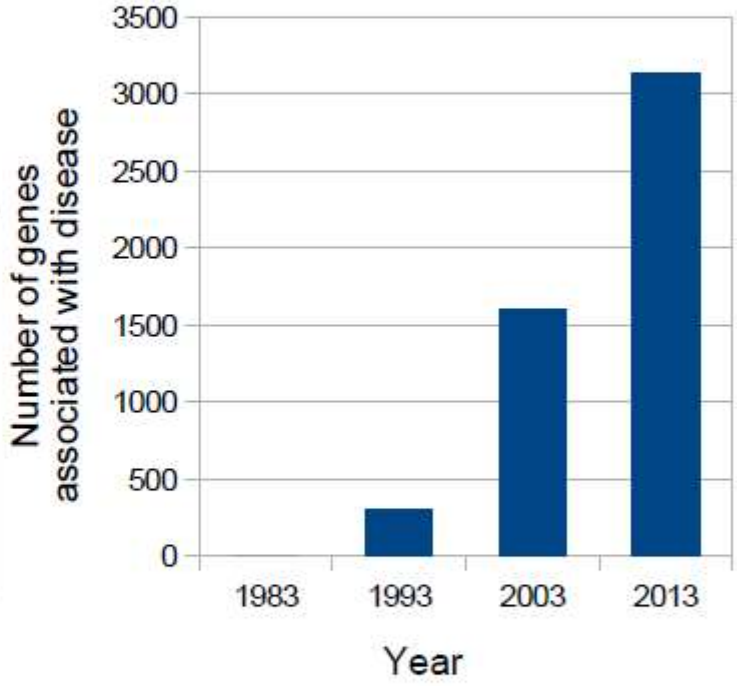
- 25 000 genes
- 12.000: identified diseases
- 8000: localized genes
- 5000: cloned

Identification de gènes responsables

OMIM®

Online Mendelian Inheritance in Man®

An Online Catalog of Human Genes and Genetic Disorders



OMIM Gene Map Statistics:

OMIM Morbid Map Scorecard (Updated 31 January 2014) :

Number of phenotypes* for which the molecular basis is known	5,123
Number of genes with phenotype-causing mutation	3,131

* Phenotypes include single-gene mendelian disorders, traits, some susceptibilities to complex disease (e.g., CFH and macular degeneration, 134370.0008), and some somatic cell genetic disease (e.g., FGFR3 and bladder cancer, 134934.0013)

OMIM Entry Statistics:

Number of Entries in OMIM (Updated 31 January 2014) :

Prefix	Autosomal	X Linked	Y Linked	Mitochondrial	Totals
* Gene description	13,723	670	48	35	14,476
+ Gene and phenotype, combined	101	2	0	2	105
# Phenotype description, molecular basis known	3,712	282	4	28	4,026
% Phenotype description or locus, molecular basis unknown	1,579	135	5	0	1,719
Other, mainly phenotypes with suspected mendelian basis	1,747	116	2	0	1,865
Totals	20,862	1,205	59	65	22,191

Maintenant un outil de diagnostic

Radboudumc university medical center

GATC BIOTECH

UCLA Health

Cincinnati Children's

Children's Mercy KANSAS CITY

EMORY GENETICS LABORATORY

Baylor College of Medicine

THE UNIVERSITY OF CHICAGO GENETIC SERVICES

UNIVERSITY OF IOWA

MAYO CLINIC

PARABASE GENOMICS

TARGETED GENOMICS

Special Report: Exome Sequencing for Clinical Diagnosis of Patients with Suspected Genetic Disorders

BlueCross BlueShield Association

Carolina Center for Genome Sciences

GeneDx DNA DIAGNOSTIC EXPERTS

Ambry Genetics

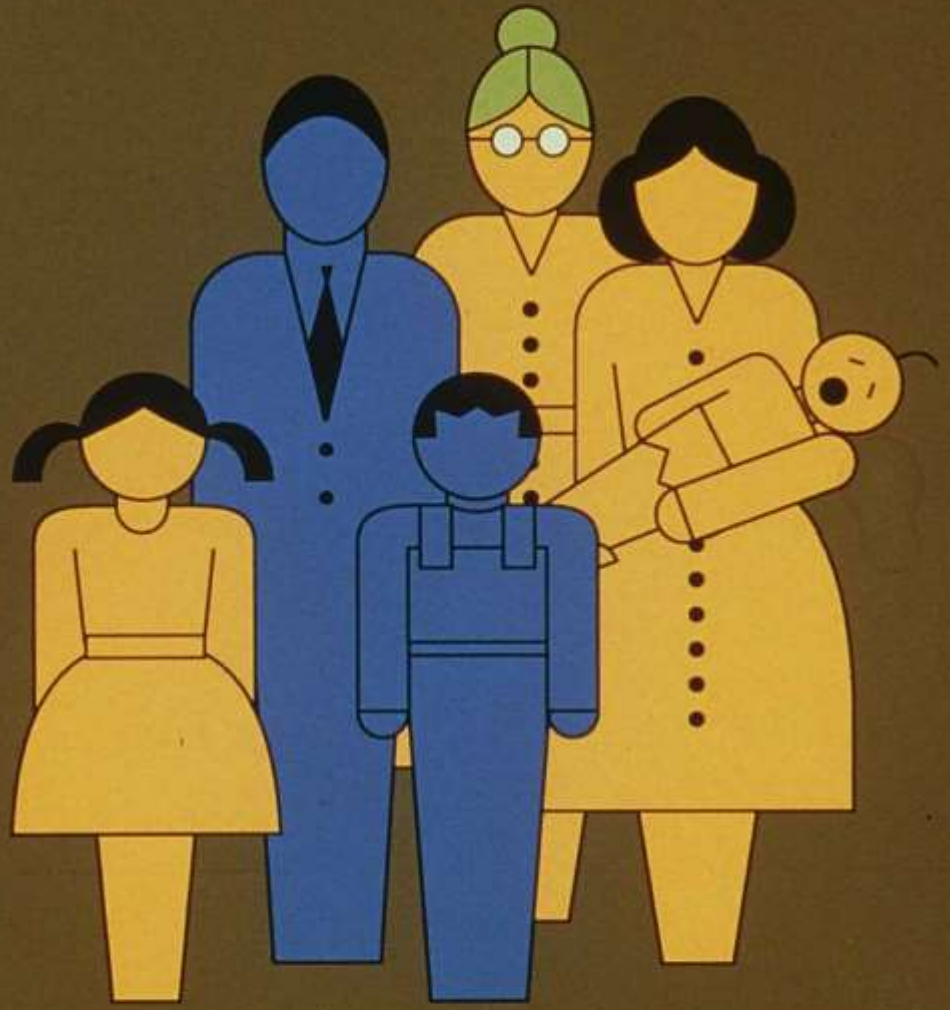
sengenics

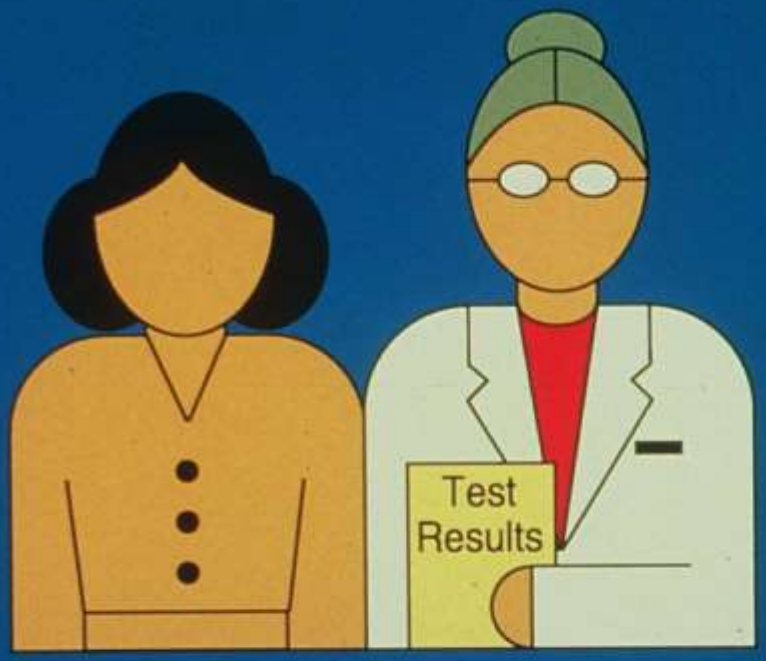
EdgeBio

华大健康 BGI health

Genetic Tests Serve Many Purposes

Candidates for Testing





Benefits of Gene Testing

- Relief
- Fewer Checkups
- Informed Decisions
- Intervention

Limitations of Gene Testing

Mutation Present But:

- May Be Acquired, Not Inherited
- May Never Lead to Disease
- May Go Undetected

Bases for Genetic Counseling

4) genetic information:

* Flow of information?
* Who should inform relatives at risk?
Consultants / The doctor?

*conflict

*confidentiality
and
failure to assist a person in danger

Qui voudrait savoir?

Psychological Consequences

Confidentiality Concerns

Personal Decision

Key Role of Genetic Counseling

- Non-directive, non-judgmental supportive counseling
- Ascertain client's perceived notion of the nature and magnitude of genetic risks
- Discuss fears & attitudes of families and friends
- Follow-up letter can help clarify patient/family misconceptions (& health care providers!)
- "I told you so"/Feelings of parental guilt
- Blame and shame

Client factors & risk perception

Coping styles

Seekers, avoiders,

dependent decision makers,

Minimizers

Perceived “burden”

Gender differences

Cultural differences

Religious differences

Stigma associated with carrier status

- Potential damage to self-concept
  - Component of self observed by others
  - Component of self that is internal, private, reflective
- Altered perception of genetic identity/inherited “endowment”
- Diminished social identity
- Altered perception of health

Threatened parental role

- Carrier status challenge “wished-for” parental role
- May differ based on age
- Carrier believe marriage plans might change for other carriers
- Carriers believed that other carriers might have negative response

Treatment

- Treatment of genetic disease by conventional means requires identification of the gene product and an understanding of the pathophysiology of the disease process.

- Very rare: lack of treatment strategies for many genetic disorders.

Take everywhere you like message…

Genetic counseling

- takes time and availability (see possibly partner separately if it is suspected misinformation, hidden secrets).
- Require psychology
- Require an understanding of genetic diseases: specific diagnosis (hereditary v / s acquired disorder …)