MENDELIAN INHERITANCE

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MGL- 6

Genetic Diseases (GD)

- Chromosomal Abnormalities
- **Single Gene Defects**
- Non-Traditional Inheritance
- Multifactorial Disorders
- Cancer Genetics

Topics of Discussion

- Basic concepts of formal genetics
- Autosomal dominant inheritance
- Autosomal recessive inheritance
- Factors that may complicate inheritance patterns
- Probability

Mendelian Inheritance
Single Gene Defects

- Autosomal recessive
- Autosomal dominant

- Factors complicating Mendelian inheritance
- X-linked recessive
- X-linked dominant
- Y-linked

Pedigree

- The family tree
- Representation of the ancestry of an individual's family.
- Symbolic representations of family relationships and inheritance of a trait

Goals of Pedigree Analysis

- Determine the mode of inheritance: dominant, recessive, partial dominance, sex-linked, autosomal, mitochondrial, maternal effect.

- Determine the probability of an affected offspring for a given cross.

Obtaining a pedigree

A three generation family history should be a standard component of medical practice. Family history of the patient is usually summarized in the form of a pedigree

Points to remember:

- Ask whether relatives have a similar problem
- Ask if there were siblings who have died
- Inquire about miscarriages, neonatal deaths
- Be aware of siblings with different parents
- Ask about consanguinity
- Ask about ethnic origin of family branches

Pedigree Symbols

Lines

= Generation

= Parents

= Adoption

= Siblings

= Identical twins

= Fraternal twins

= Parents closely related (by bl

= Former relationship

= Person who prompted pedigr analysis (proband)

Numbers

Roman numerals = generations

Arabic numerals = individuals in a generation

Male

Female

Sex unspecified

Number of children of sex indicated

Affected

Nonpenetrant carrier, may manifest disease

Obligate carrier, will not manifest disease

Proband

Deceased individual

Stillbirth

Adopted into family

Adopted out of family

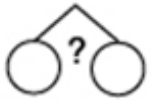
Marriage or union

Divorced

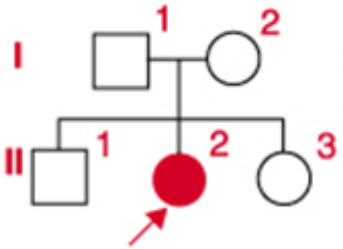
Consanguinity

Monozygotic twins

Dizygotic twins



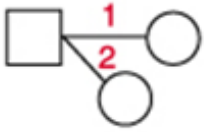
Twins of unknown zygosity



Pedigree with generations and individuals numbered

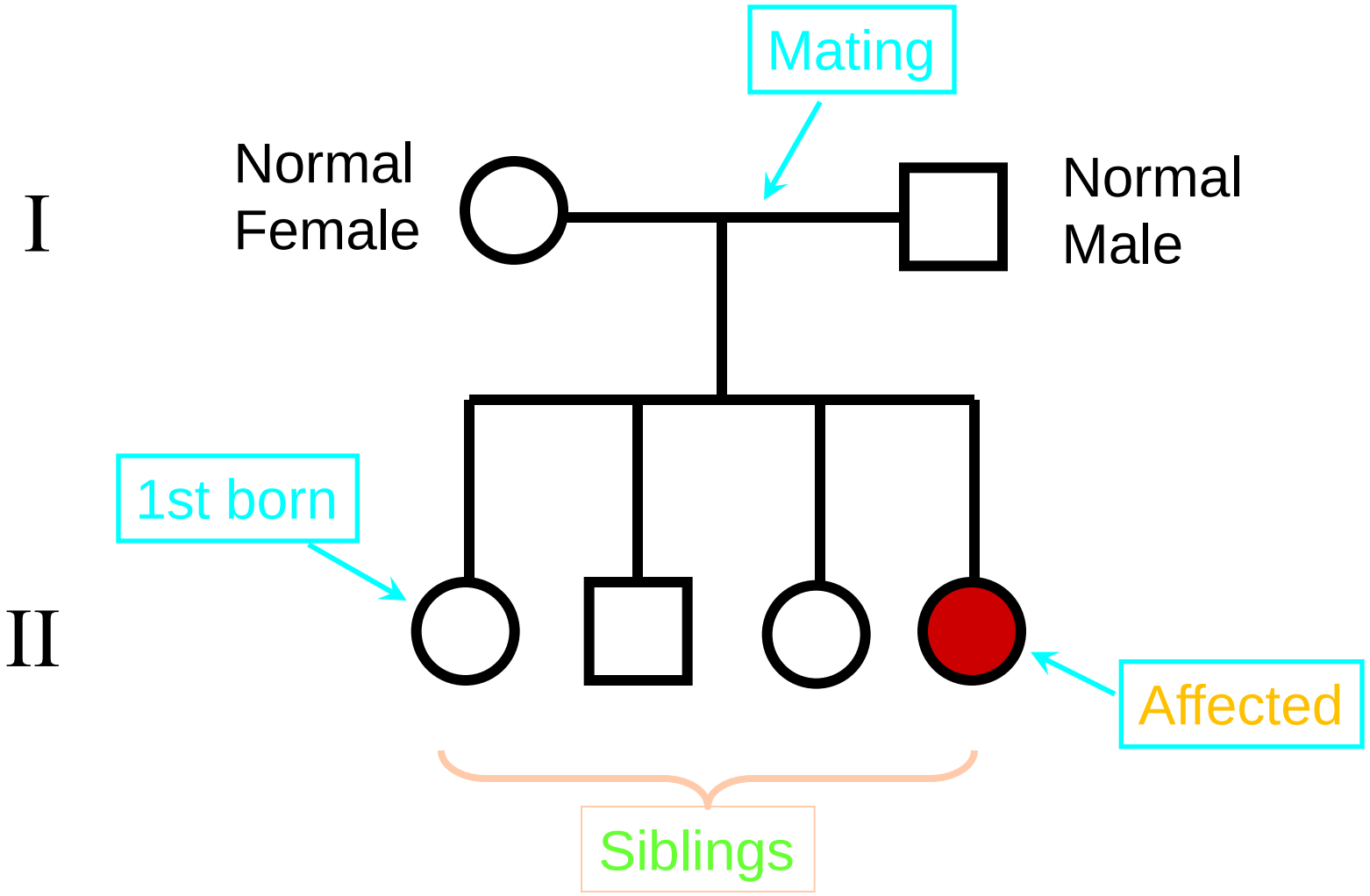
Miscarriage

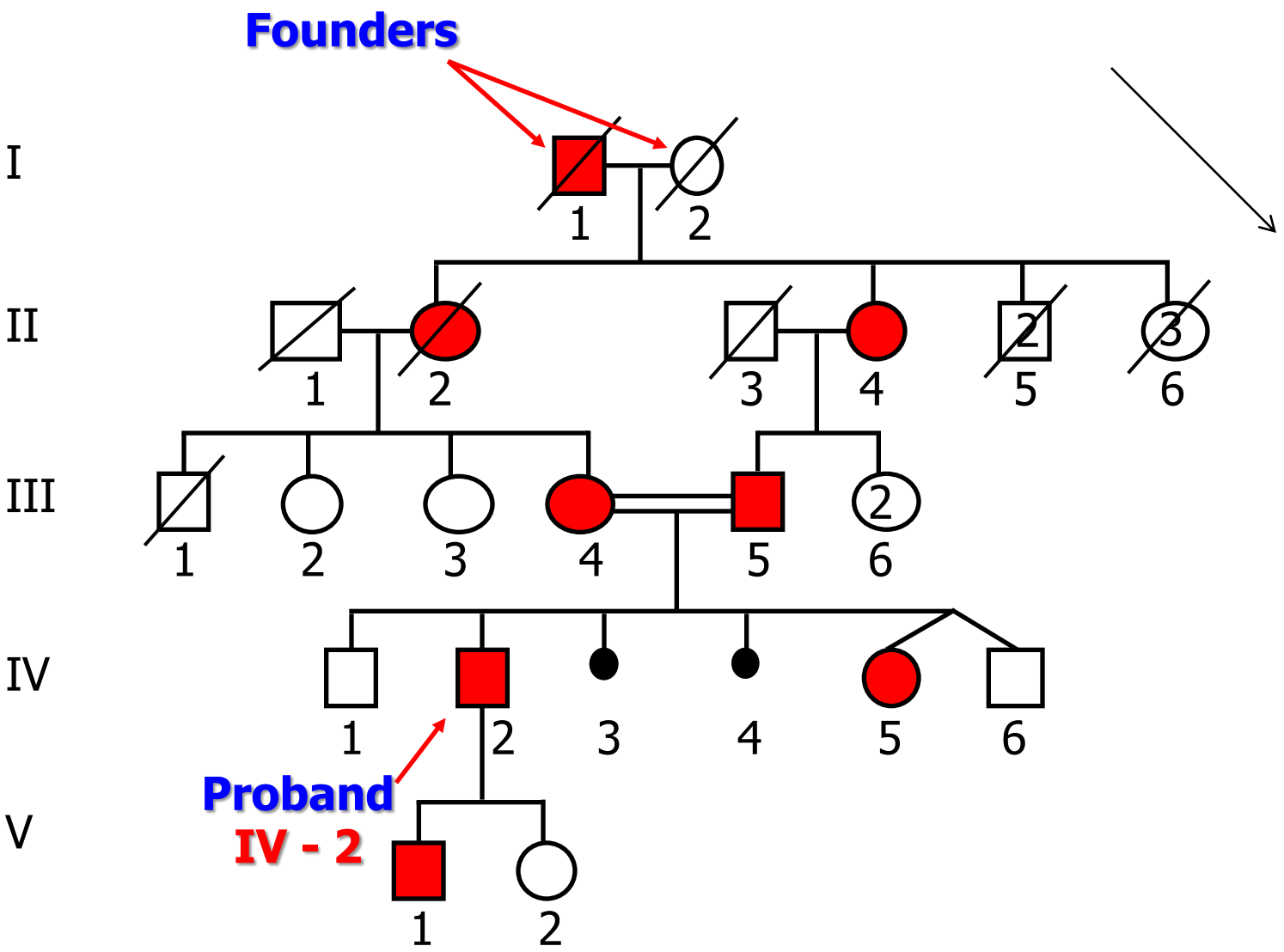
No offspring



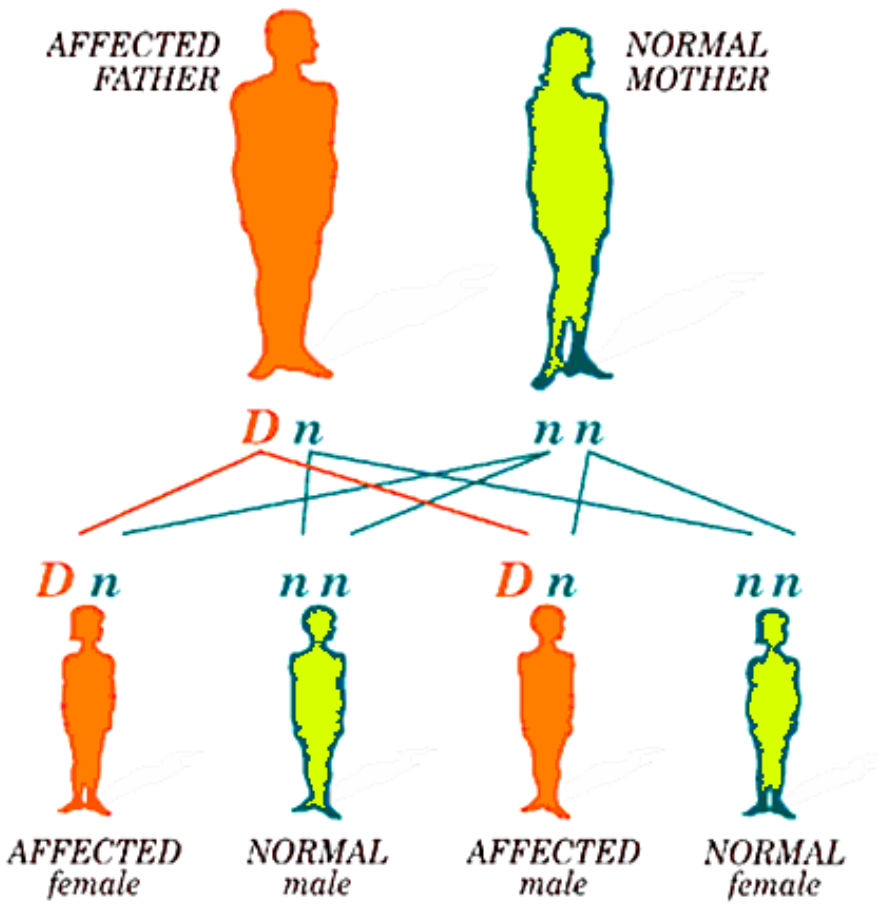
Multiple unions

Pedigree Analysis




Founders
I
II
III
IV
V
1
2
1
2
3
4
5
6
1
2
3
4
5
6
1
2
3
4
5
6
Proband
IV - 2
1
2

Autosomal dominant inheritance



- **D** abnormal gene
- **d** normal gene
- Each child of an affected person has a 50% chance of being affected
- Affected persons are usually heterozygous

Characteristics of autosomal dominant inheritance:

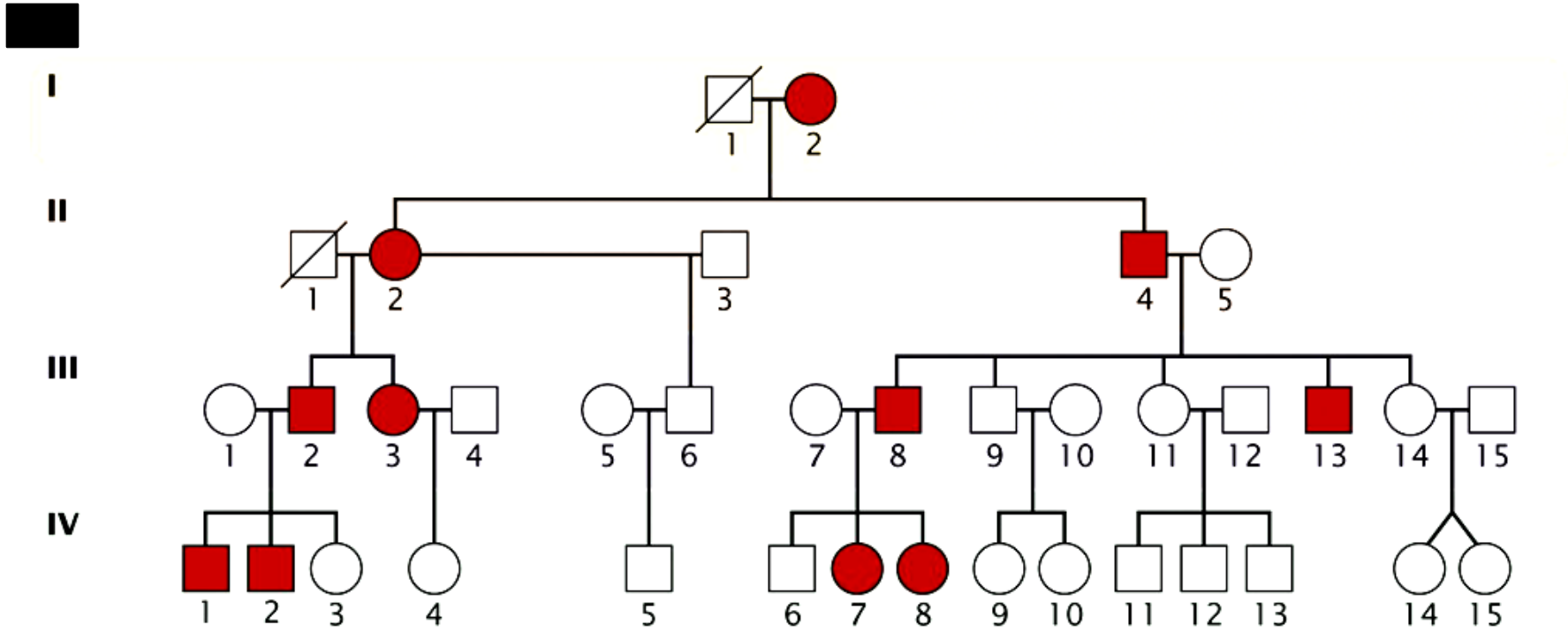
1. A gene is dominant if it is expressed when heterozygous
2. An affected individual has a 50% chance of having an affected child.
3. An affected child will have one affected parent
4. The affected parent can be either the mother or the father
5. Autosomal dominant traits have low frequencies in the population
6. Autosomal dominant traits are usually lethal when homozygous
7. No skipping of generations

Autosomal Dominance

Example:

Waardenburg Syndrome

Hearing loss and changes in coloring (pigmentation) of the hair, skin, and eyes.



- **Hemizygous:** Having half the number of alleles (e.g. males are hemizygous for all X chromosome genes)
- **Expressivity:** The severity or intensity of the phenotype of an allele.
- **Penetrance:** The degree to which a gene expresses any observable phenotype

Pitfalls in Recognizing AD Inheritance

- **Incomplete Penetrance**. Some people who have the gene mutation do not show the clinical effects.
- **Penetrance Limited to one gender**. For example, when prostate cancer risk is inherited in an autosomal dominant manner, women who inherit the mutation are not affected; they can, however, pass the mutation on to their sons
- **Variable Expressivity**. The gene mutation has variable clinical manifestations: the disorder may range from mild to severe; or a range of different complications may occur among people with the mutation.

Pitfalls in Recognizing AD Inheritance

- **New Mutation.** An affected person may be the first person in the family with the condition, due to a mutation arising for the first time in sperm, egg, or embryo

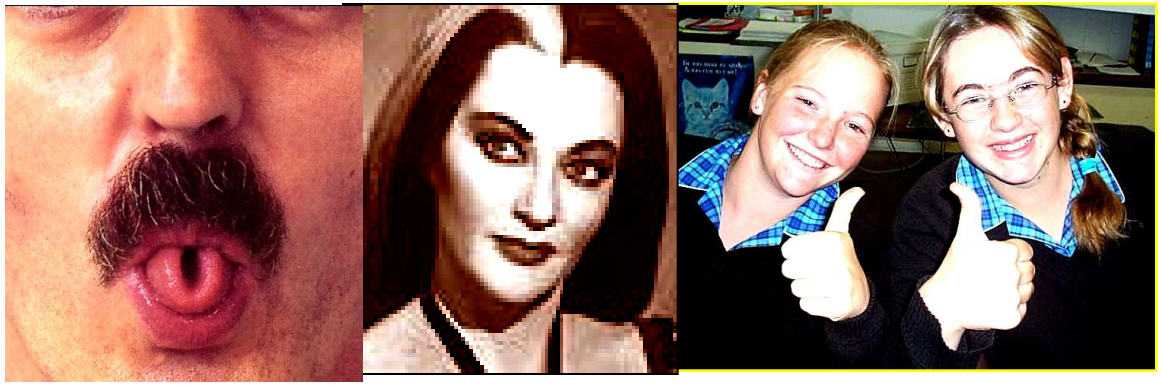
- **Germline Mosaicism.** A new mutation may arise in testis or ovary, resulting in an unaffected parent transmitting the condition to two or more children

AD Disorders

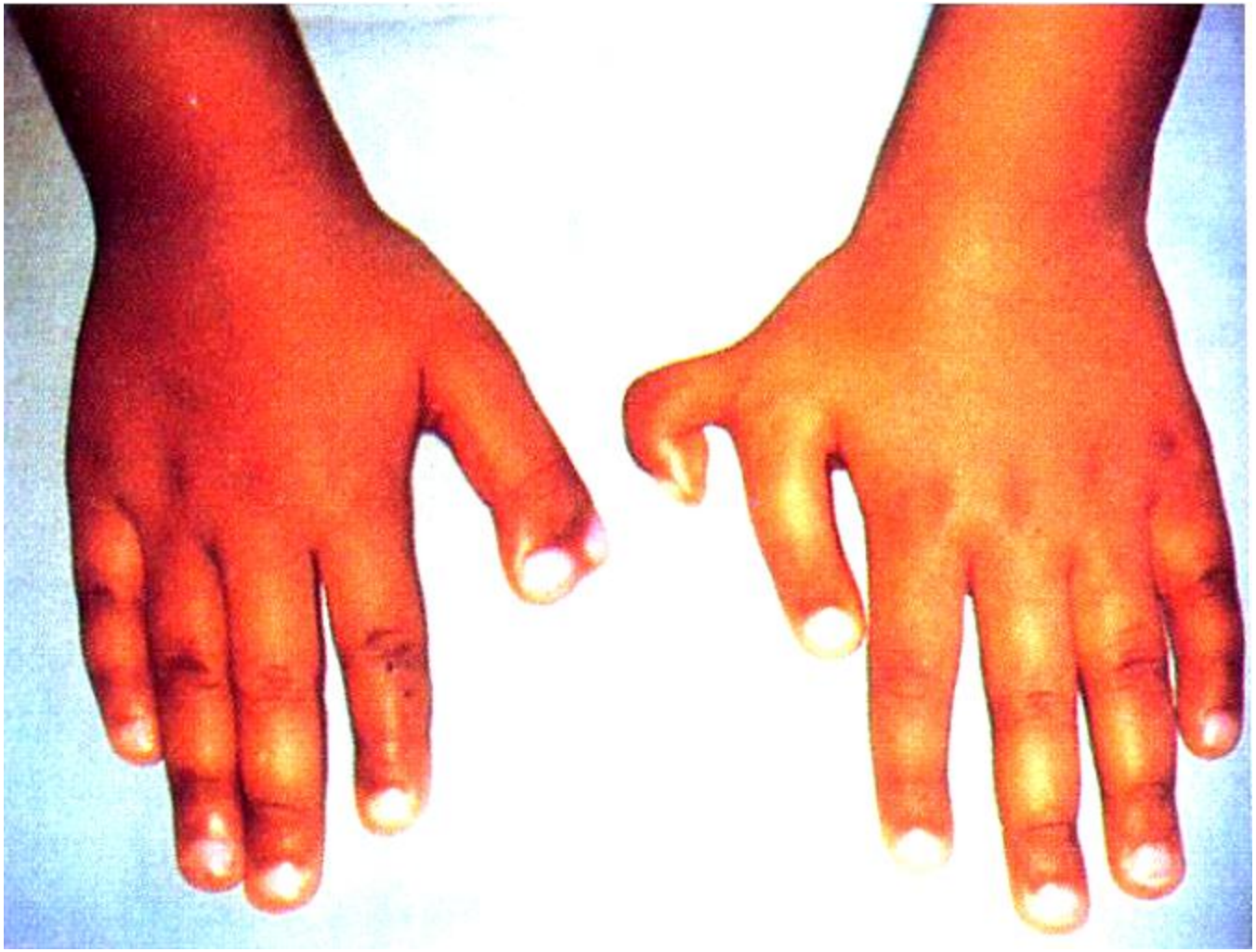
- **Marfan's Syndrome**
- **Huntington's Chorea**
- **Osteogenesis imperfecta**
- **Neurofibromatosis**
- **Retinoblastoma**
- **Tuberous sclerosis**
- **Apert's Syndrome**
- **Multiple polyposis of colon**
- **Achonroplacia**
- **Brachydactylyl**
- **Ehlers-Dalton Syndrome**
- **Familial Hypercholeserolemia**
- **Porphyria**

GENETIC TRAITS IN HUMANS CAN BE TRACKED THROUGH FAMILY PEDIGREES

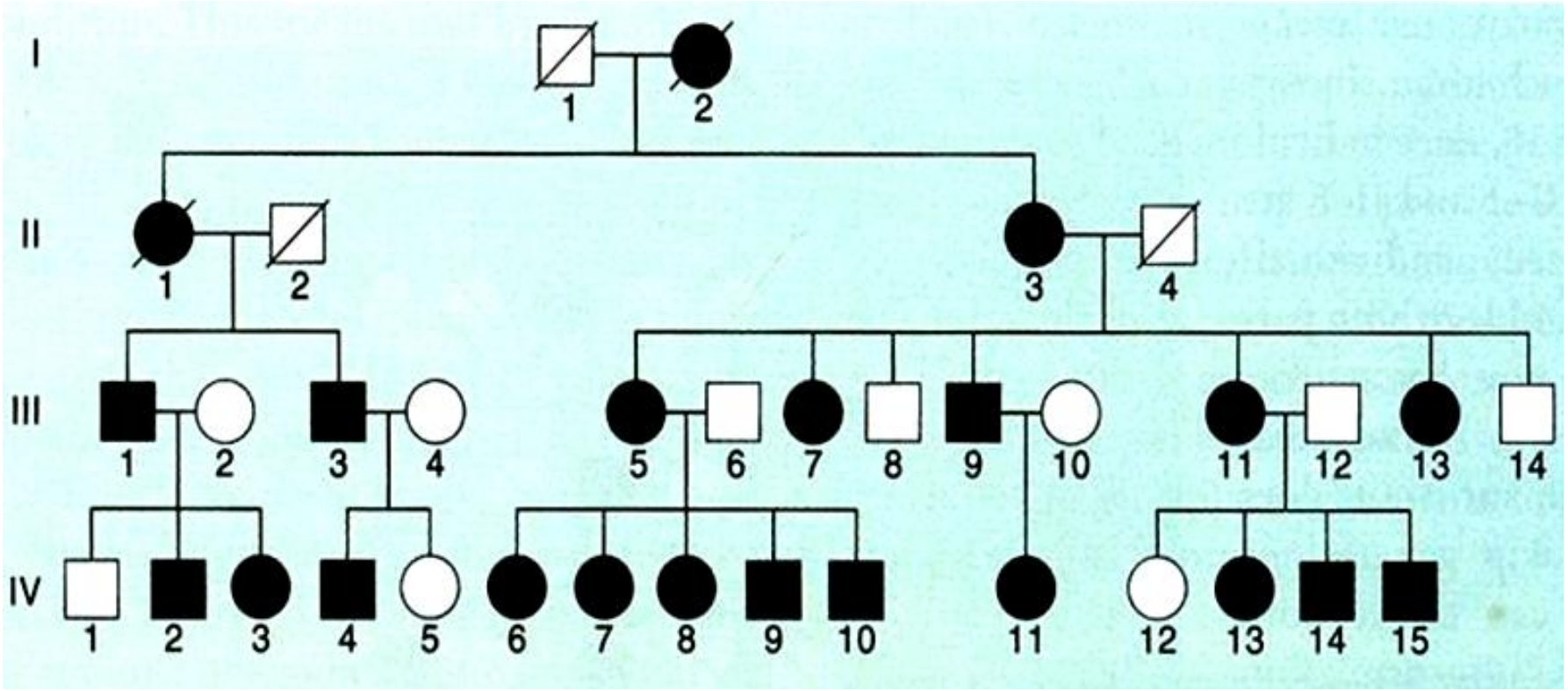
- Recessive traits are often more common in the population than dominant ones.
- E.g. absence of freckles more common than presence.



Polydactyly



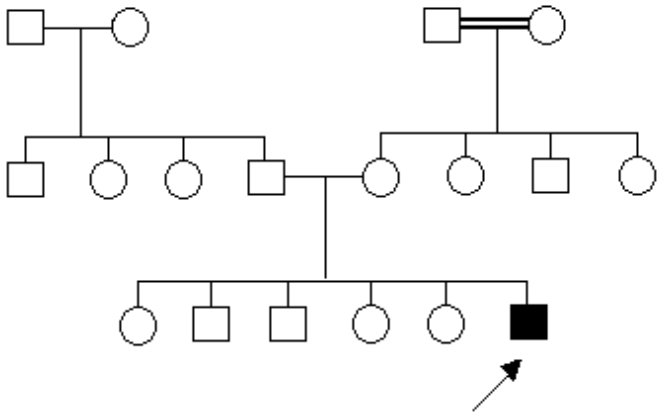
Polydactaly

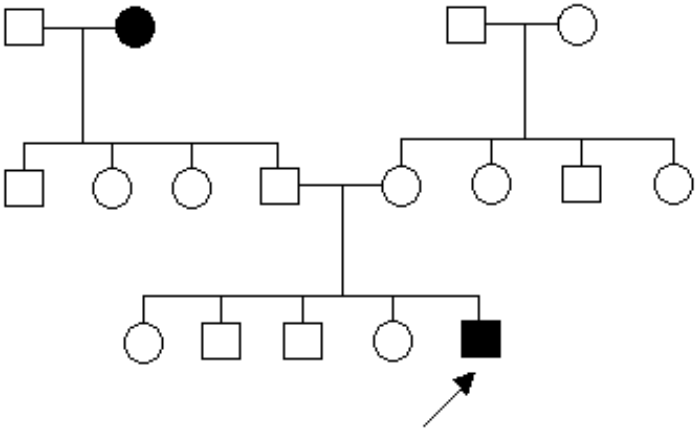


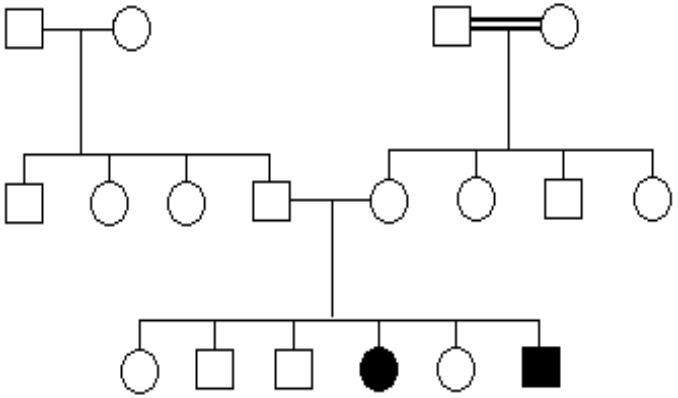
Autosomal Dominant Inheritance

Possible explanations for apparent sporadic cases

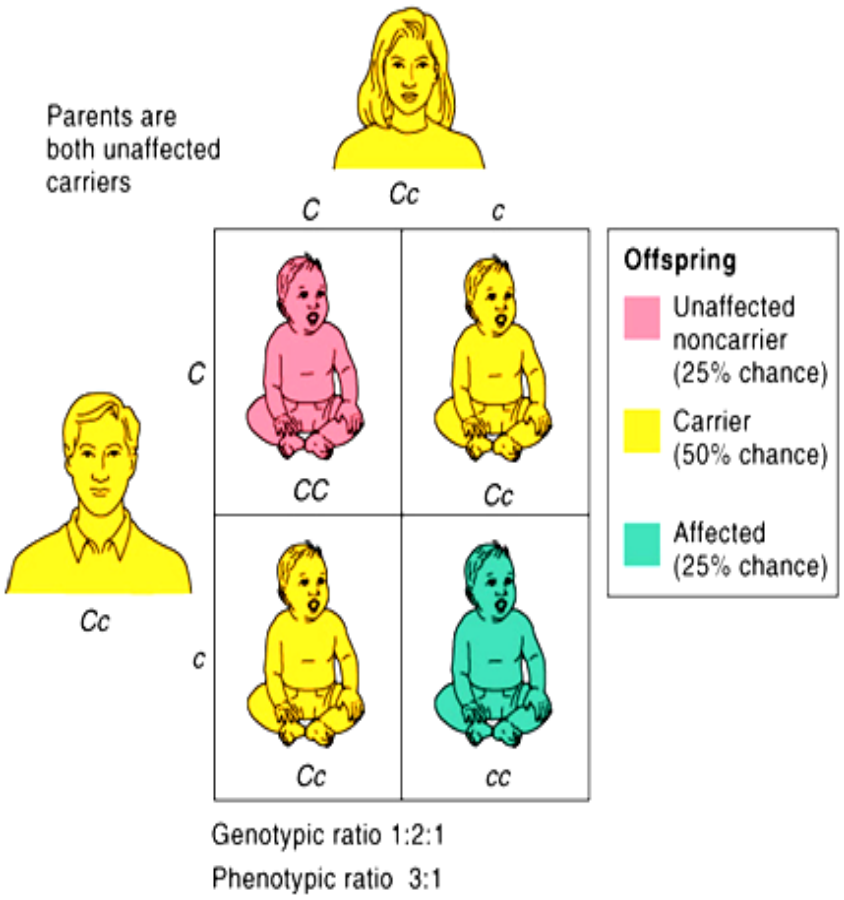
- Variable expressivity
- New mutation
- Non-penetrance
- Gonadal mosaicism





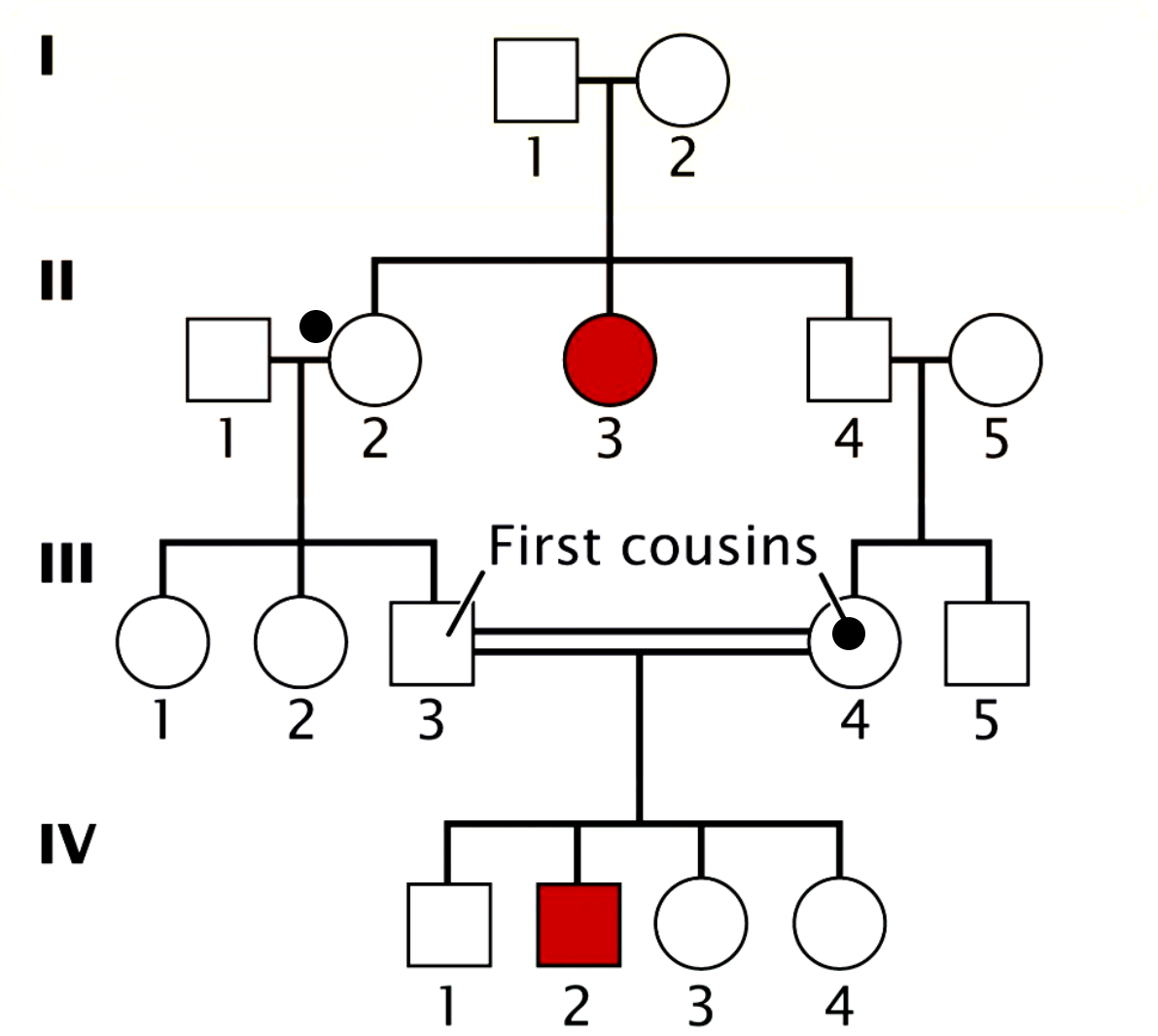


Autosomal Recessive



- **Carrier parents are Heterozygotes carry the recessive allele but exhibit the wild type phenotype.**
- **Normal parental phenotype**
- **75% chance for normal offspring**
- **25% chance for affected offspring**
- **Males & females equally affected**
- **“Inborn errors of metabolism”**
- **Associated with specific ethnic groups**

Autosomal Recessive



Risks to children:

- *When both parents are carriers*, every child they have has a 25% chance of being affected, a 50% chance to be a carrier, and a 25% to neither be affected nor a carrier.
- *When one parent is a carrier and the other is not a carrier or affected,* every child they have has a 50% chance to be a carrier and a 50% chance to neither be a carrier nor affected. No child will be affected.
- *When one parent is affected, and the other parent is a carrier,* every child they have has a 50% chance to be affected and a 50% chance to be a carrier.
- *When one parent is affected and the other is not a carrier or affected,* every child they have will be a carrier. No child will be affected.

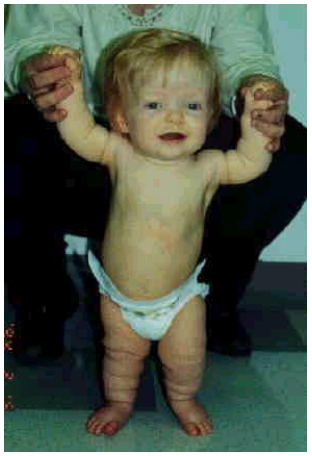
Heterozygote Advantage in Recessive Conditions

Condition	Carriers protected against
1. Thalassaemia	falciparum malaria
2. Sickle cell	falciparum malaria
3. (G-6-PD deficiency	falciparum malaria)

Examples of AR conditions

- Beta thalassemia
- Sickle cell anemia
- Congenital adrenal hyperplasia
- Familial Mediterranean fever
- Cystic fibrosis
- Phenylketonuria

Dominant Versus Recessive



1. **Achnondroplassia**

   Homozygote – Reduced Stature, Usually Die in Infancy

   Heterozygote - Usually normal life

2. **Familial Isolated Growth Hormone Deficiency (IGHD)**

   Several mutations on Ch 17 (GH1)

   RECESSIVE: Nonsense Mutation

   1. Heterozygote : Produce sufficient GH – Normal

   2. Homozygote: No GH production – Affected

   DOMINANT: Splicing Site mutation at exon 3, Mutated GH produce Disulfide bond with the normal GH produced by normal gene

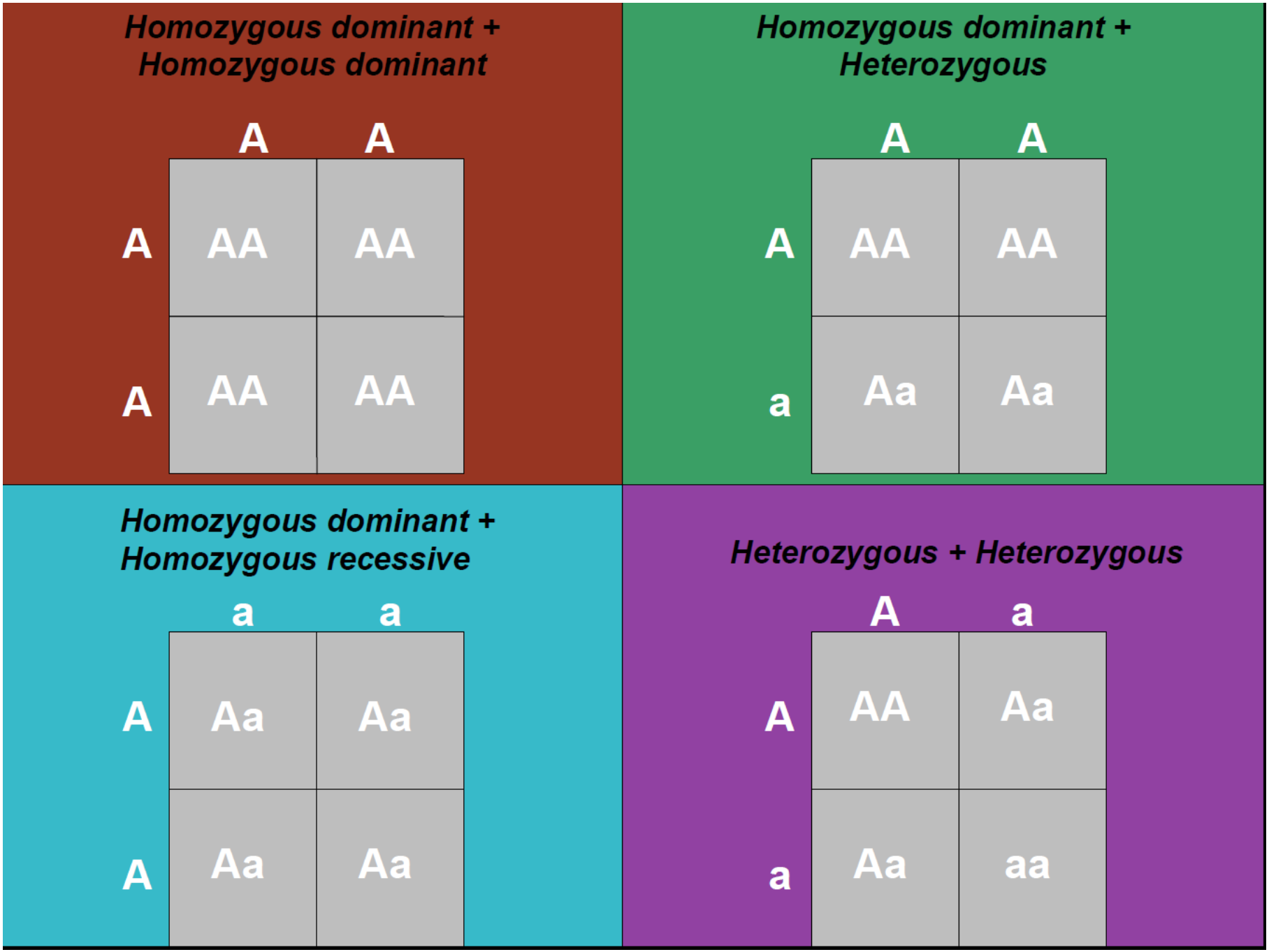
3: **Sickle Cell Anemia**

   Normal Altitude - Trait is living normal Recessive

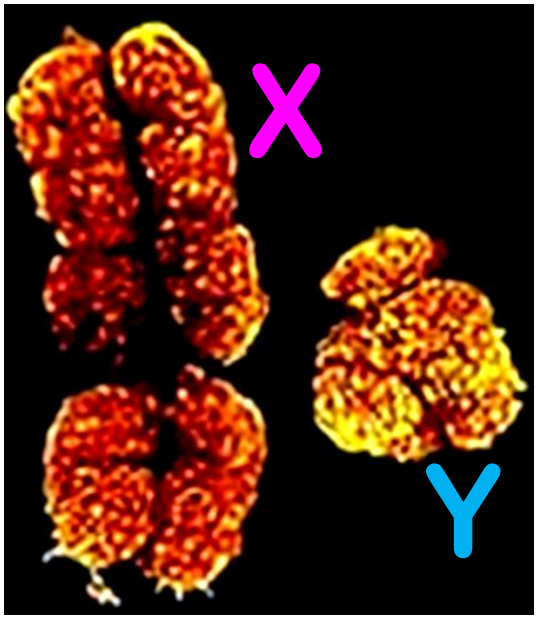
   High Altitude - Trait is Affected Dominant

Factors that may complicate Inheritance Patterns

- Codominance
- Epistasis
- New mutation
- Germline Mosaicism
- Delayed age of onset
- Reduced penetrance
- Variable expression
- Pleiotropy and Heterogeneity
- Genomic Imprinting
- Anticipation


Homozygous dominant + Homozygous dominant
A A
A AA AA
A AA AA
Homozygous dominant + Heterozygous
A A
A AA AA
a Aa Aa
Homozygous dominant + Homozygous recessive
a a
A Aa Aa
A Aa Aa
Heterozygous + Heterozygous
A a
A AA Aa
a Aa aa

Sex-Linked Disorders



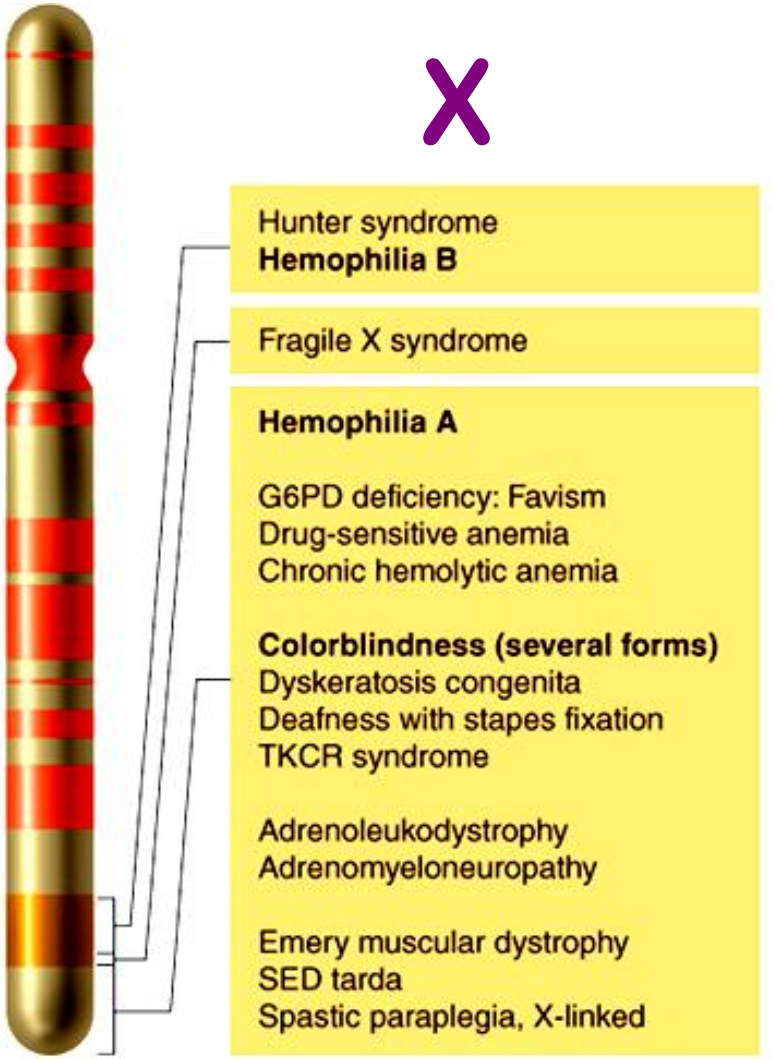
Y-linked Traits

- The Y chromosome is small and therefore does not contain many genes
- Y linked diseases are very rare
- Only passed from father to son.
- Example: Male infertility

Sex-linked inheritance

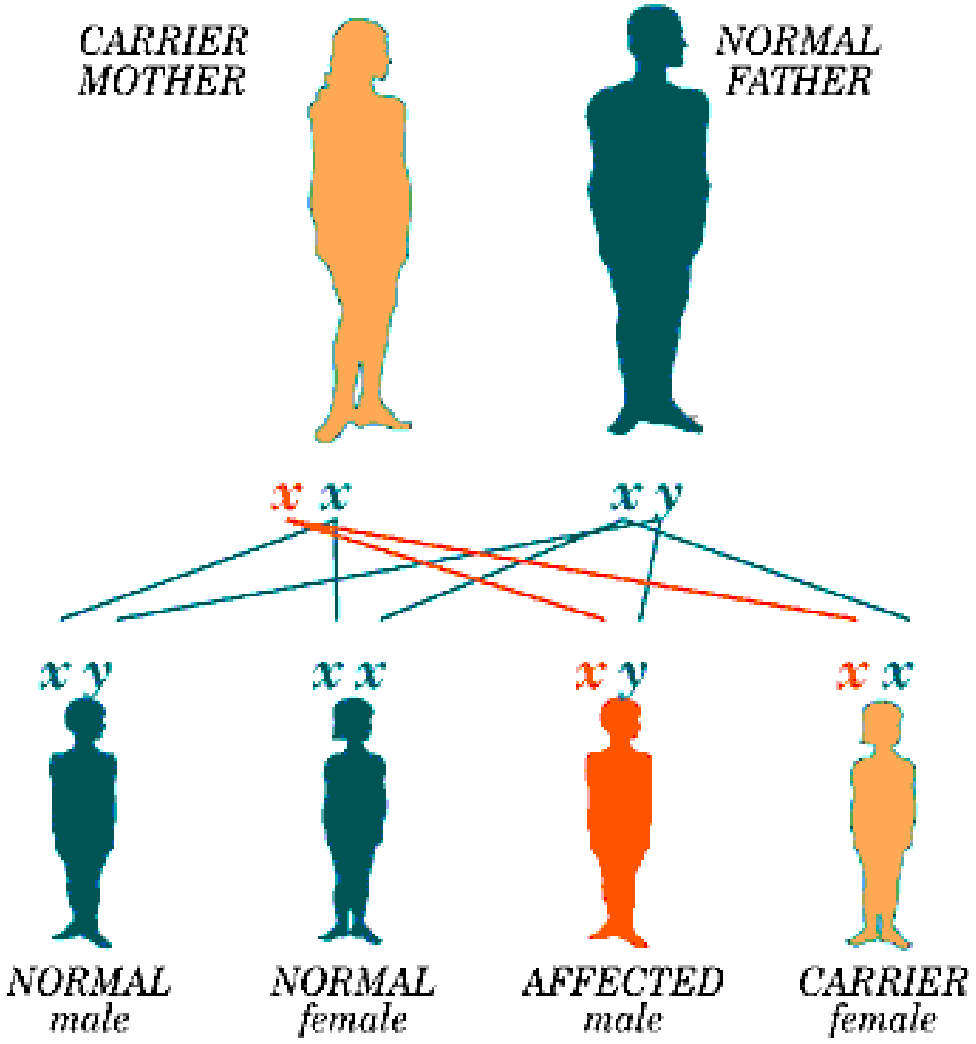
- Males are XY and females are XX
- Two sex chromosomes are very different in size
  Y about ¼ the size of the X
- They are not genetically equivalent
- Traits associated with genes on the X chromosome
  - X-linked
- Traits associated with genes on Y chromosome
  - Y-linked

X Chromosomes Inheritance

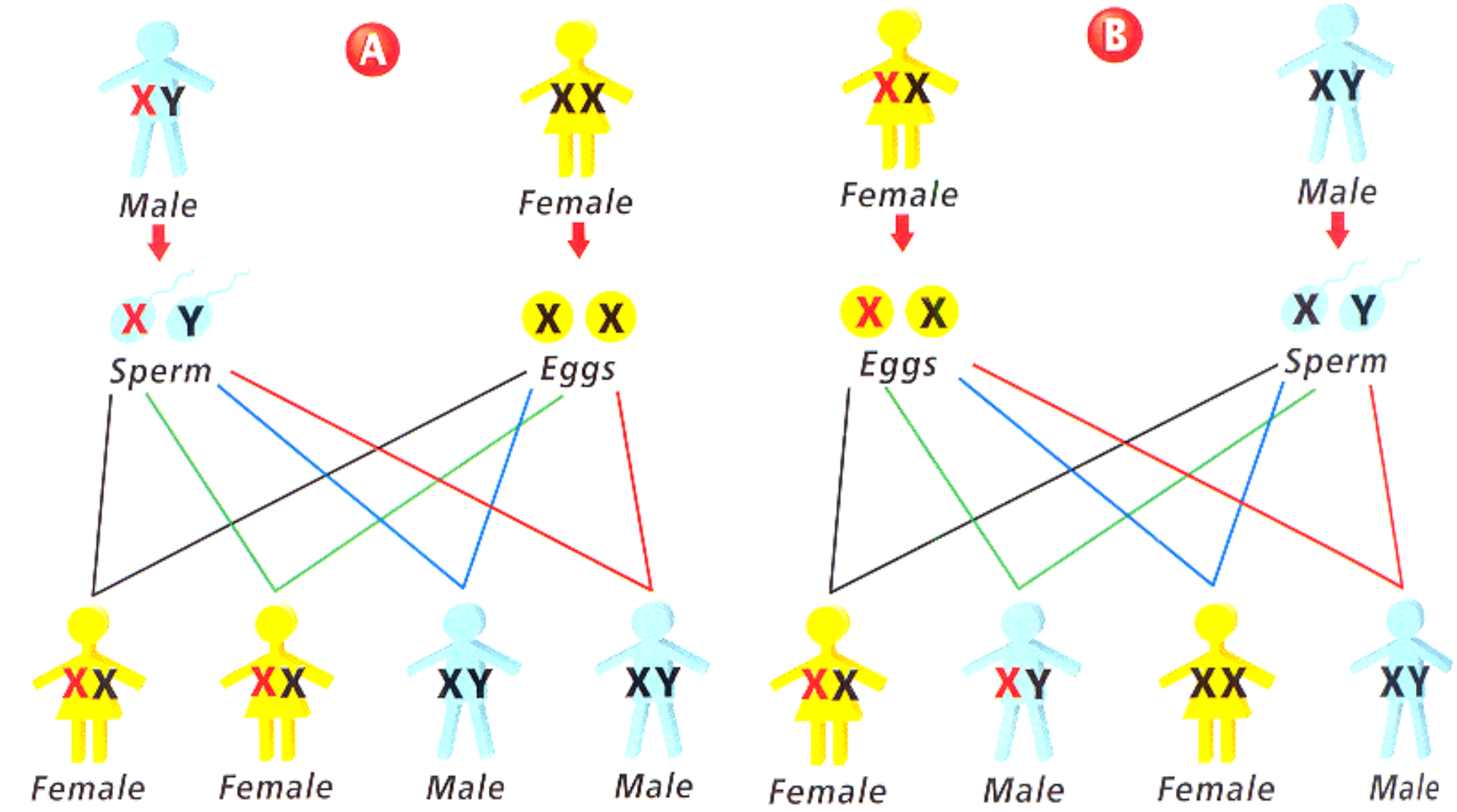


- X-Chromosome = 5% of the human genome Approximately 160 million bp (160Mb).
- > 700 genes identified, most of them are Recessive
- Few of them are Dominant

X-Linked Disorders: Males are at Risk



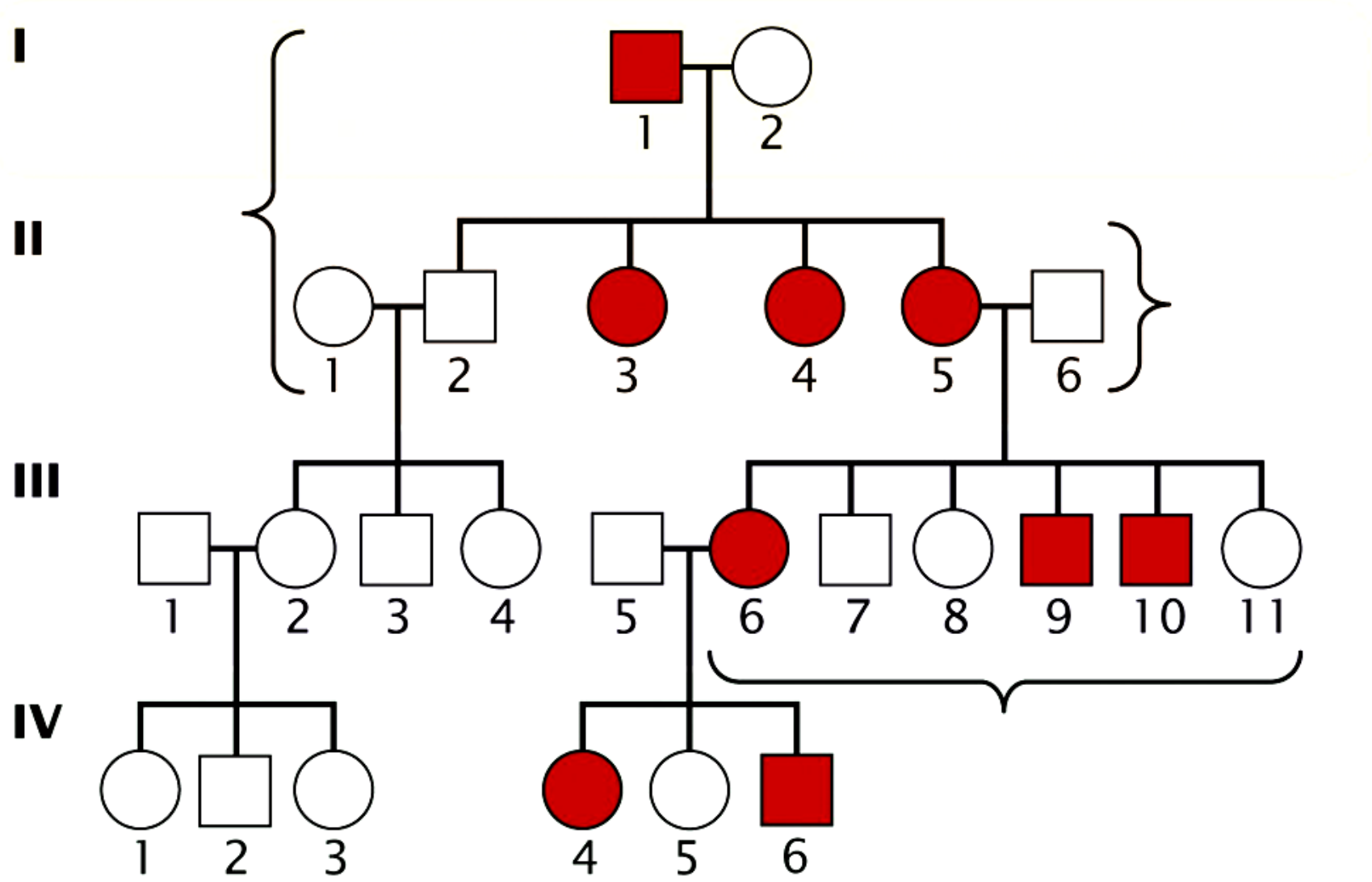
X-linked Inheritance



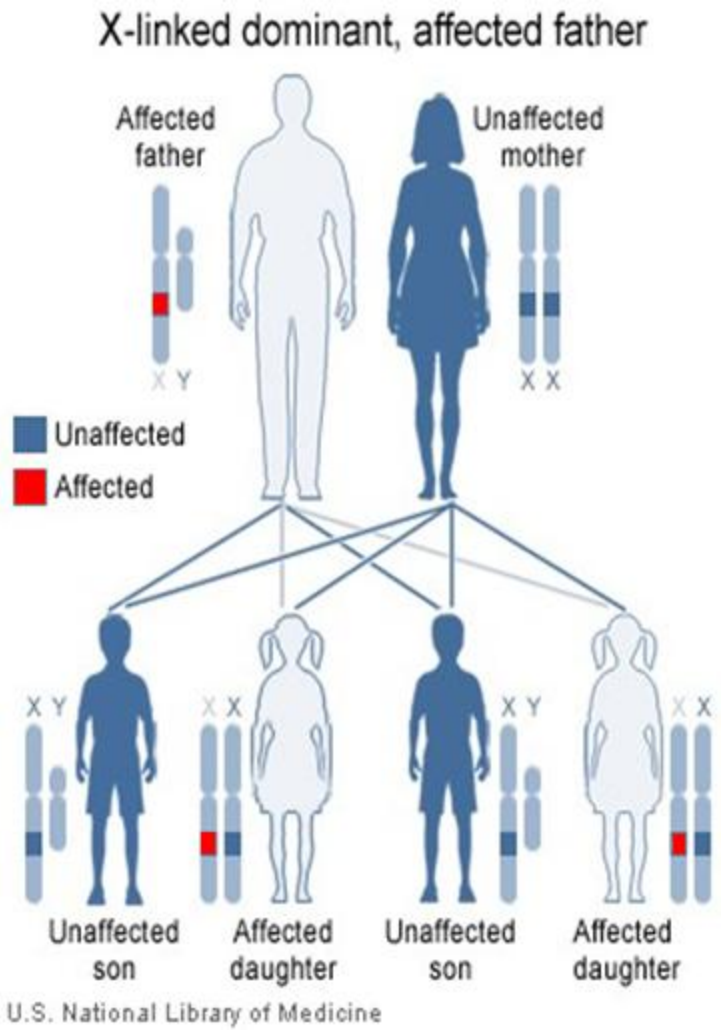
X-linked Dominant Disorders

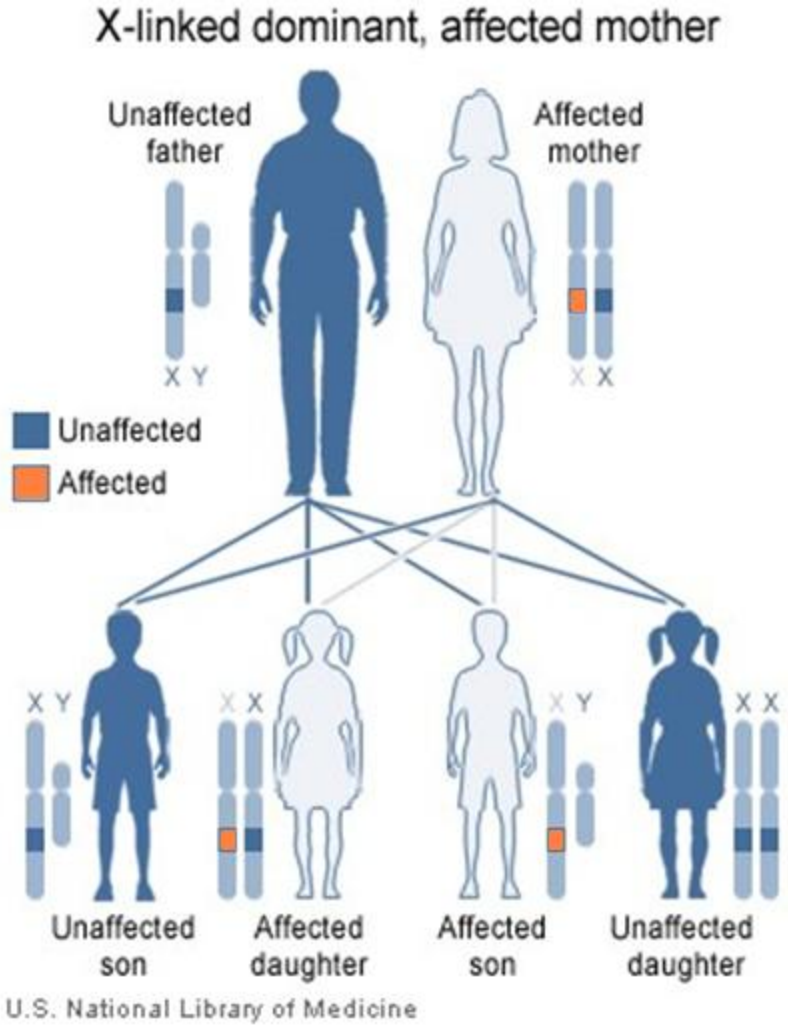
- Affected males will produce all affected daughters, but no affected sons.
- 50% chance that a heterozygous affected female will pass trait to either son or daughter.
- Homozygous females pass on trait to all offspring.
- On average, twice as many females afflicted as males
- Expressed in females with one copy.
- Males are often more severely affected.
- Typically associated with miscarriage or lethality in males.

X-Linked Dominant



X-Linked Dominant Inheritance

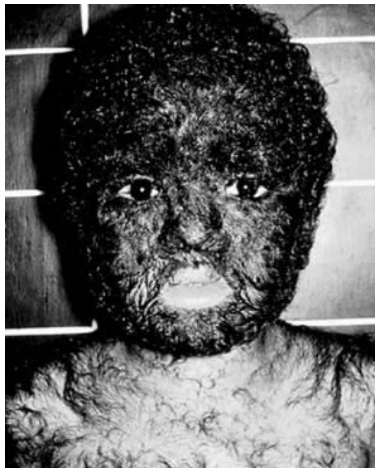


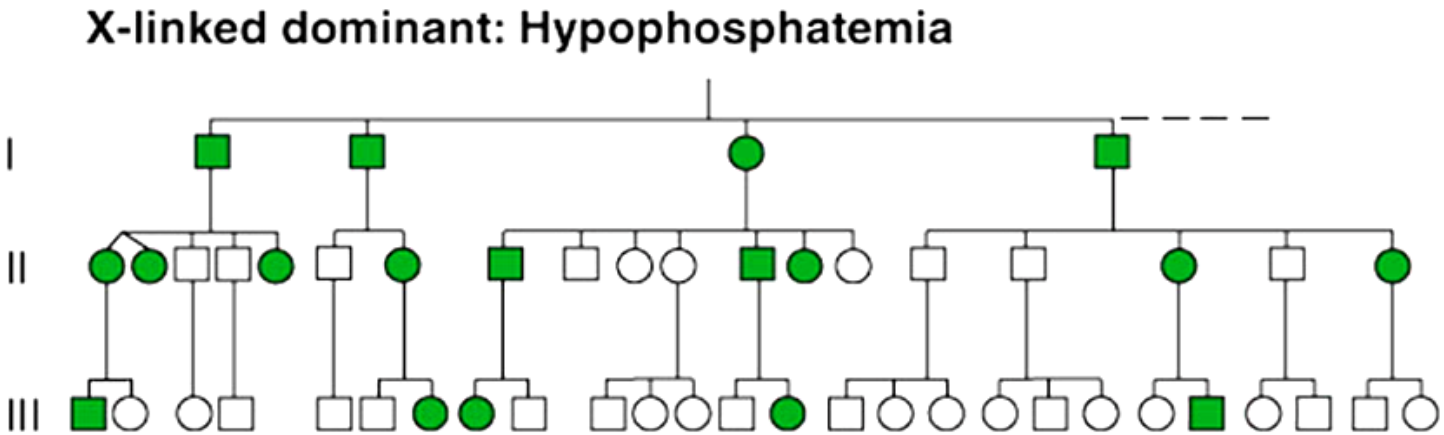


X-Linked Dominant Inheritance

There are very few X-linked dominant traits.

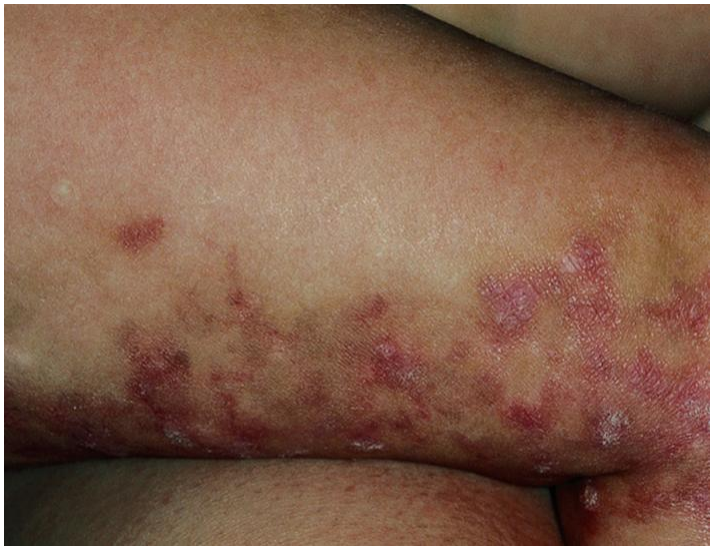
- Dwarfing conditions due to X-linked dominant conditions include another form of chondrodysplasia punctata (X-linked dominant type)
- Incontinentia Pigmenti
- Congenital Generalized Hypertrichosis CGH:
- X-linked hypophoshatemic (Vitamin D-resistant rickets).





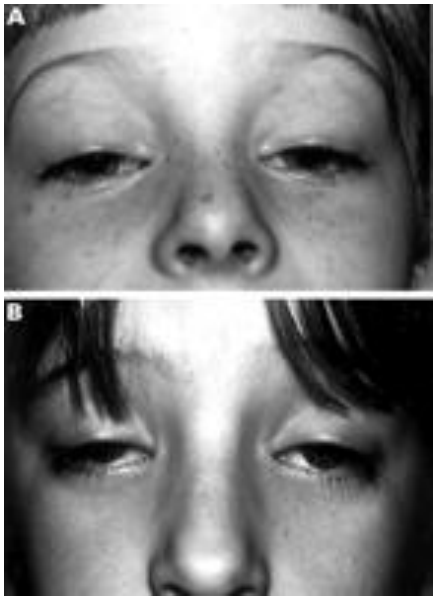
Incontinentia pigmenti

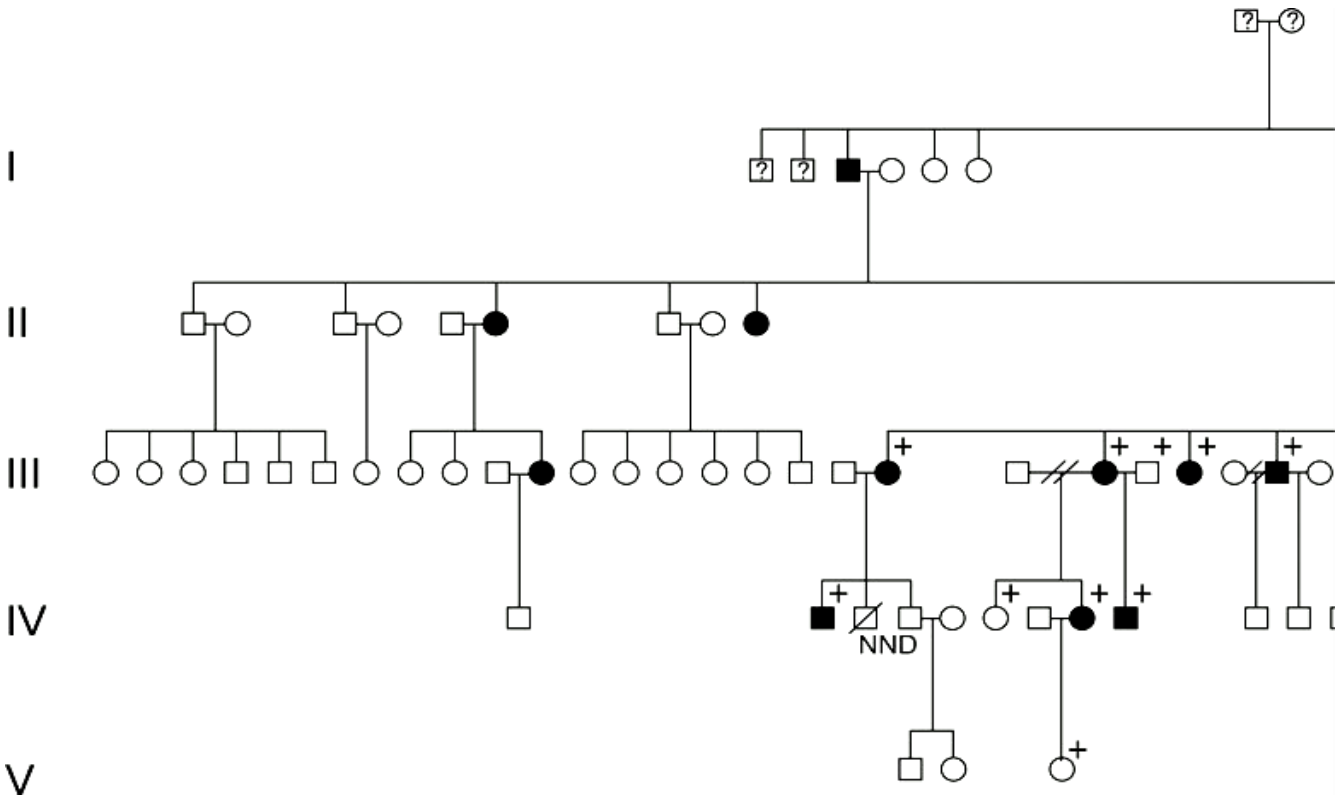
- X-linked dominant trait
- Heterozygous female - pigment swirls on skin, hair and tooth loss, seizures
- Male - death in uterus
- No homozygous females because no males reproduce



X-Linked Dominant Example

Congenital Bilateral Ptosis: Droopy Eyelids Locus:
Xq24-Xq27.1

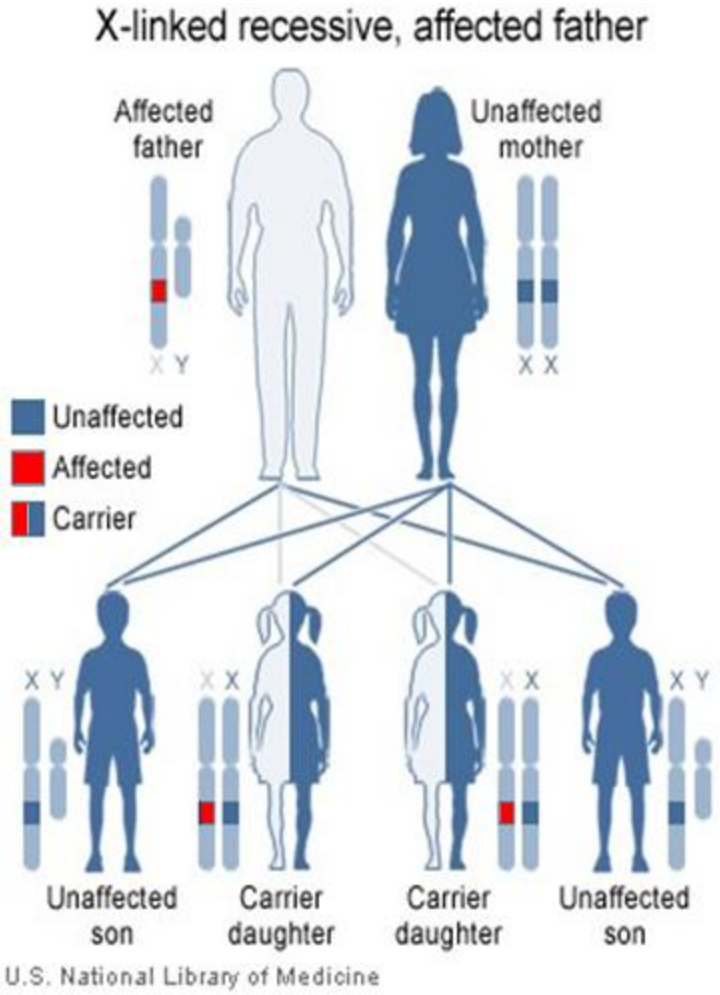


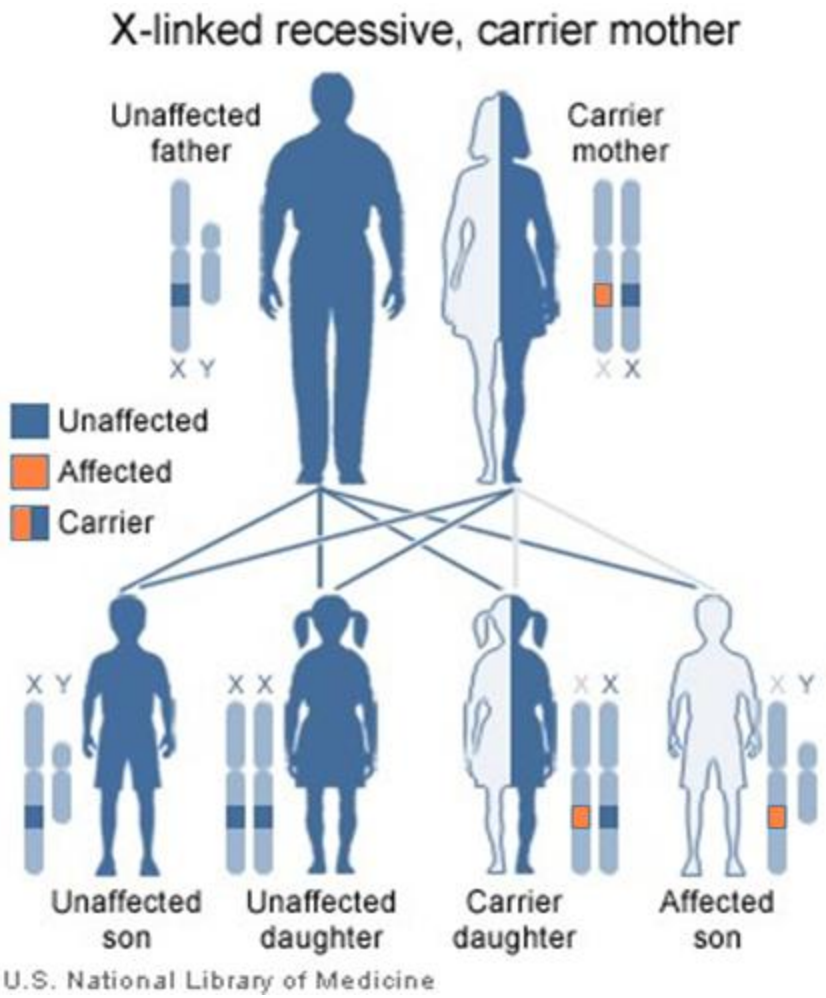


X-linked Recessive Disorders

- Abnormal disorder-causing allele is *recessive* and is located on the X-chromosome
- Normal, wild type allele is *dominant*
- Affects hemizygous males and homozygous females.
- Expressed phenotype much more common in males
- Affected males get the mutant allele from their mothers
- Affected males transmit the mutant allele to all daughters, but not to sons
- Daughters of affected males are usually heterozygous – thus unaffected
- Sons of heterozygous mothers have a 50% chance of being afflicted

X-Linked Recessive Inheritance

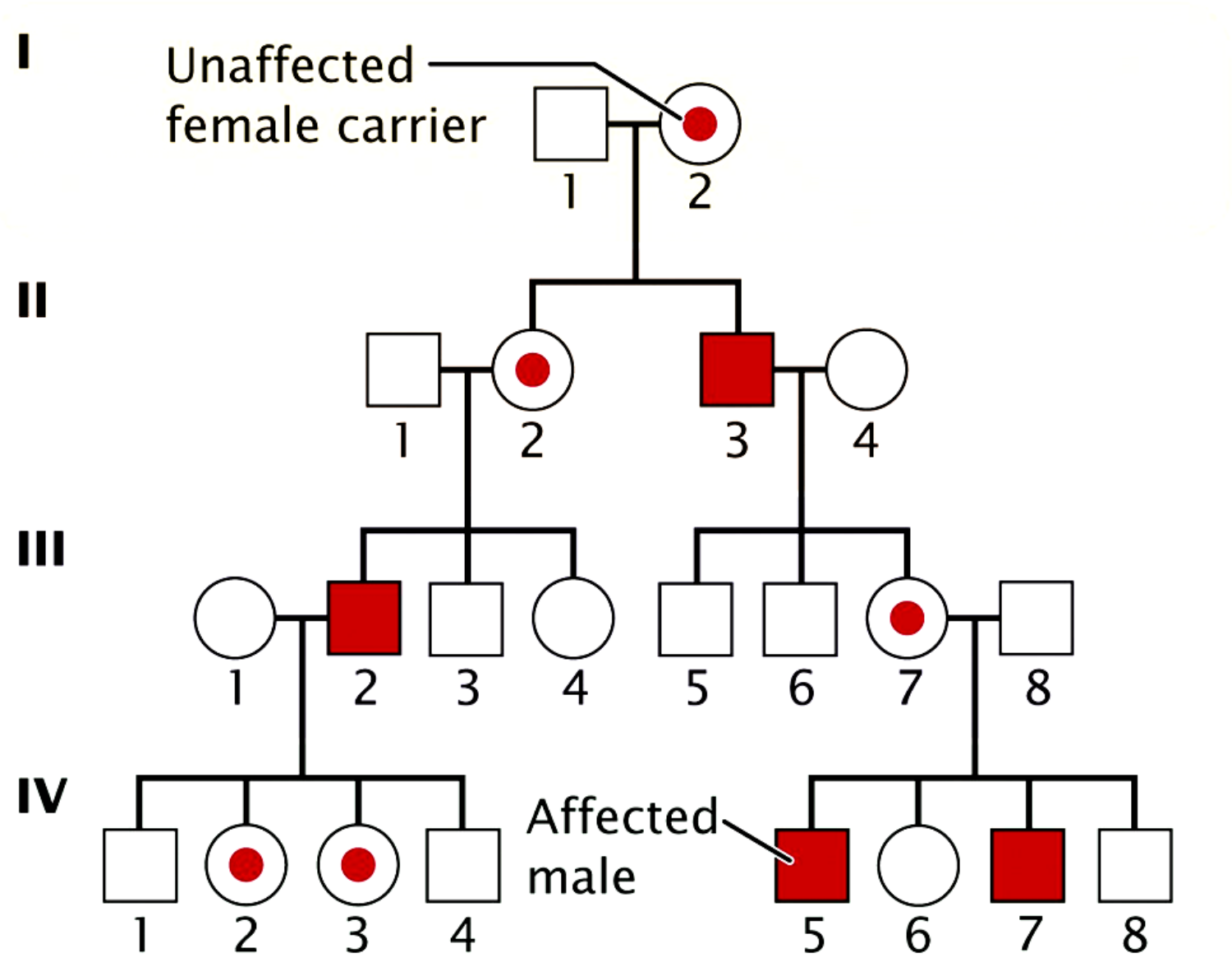




X-linked Recessive Inheritance: Recurrence Risks

- In the usual mating between a heterozygous affected female and a normal male, the risks for offspring are as follows:
  - 25% chance affected male
  - 25% chance normal male
  - 25% chance carrier female (normal)
  - 25% chance non-carrier female (normal)
  - Total risk for an affected child: 25%

X-linked Recessive

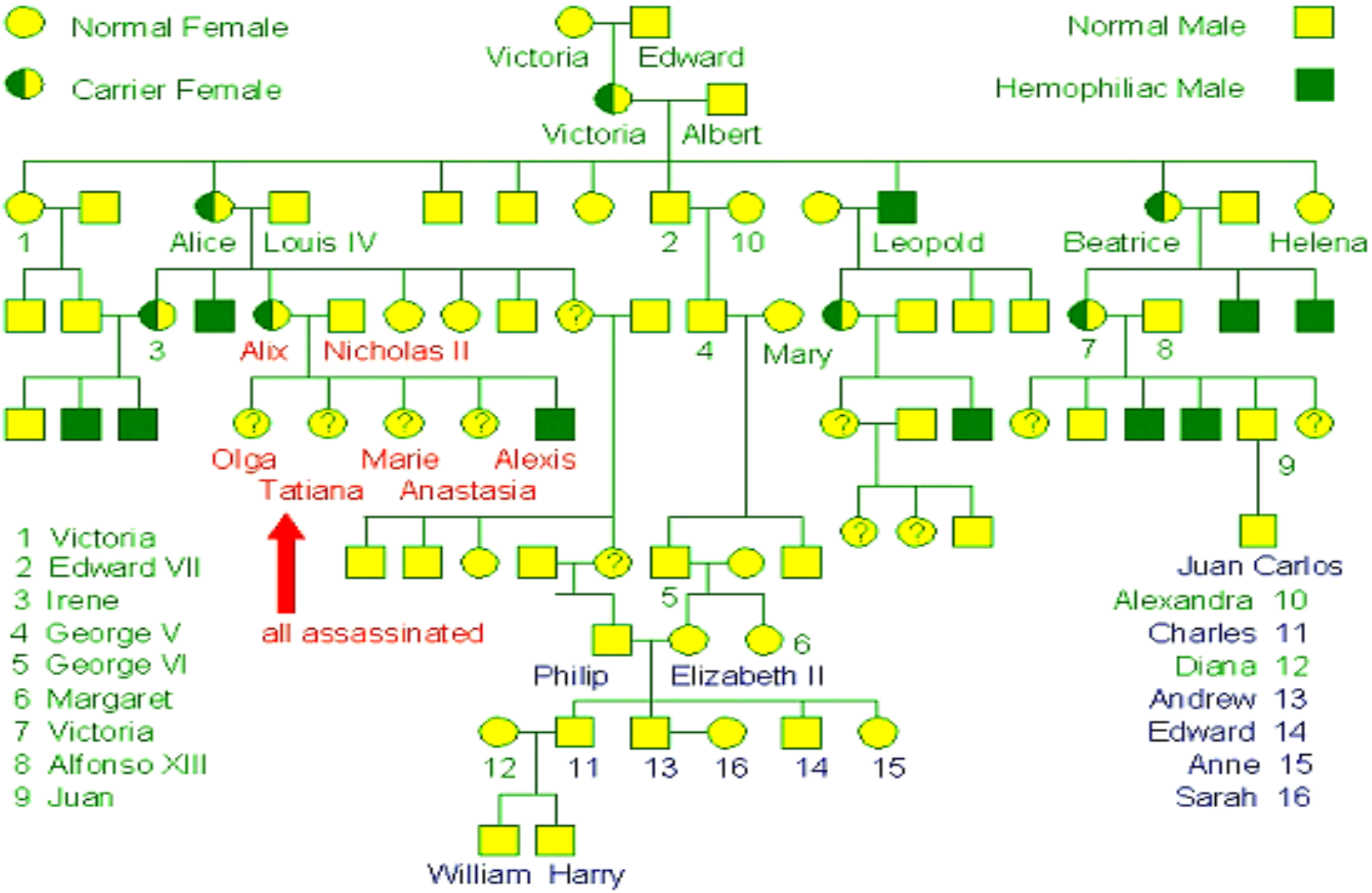


X-Linked Recessive Inheritance

Pitfalls in Recognizing X-Linked Recessive Inheritance and Providing Genetic Counseling

- **Small Families.** Small family size and few male children may make the pattern of an X-linked recessive disorder difficult to diagnose.
- **New Mutation.** An affected male may be the first person in the family with the condition, due to a mutation arising for the first time . sperm, egg or embryo.
- **Germline Mosaicism.** A new mutation may arise in testis or ovary, resulting in a parent who can pass on the condition or the carrier state to children, without being either affected (in the case of a male parent) or a carrier (in the case of a female parent).

Intermarriage caused the disease hemophilia to spread through the royal families of Europe



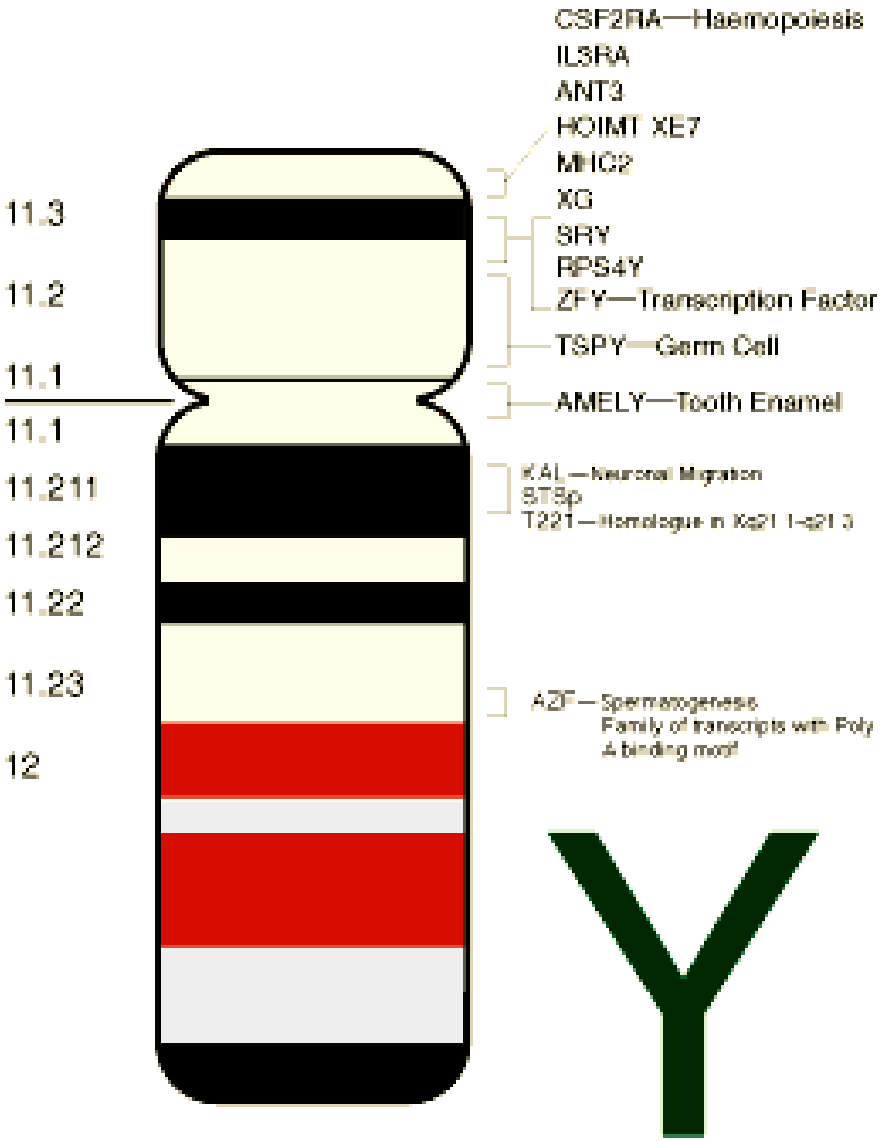
Rules for X-linked conditions

- **X-linked recessive**
  - Males have the condition
  - Females are carriers
  - If a male has the allele
    - All daughters are carriers
    - All sons are normal
  - If a female has the allele
    - ½ daughters are carriers
    - ½ sons have the condition
- **X-linked dominant**
  - If a male has the allele
    - All daughters have the condition
    - All sons are normal
  - If a female has the allele
    - ½ offspring have the condition (whether sons or daughters)

X-linked Recessive Disorders

TRAIT	Phenotype
• Adrenoleukodystrophy	Atrophy of the adrenal gland; maternal Deterioration; death 1-5 Y after onset
• Color Blindness	Green (60-75%); Red (25 – 40%)
• Fabry disease	MD α-Galactozidase A deficiency Cardiac and Renal , Death
• G-6-P-D	Benign, can cause sever fetal anemia Due to certain food and drugs
• Hemophilia A	Lack of factor VIII
• Hemophilia B	"Christmas Disease" lack of factor IX
• Ichethiosis	Skin disorder causing large, dark scales on extremities
• Lynch-Nyhan S	MD Hypoxanthine guanine Phosphoribisyl transferase (HGPRT) Deficiency: MR, Self-mutilation Early death
• Muscular dystrophy	Many types

Y-Linked Inheritance



Y-linked

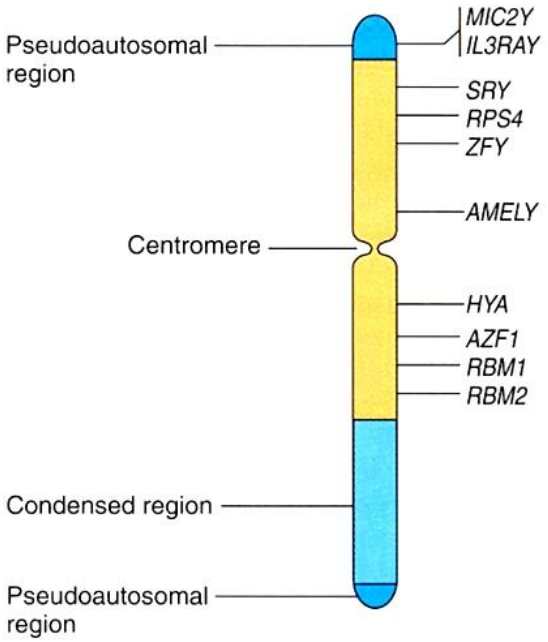
Father's Gametes

Mother's Gametes

	X	Y
X	XX	XY
X	XX	XY

Y Chromosome Inheritance

- Y-Chromrosome = 70Mb
- Few dozen genes **(Holandric)** are found on Y
- Male differentiation genes
- Testis-specific spermatogenesis factor
- Minor Histocompatibility genes (HY)
- Several housekeeping genes
- Transmission strictly from father to son



Y-linked traits

- -Related to genes unique to the Y chromosome
  - are present only in males (no afflicted females)
  - passed directly from fathers to sons
    hemizygous – always expressed

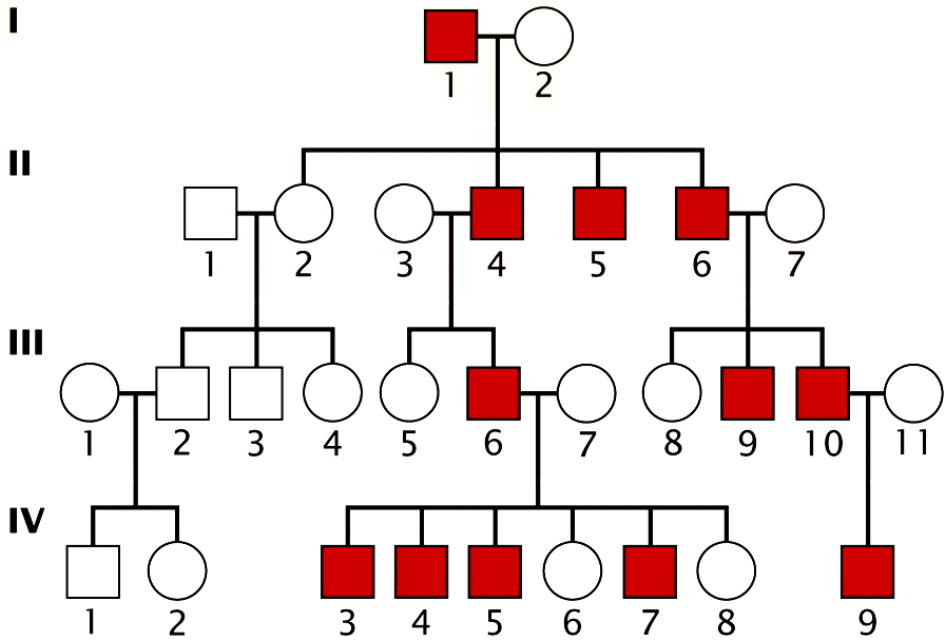
- Very rare - only about 3 dozen Y-linked traits known
  - Often associated with infertility

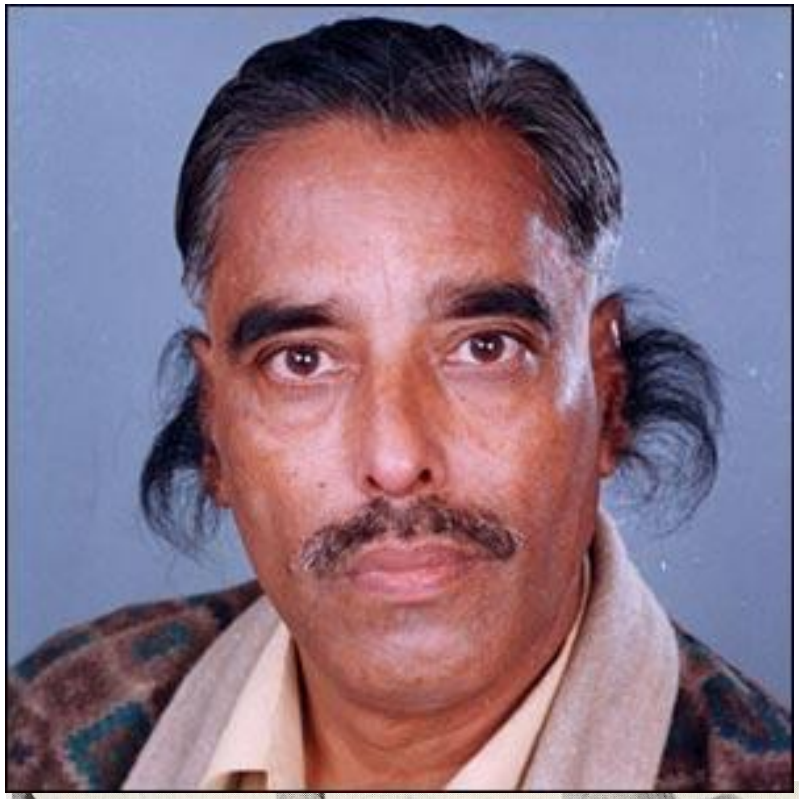
- One important gene

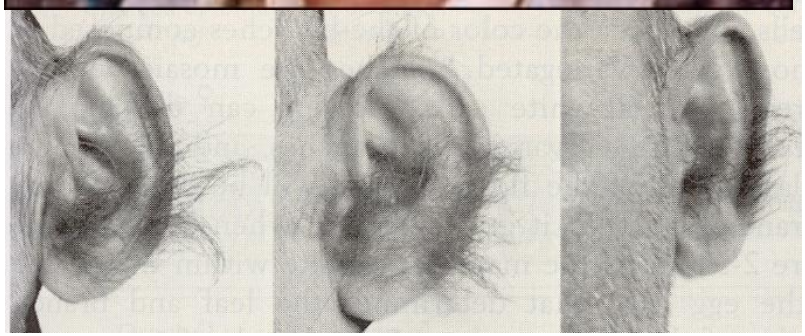
  - TDF – testis determining factor
  - Also known as SRY
  - Sex determining region of the Y chromosome

Y-Linked Traits

HYPERTRICHOSIS PINNAE AURIS (Hairy ears),







Can happen later in life.

Y-linked

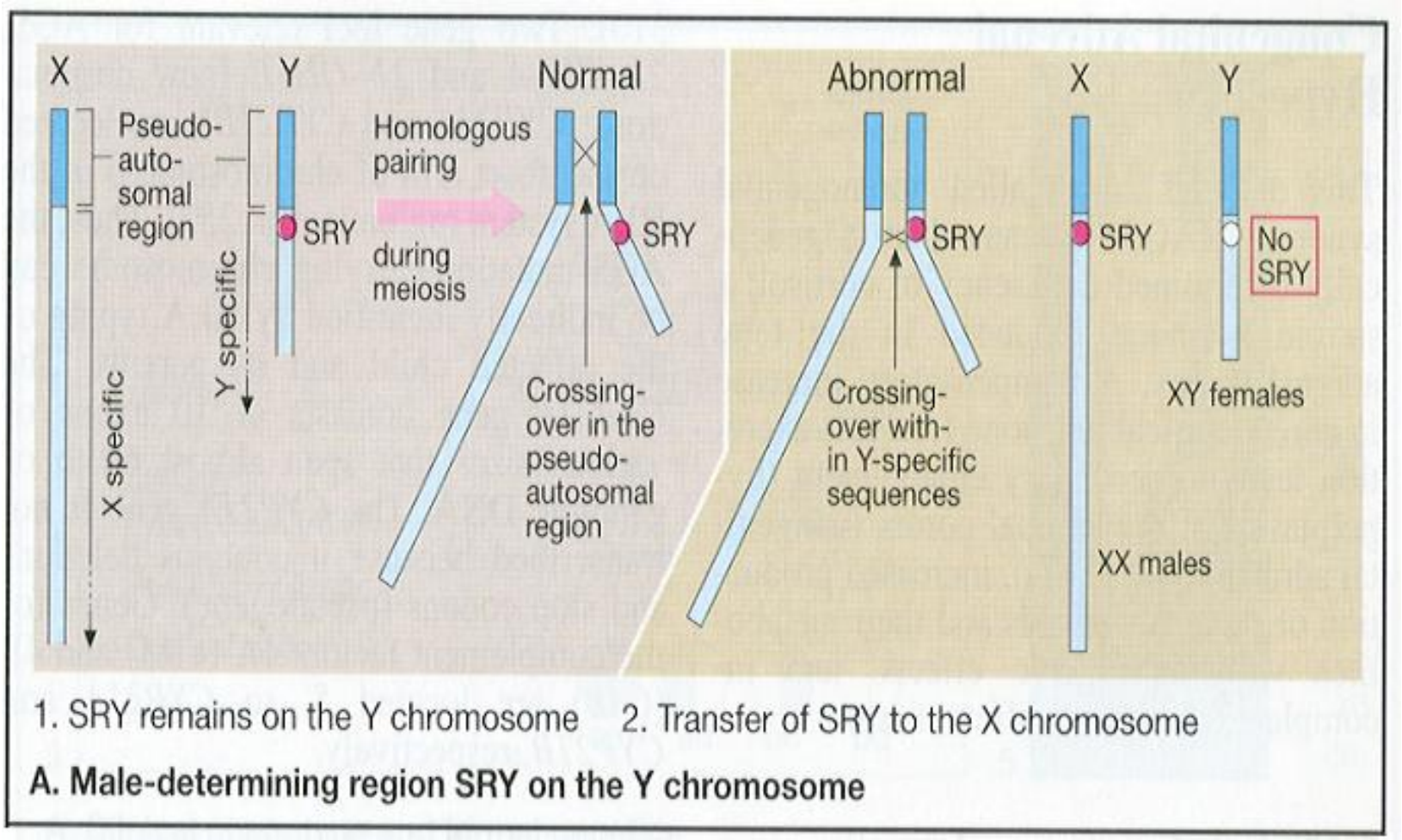
Sex-Limited, Sex-Influenced

- **Sex-Limited:** Autosomal genes
  - Affects a structure/process/behavior found only in one sex due to anatomical differences, Inherited Uterine or Testicular defects

- **Sex-Influenced:** Autosomal genes

  Baldness, Dominant in males and recessive in females, carrier females have thinner hair

Male-Determining Region SRY on the Y Chromosome



X-Chromosome Inactivation

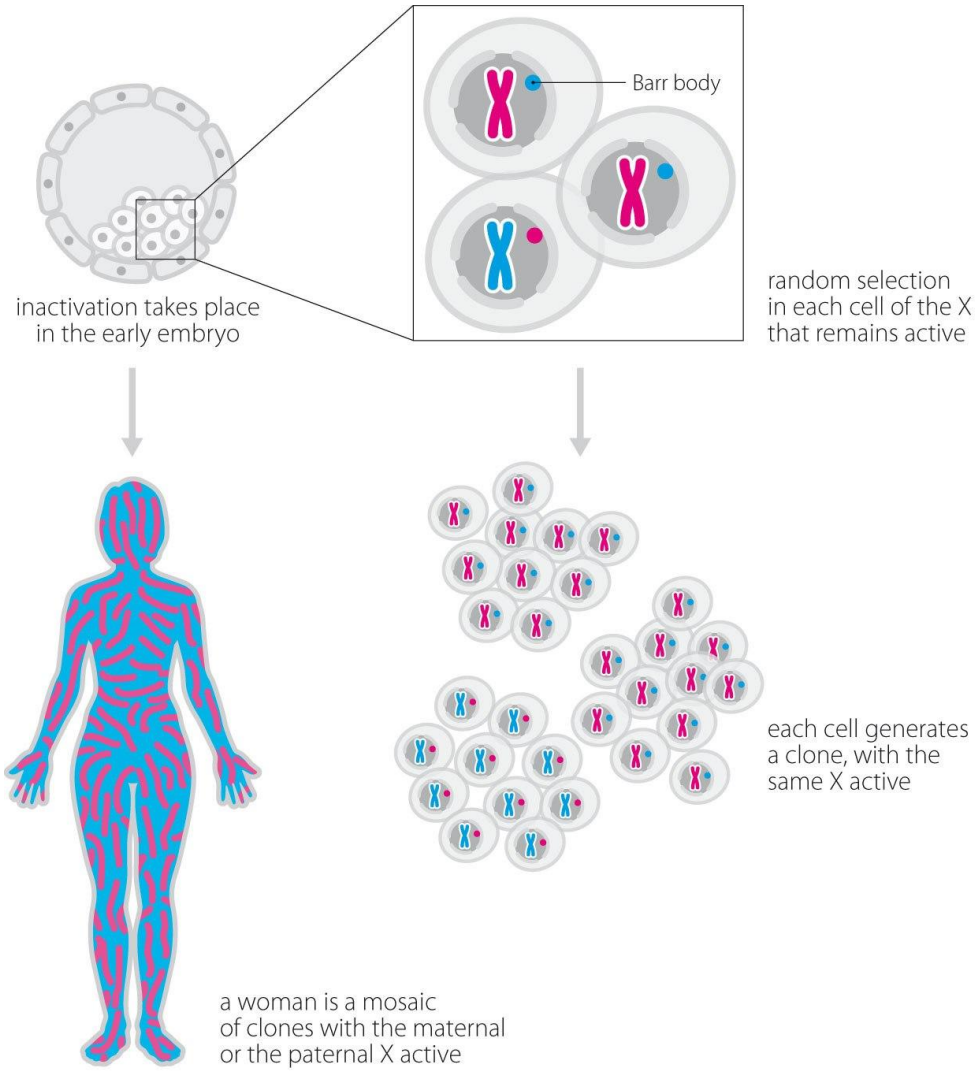
The Lyon Hypothesis of X Inactivation

- Proposed by Mary Lyon and Liane Russell (1961)

- Which X is inactivated? Inactivation of X chromosome occurs randomly in somatic cells during embryogenesis

- Progeny of cells all have same inactivated X chromosome as original, creating mosaic individual

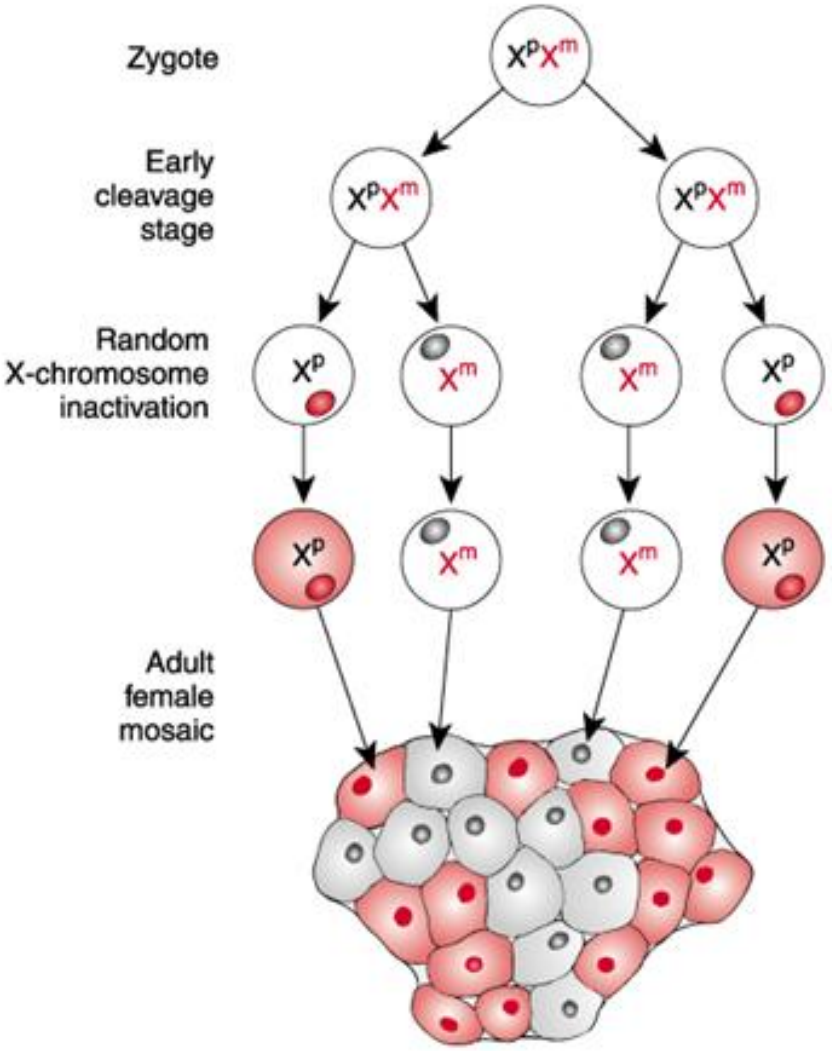
X-inactivation is an epigenetic process.



- Because of X-inactivation every female is a mosaic of cell lines with different active X chromosomes
- Early in the development of female, one **X**-chromosome is inactivated at random **(7-10 days after fertilization)**
- Zygout around 24 cell

X - Inactivation

- The Lyon hypothesis states that one X chromosome in the cell is randomly inactivated early in the embryonic development of females
- Inactivation results in 'dosage compensation',
- The X inactivation center is located on Xq 13 (1 Mb). The **XIST** : **X** **I**nactive **S**pecific **T**ranscript. gene is transcribed only from the inactive X - chromosome.

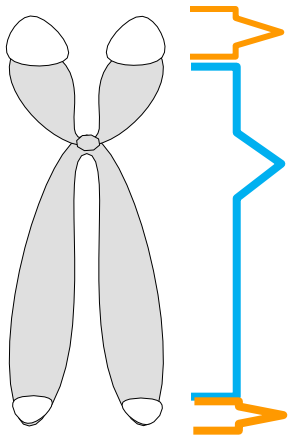


X Chromosome Inactivation

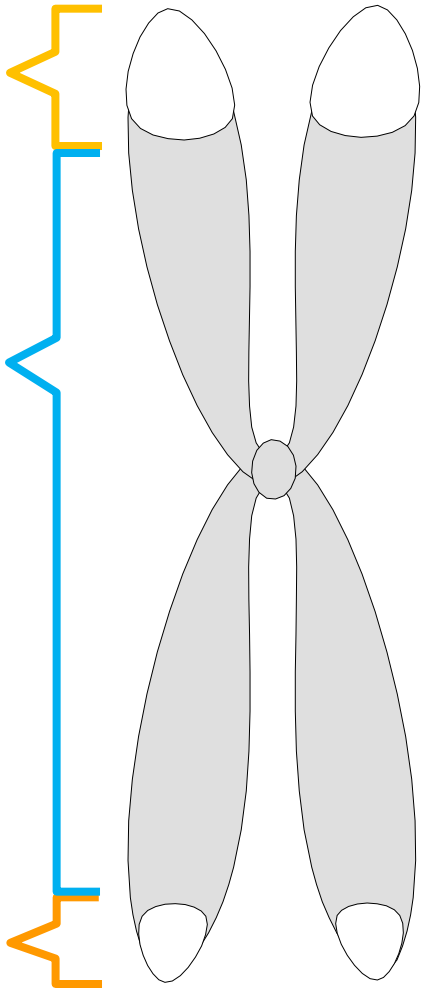
- Mechanism of X Chromosome inactivation

- XIC – X chromosome Inactivation Center
  - XIC controls expression of the *XIST* gene
  - *XIST*: X-inactive-specific transcript
  - *XIST* produces a non-coding 17 kb RNA molecule
  - "Coats" the entire *local* X-chromosome – *cis*-acting

Organization of Human Sex Chromosomes



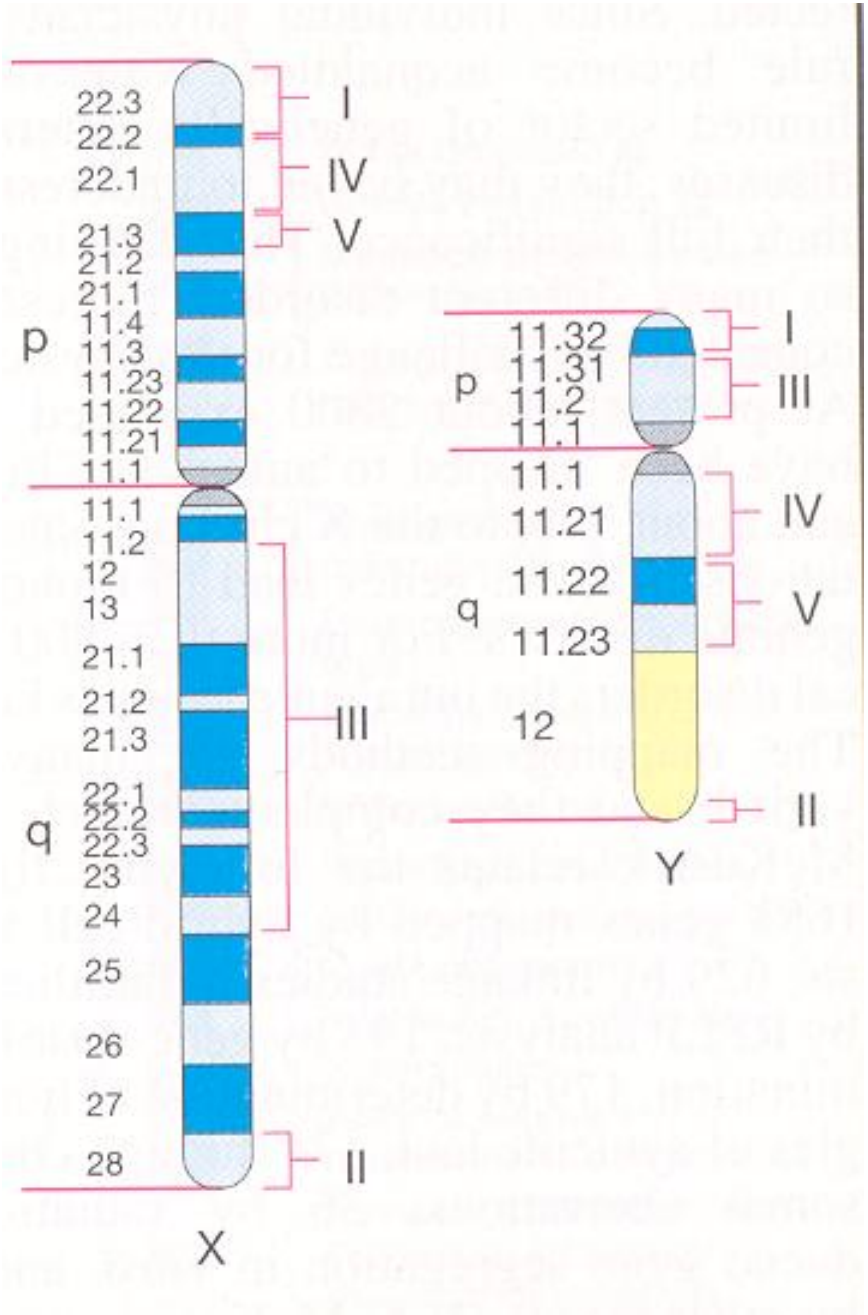
Length: 50,286,555 bp
Gene Count: 160



Many genes escape inactivation

Xce – X chromosome inactivation center

Length: 153,692,391 bp
Gene Count: 1228

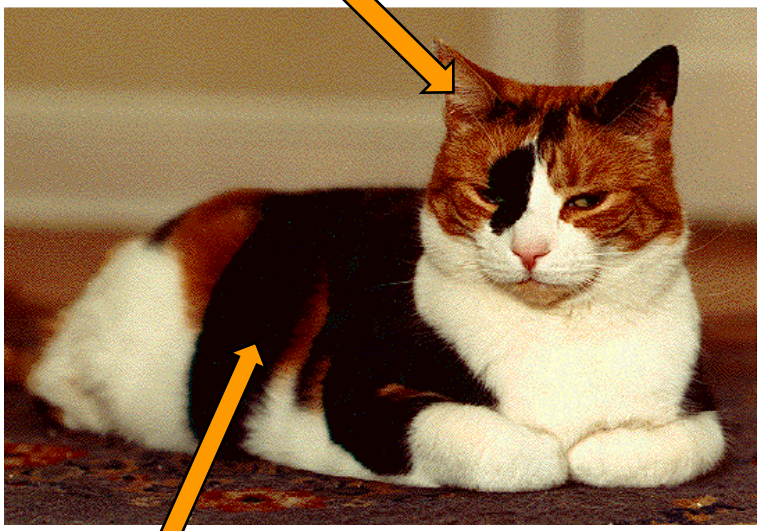


Sequence Homologies of the X and Y Chromosomes

- 15% ox X Chr. Escape Inactivation
- Tips of P and q arms escape inactivation
- Steroid sulfatase
- Xg blood group
- Kallman Syndrome (hypogonadism inability to perceive odor)
- Housekeeping genes

Mosaicism Reveals the Random Inactivation of one X chromosome

X^b active



X^B active

- G6PD
- Melanine
- *Barr Bodies*

Anhidrotic Ectodermal Dysplasia Calico Cat Fur Color

Regions where sweat glands are absent.

Non-Traditional Types of Gene Disorders (NTGD)

Classification of genetic disorders

- Chromosomal
- Single gene
  - Autosomal recessive
  - Autosomal dominant
  - X-linked recessive
  - X-linked dominant
- Nontraditional GD
- Multifactorial
- Somatic mutations (cancer)

Non-Traditional Types of Gene Disorders (NTGD)

- Mosaciasm
- Imprinting
- Trinucleotide expansion
- Uniparental Disomy
- Mitochondrial
- Fragile X Syndrome

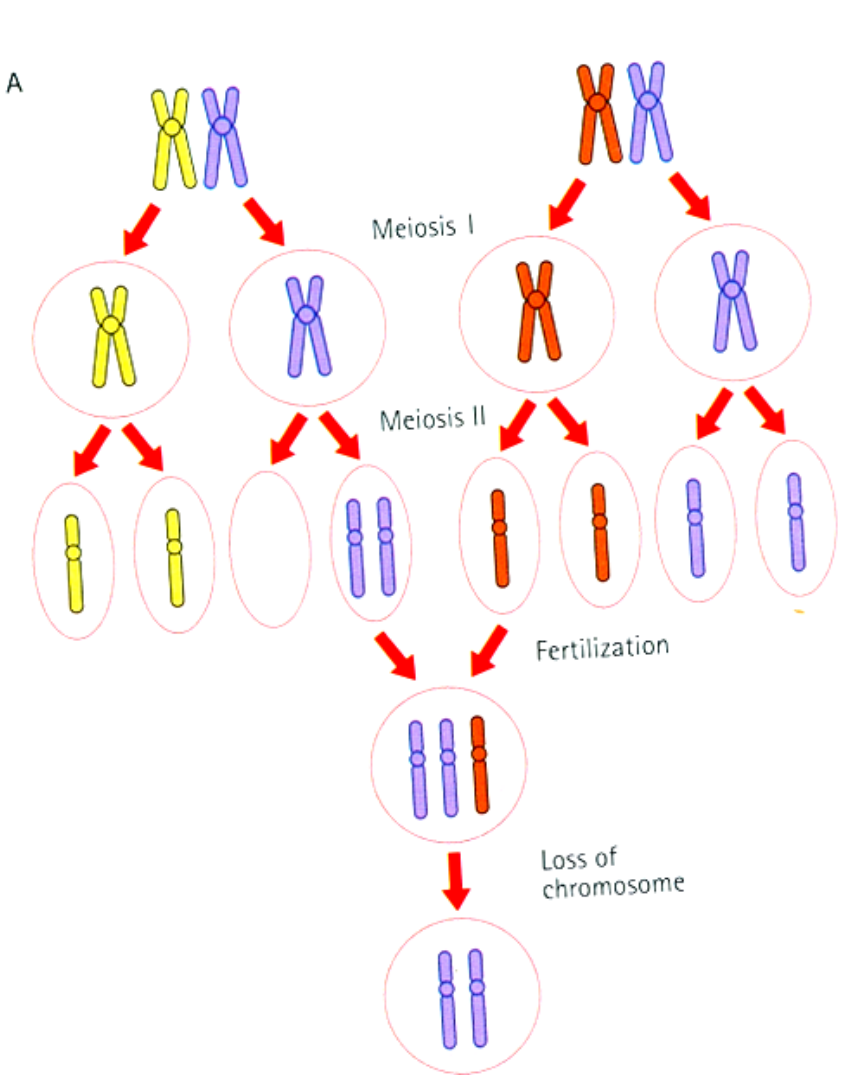
Uniparental Disomy

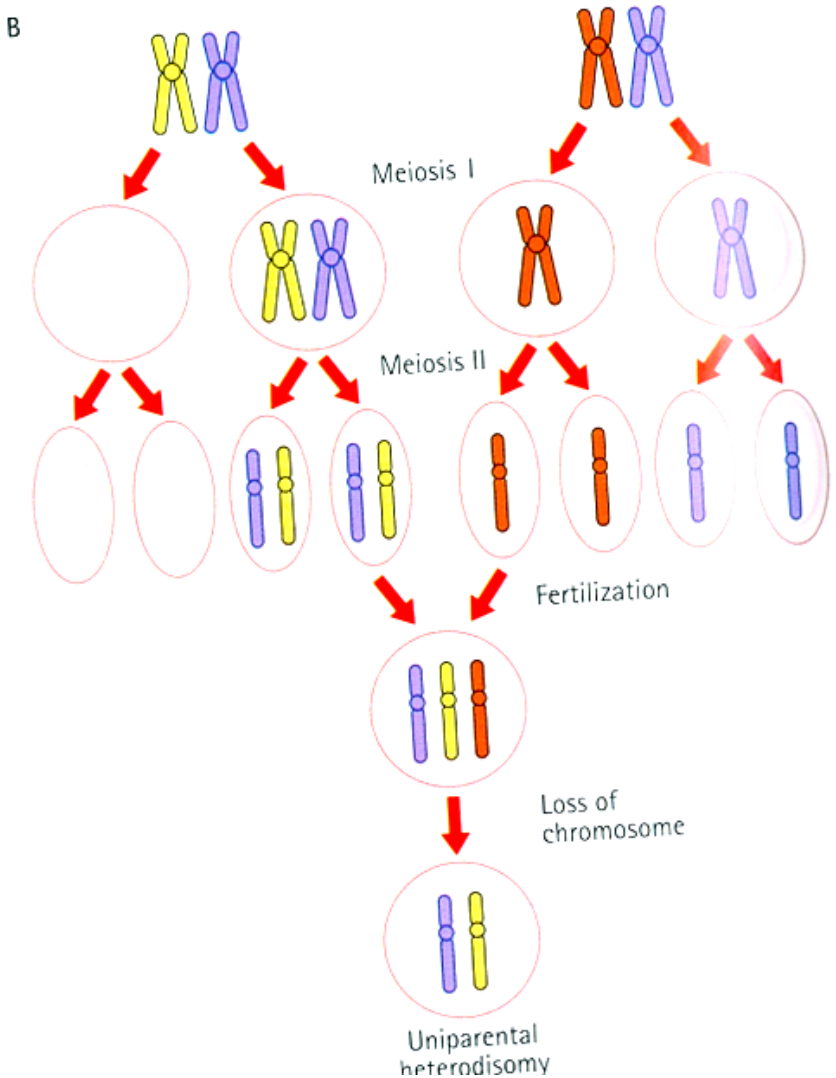
- **Uniparental disomy** (UPD) is defined as the presence of two homologous chromosomes inherited in part or in total from only one parent.
- This means that one parent has contributed two copies of a chromosome and the other parent has contributed no copies.
- The incidence of UPD is estimated to be as high as 2.8 to 16.5 per 10,000 conceptions.

- **Isodisomy:** If the parent passed on two copies of the same chromosome (as results from non-disjunction in meiosis II).

- **Heterodisomy**. If the parent provides one copy of each homolog (as results from non-disjunction in meiosis I),

Uniparental Disomy



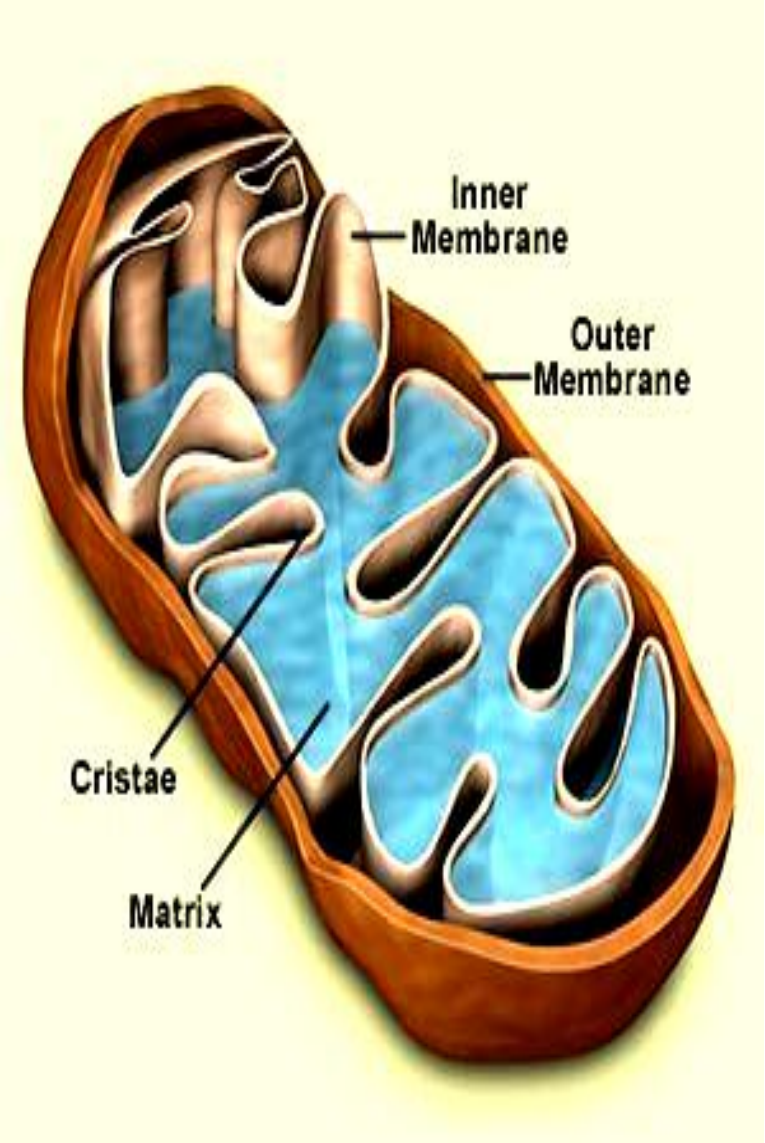


Examples

- Cases of PWS & AS
- Two CF patients with short stature, inherited two identical copies of most or all of their maternal chr. 7. In both cases, the mother happened to be a carrier for CF
- Father-to-son transmission of hemophilia, affected boy inherited both X & Y from father
- Expression of X-linked in homozygous form in a female offspring of a carrier mother and a normal father

MITOCHONDRIAL GENETICS

Mitochondrion



- A cellular organelle probably of endosymbiotic origin that resides in the cytosol of most nucleated (eurkaryotic) cells.
- This organelle produces energy by oxidising organic acids and fats with oxygen by the process of **oxidative phosphorylation** and generates oxygen radicals (reactive oxygen species ROS)as a toxic by-product
- Contains small circular DNA.
- No crossing over or DNA repair.
- Many copies of the mitochondrial genome per cell.
- 37 genes, no histones, no introns.
- Maternal inheritance

Mitochondrial Inheritance

- Each cell contains hundreds of mitochondria, each of which contains multiple copies of a 16.5 Kb circular DNA molecule.
- The entire human mitochondrial chromosome has been cloned and sequenced.
- Oxidative Phosphorolation to produce ATP
- Although most proteins functioning in the mitochondria are encoded by nuclear genes, some are encoded by mitochondrial genes, and mutations can lead to energy failure.

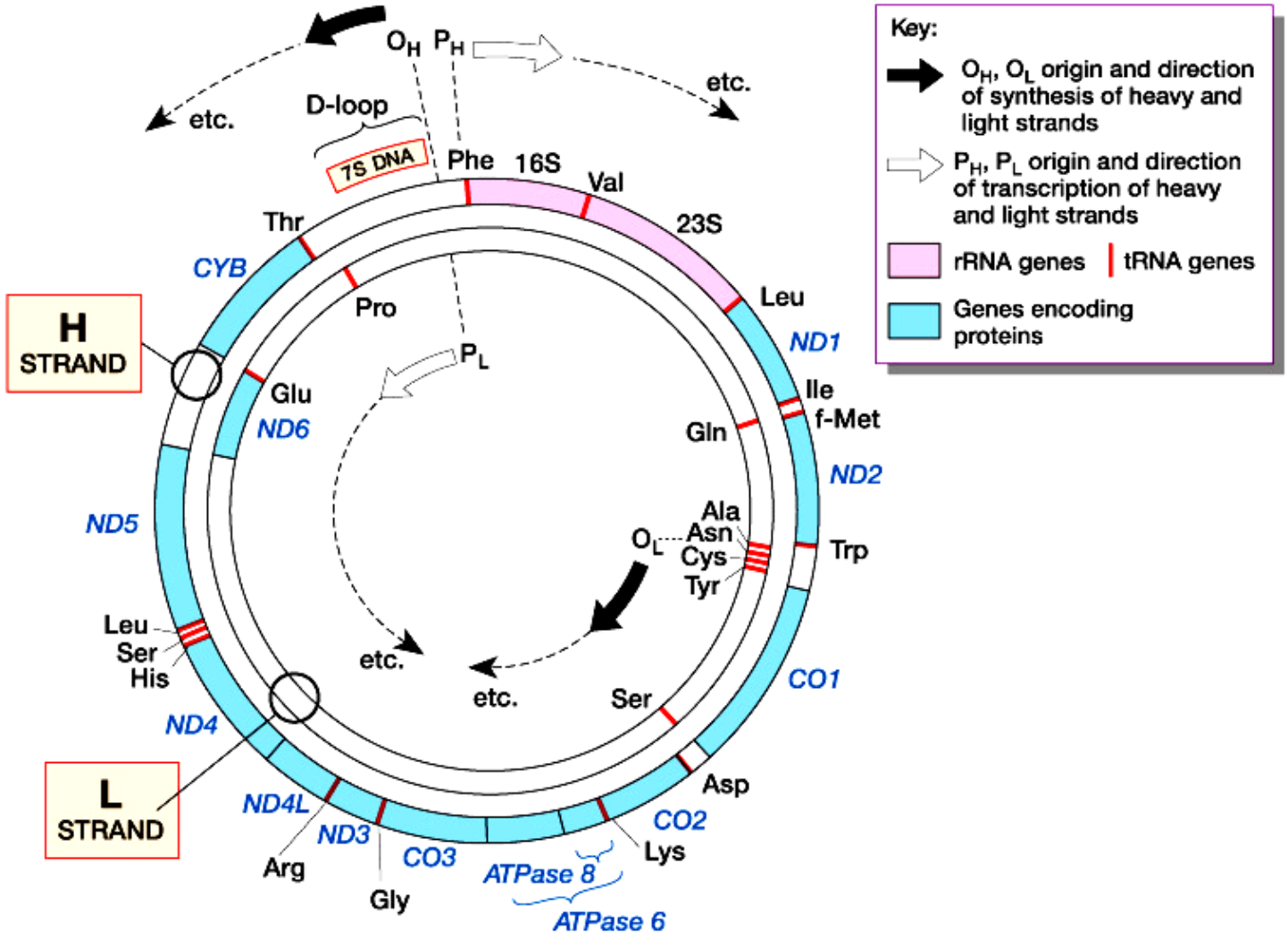


Figure 9-2 Human Molecular Genetics, 3/e. (© Garland Science 2004)

Mt Enzymes

- Mitochondria perform cellular respiration after the cytosolic glycolysis step.
- The enzymes needed, include:

a. Pyruvate dehydrogenase.
b. Electron transport and OP enzymes.
c. Citric acid cycle enzymes.
d. Fatty acid oxidation enzymes

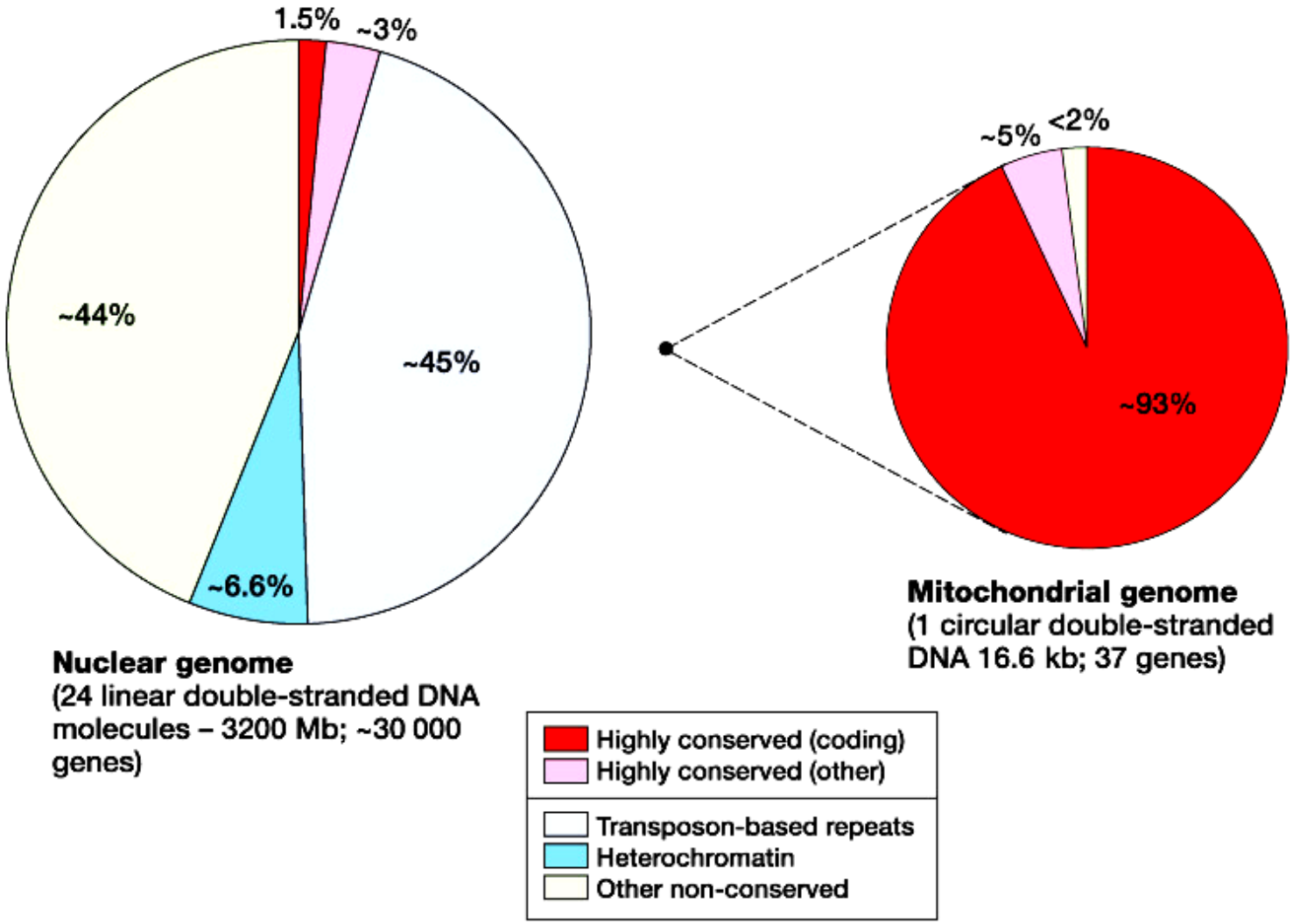


Figure 9-1 Human Molecular Genetics, 3/e. (© Garland Science 2004)

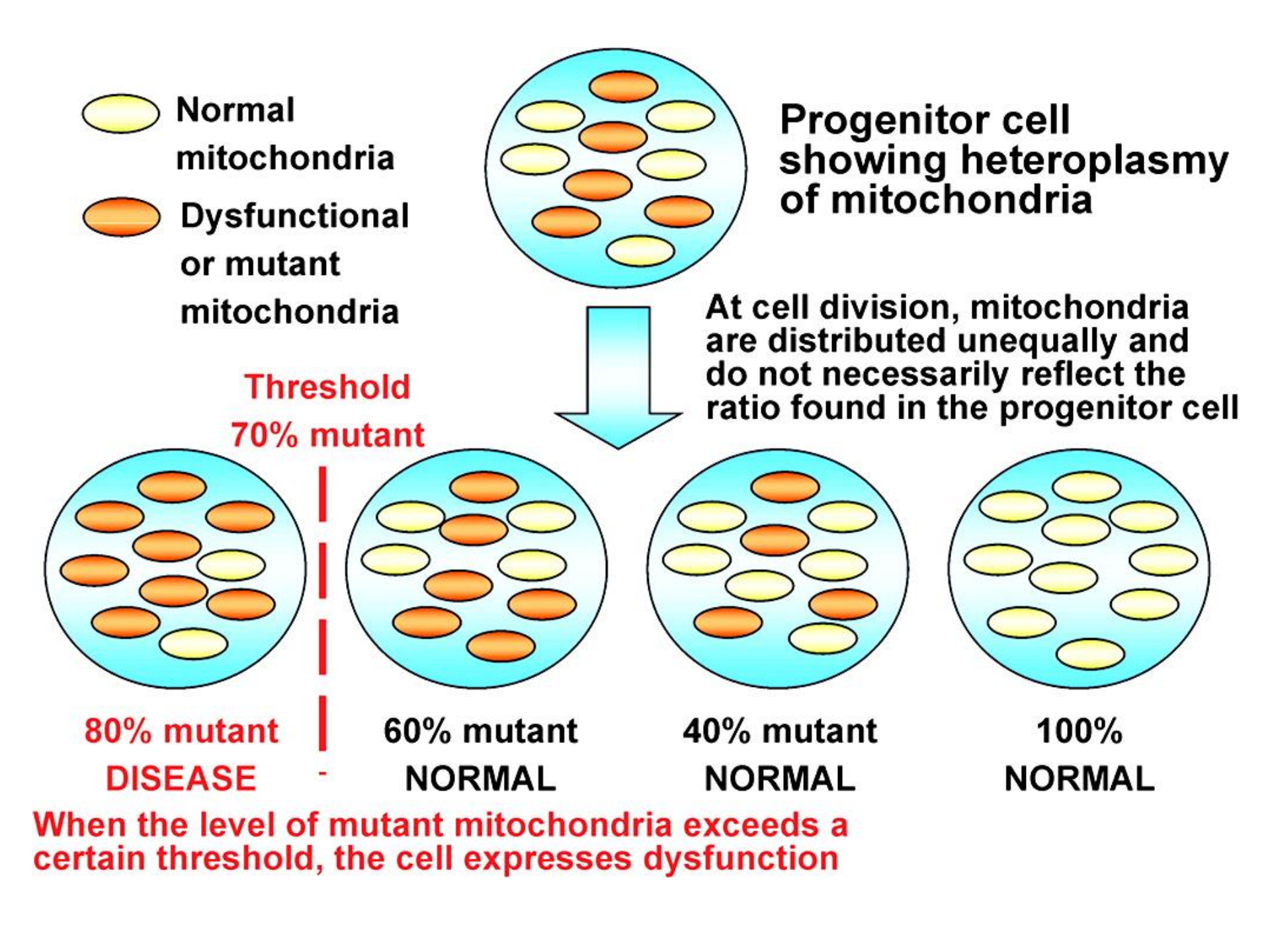
Mitochondrial Inheritance

- In humans, at fertilization, the ovum contributes significantly more cytoplasm to the zygote than does the sperm.
- The sperm mitochondria degenerate upon penetration of the ovum.
- Mitochondria in offspring are exclusively maternal in origin.
- Phenotype results from maternal transmission

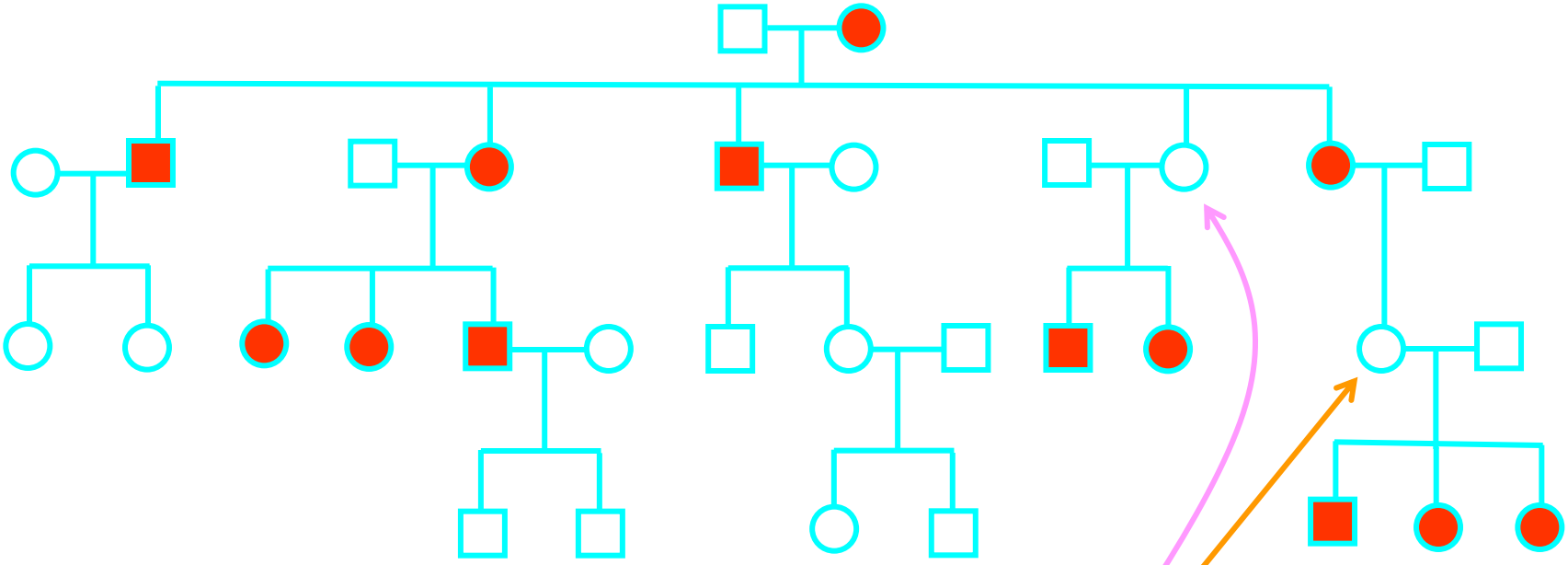
Mitochondrial Inheritance

- Mutations in mitochondrial genes are also the cause of several single gene disorders.

- Mutation rate in mt is 10 times more than in nuclear DNA due to the lack of DNA repair mechanism and free oxygen radicals?


Normal mitochondria
Dysfunctional or mutant mitochondria
Progenitor cell showing heteroplasmy of mitochondria
At cell division, mitochondria are distributed unequally and do not necessarily reflect the ratio found in the progenitor cell
Threshold
70% mutant
80% mutant
DISEASE
60% mutant
NORMAL
40% mutant
NORMAL
100%
NORMAL
When the level of mutant mitochondria exceeds a certain threshold, the cell expresses dysfunction

Mitochondrial inheritance



Complications

- Incomplete penetrance
- Variable expression

Examples of Diseases Due to Mutations and Deletions in Mitochondrial DNA

Abbreviation	MIM No.	Designation
LHON	535000	Leber's hereditary optical neuropathy (Missence M)
MELAS	540000	Mitochondrial encephalomyopathy
	540050	Lactic acidosis with stroke-like signs (Single base M)
MERRF	545030	Myoclonic epilepsy and ragged red fibers (Single base M)
MMC*	590050	Maternally inherited myopathy and cardiomyopathy
NARP*	551500	Neurogenic muscular weakness with ataxia and retinitis pigmentosa
CEOP*	258470	Progressive external ophthalmoplegia
KSS*	530000	Kearns-Sayre syndrome (ophthalmoplegia, pigmental degeneration of the retina, and cardiomyopathy)
PEAR*	557000	Pearson syndrome (bone marrow and pancreatic failure)
ADMIMY*	157640	Autosomal dominant inherited mitochondrial myopathy with mitochondrial deletion in the D loop (type Zeviani)

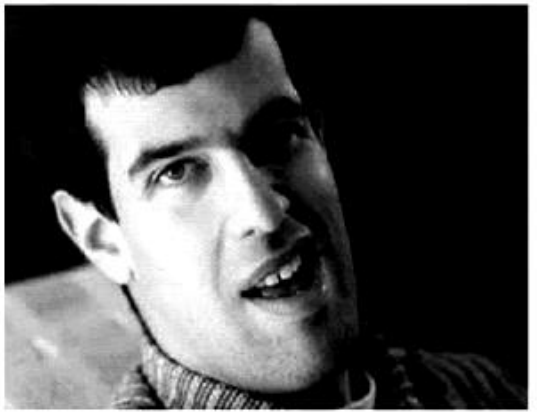
FRAGILE S SYNDROME

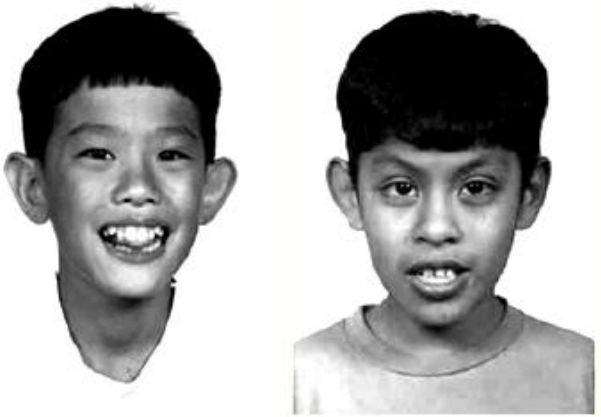
Fragile X Syndrome

- The most common cause of inherited mental retardation (MR).
- Second only to Down syndrome as an etiology for MR.
- Incidence of approximately 1 in 4000 males and 1 in 8000 females
- Found among all ethnic groups and occurs in families with no history of mental retardation
- 1 in 259 women are carriers of the fragile X premutation
  - Only the mother has to be a carrier for the fetus to be at risk for fragile X syndrome

Fragile X Syndrome

- Males:
  - Moderate to severe mental retardation, learning disabilities
  - Long face, prominent ears, macro-orchidism
  - Physical phenotype can be subtle, especially in young boys
  - Hyperactivity, autism (approx. 1/3), hand flapping, hand biting, disordered speech and language
  - males are generally unable to live independently

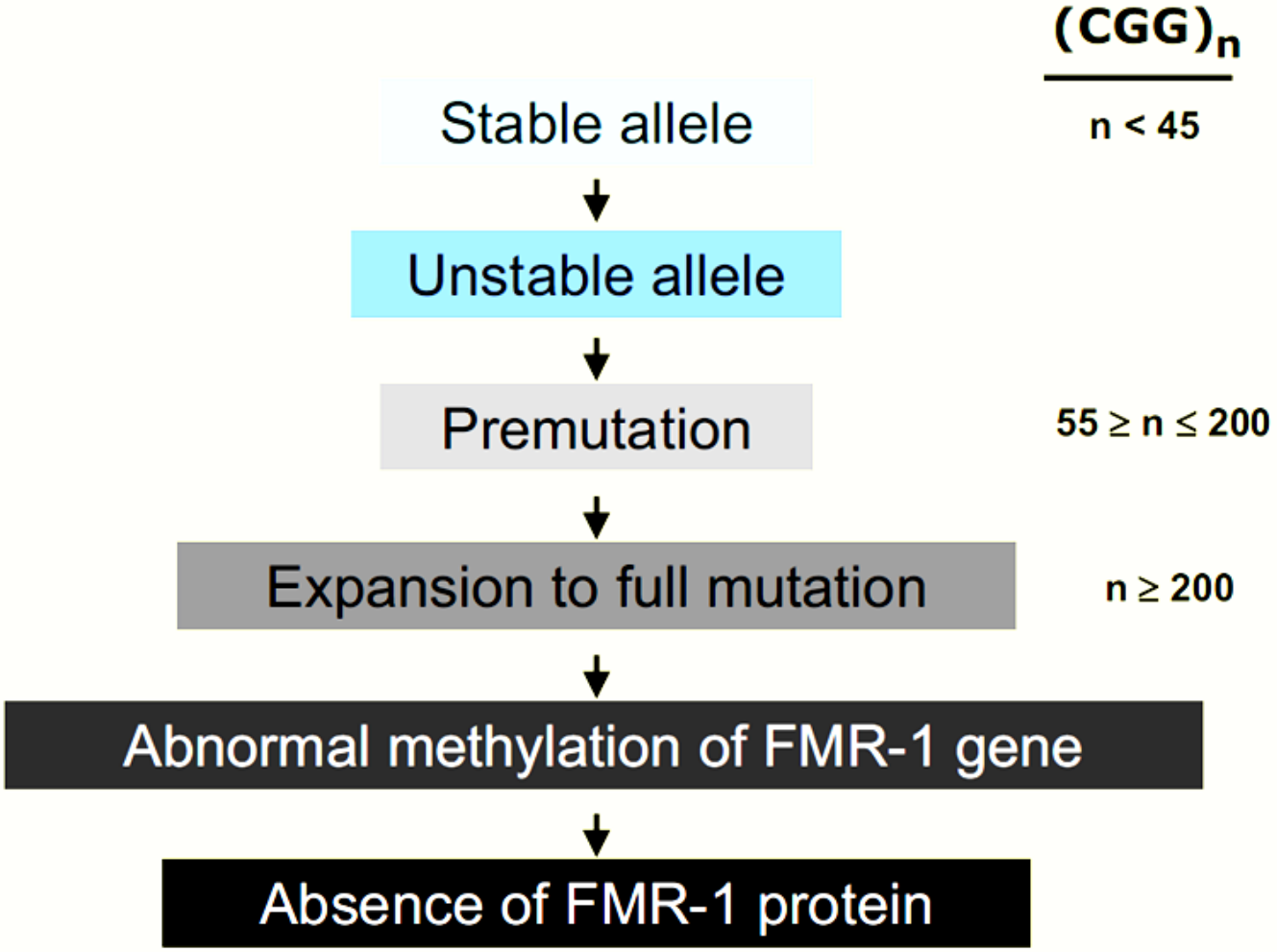




Fragile X Syndrome

- **Females:**
  - Less frequent and less severe in females
  - Mild to moderate mental retardation, learning disabilities
    - About 1/3 of females have significant intellectual disability.
  - Long face, prominent ears (more subtle in females than in males)
  - Poor eye contact, attention problems, shyness and social anxiety

FMR-1 gene: a triplet repeat disease



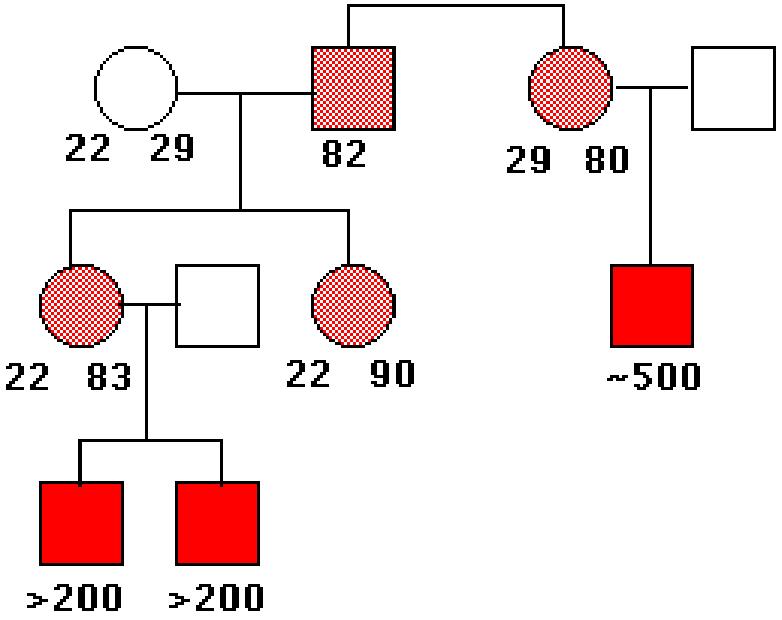
Risk of Premutation Expansion: size of repeat and gender

Maternal Repeat Size	% Of Offspring With a Full Mutation
55-59	3.7%
60-69	5.3%
70-79	31.1%
80-89	57.8%
90-99	80.1%
>100	94-100%

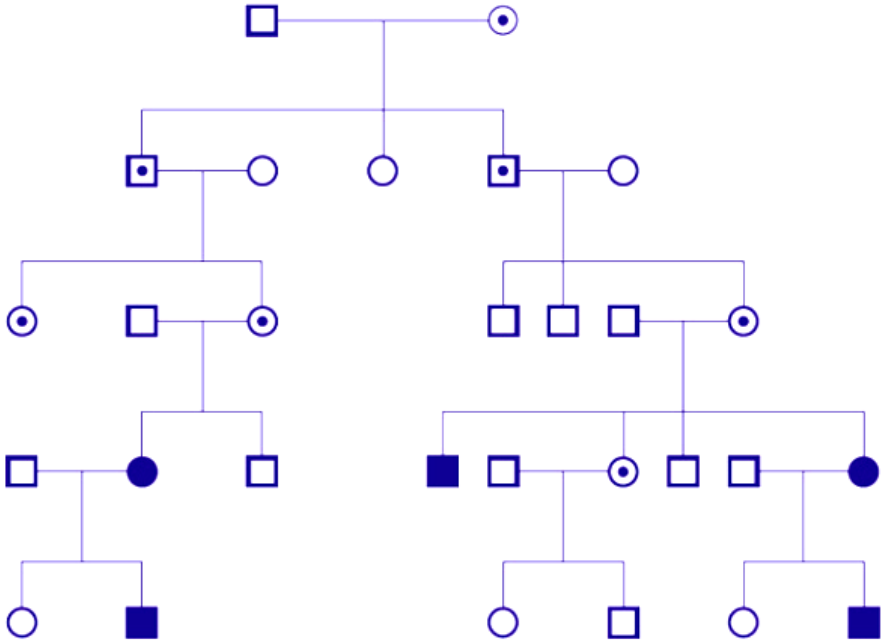
Source: Nolin et al., 2003

Genetic Anticipation Explained

A Fragile X family

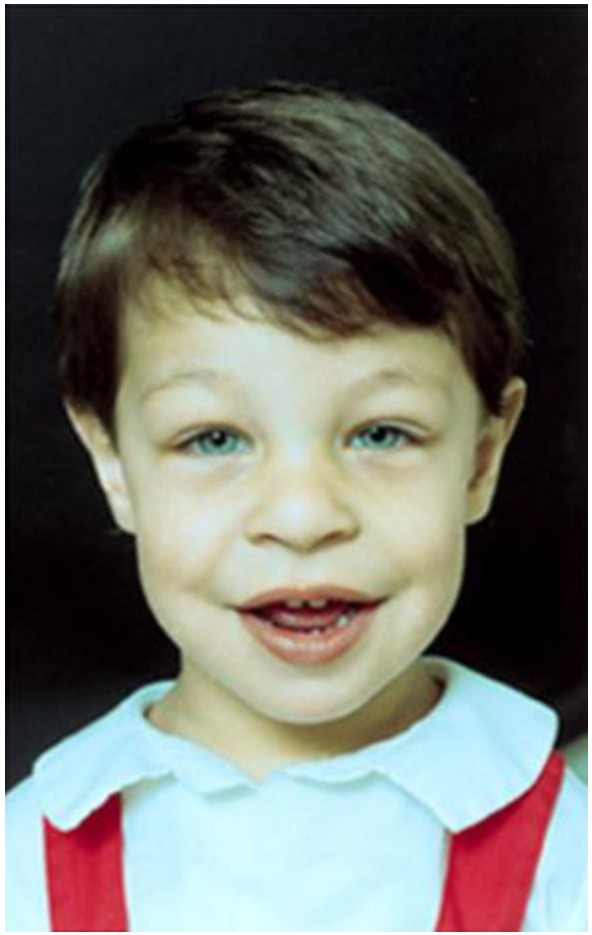


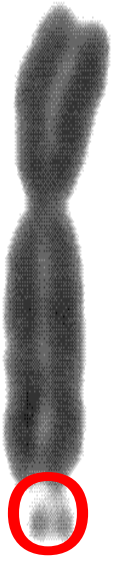
Fragile X syndrome has a complicated inheritance

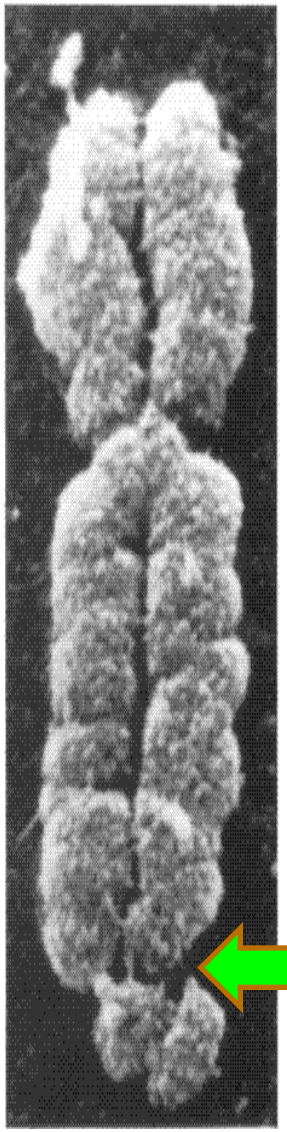


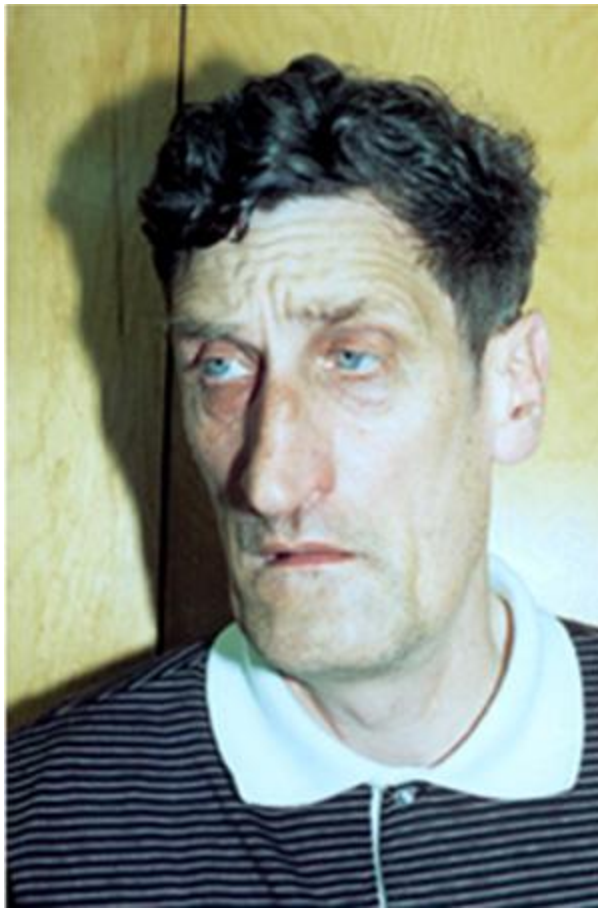
- Progressive increase in size of CGG repeat
- Requires a female transmission to go to full mutation

FRAGILE X SYNDROME









Fragile Site

Rules of Inheritance

Autosomal Recessive

- Appears in both sexes with equal frequency
- Trait tend to skip generations
- Affected offspring are usually born to unaffected parents
- When both parents are hetzyg. ~1/4 of the progeny will be affected
- Appears more frequently among the children of consanguine marriages

Autosomal Dominant

- Appears in both sexes with equal frequency
- Both sexes transmit the trait to their offspring
- Does not skip generations
- Affected offspring must have an affected parent unless they posses a new mutation
- When one parent is affected (het.) and the other parent is unaffected, ~ 1/2 of the offspring will be affected
- Unaffected parents do not transmit the trait

Mitochondrial

- Trait is inherited from mother only
- All children of a mother are at risk to be affected or carriers
- An individual will be affected with a mitochondrial disorder if the percentage of mitochondria possessing mutated mtDNA reaches a threshold value beyond which the normal mtDNA does not compensate for the mutated mtDNA.

X-Linked Dominant

- Both males and females are affected; often more females than males are affected
- Does not skip generations. Affectd sons must have an affected mother; affected daughters must have either an affected mother or an affected father
- Affected fathers will pass the trait on to all their daughters
- Affected mothers if heterozygous will pass the trait on to 1/2 of their sons and 1/2 of their daughters

X-Linked Recessive

- More males than females are affected
- Affected sons are usually born to unaffected mothers, thus the trait skips generations
- Approximately 1/2 of carrier mothers' sons are affected
- It is never passed from father to son
- All daughters of affected fathers are carriers

Y-Linked Dominant

- Only males are affected
- It is passed from father to all sons
- It does not skip generations

Extra Slide

- It turns out that Mendel's laws apply to all of the genes encoded by chromosomes in the nucleus
- But it turns out that a few additional traits are due to DNA sequences found in other organelles, namely the mitochondria and the chloroplasts
- Mitochondria and chloroplasts are thought to have arisen from a bacterial precursor that was internalized by a cell and whose presence was maintained by a sybiotic relationship - bact cell made energy but got what it needed from the rest of the cell
- Both of these plastids have their own chromosomes (circular) that encode cellular genes, many of which are utilized by the organelle.
- It turns out that the pattern of inheritance from these genes does not follow a Mendelian pattern
- In fact in most cells all mitochondria are inherited from their mother (think about the big egg and the little sperm)