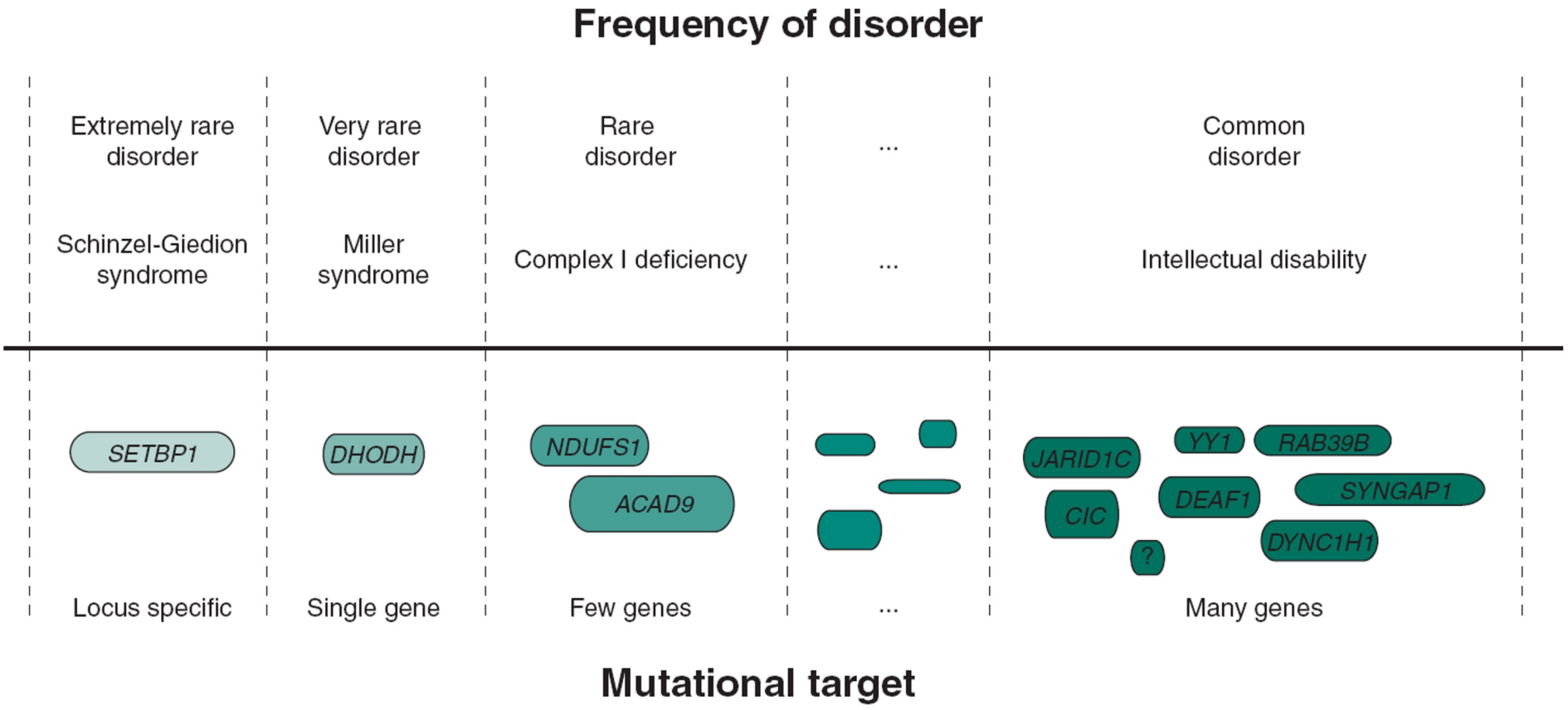
Disease prevalence and genetic model



From: Gilissen *et al. Genome Biology 2011,* ***12:228***

Many human diseases are caused by mutations in single genes

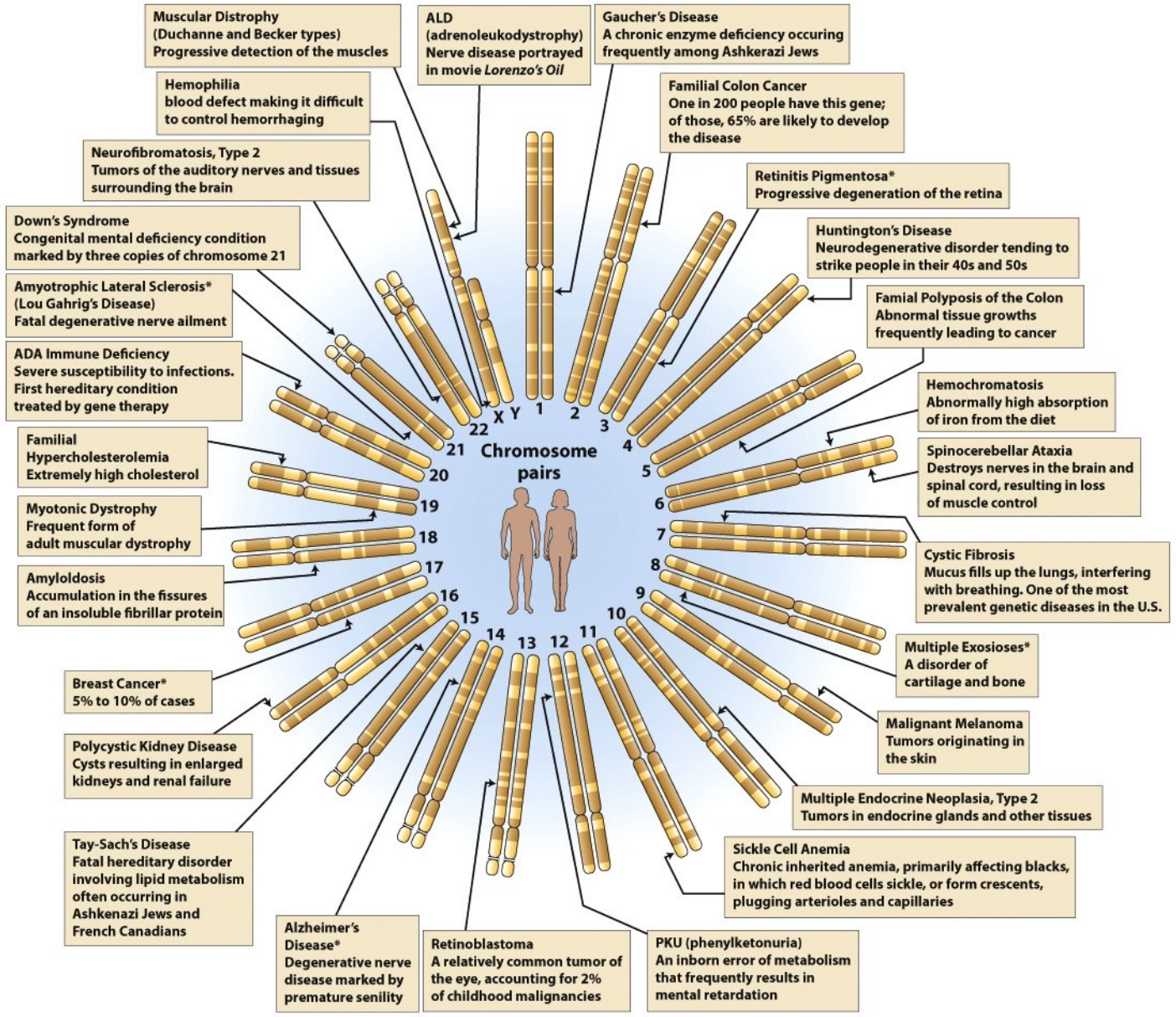


Figure 1-17
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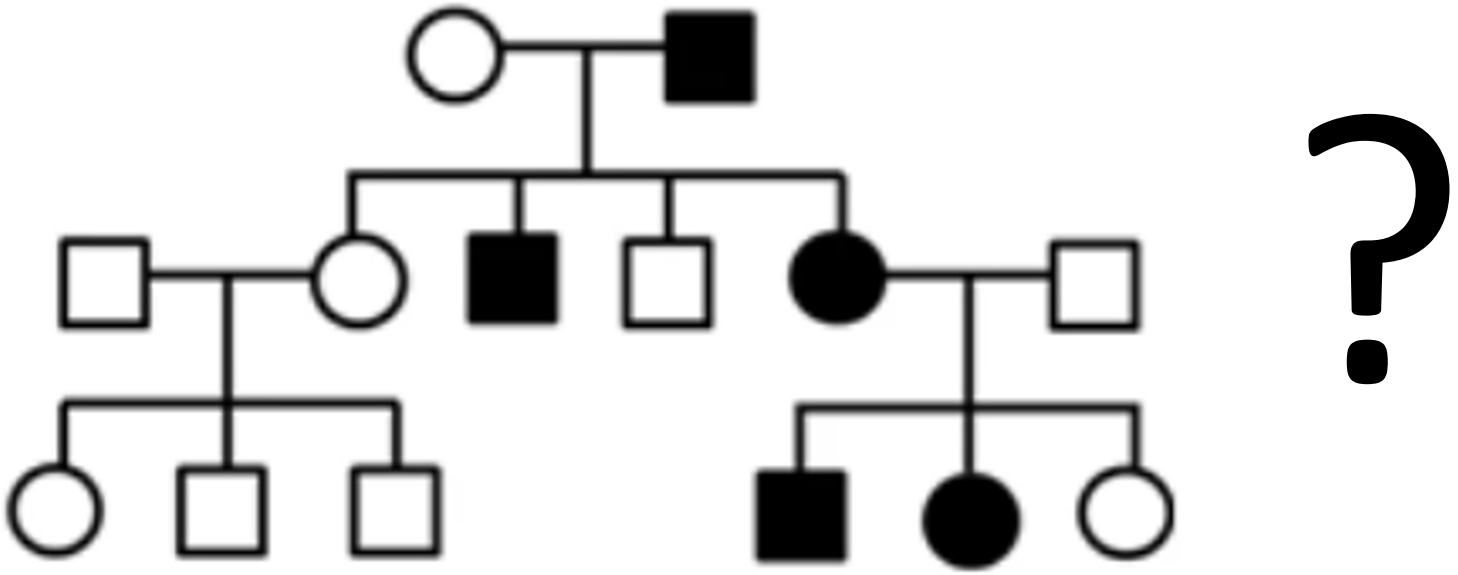


Pedigree symbols

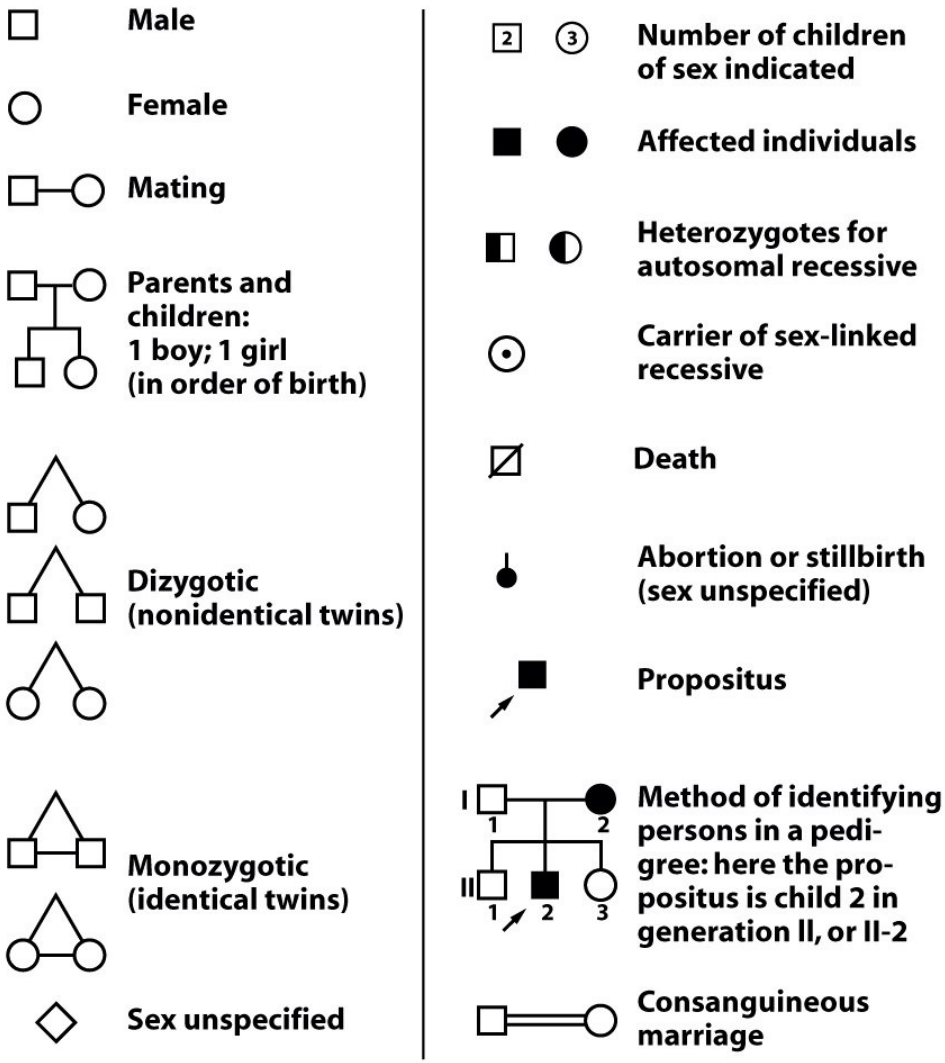


Figure 2-20
Introduction to Genetic Analysis, Tenth Edition

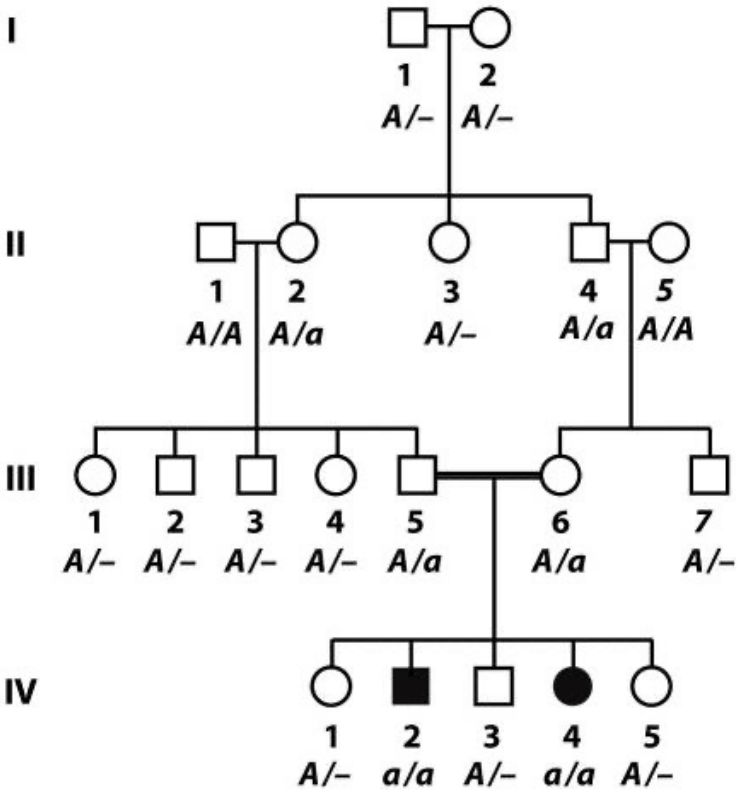
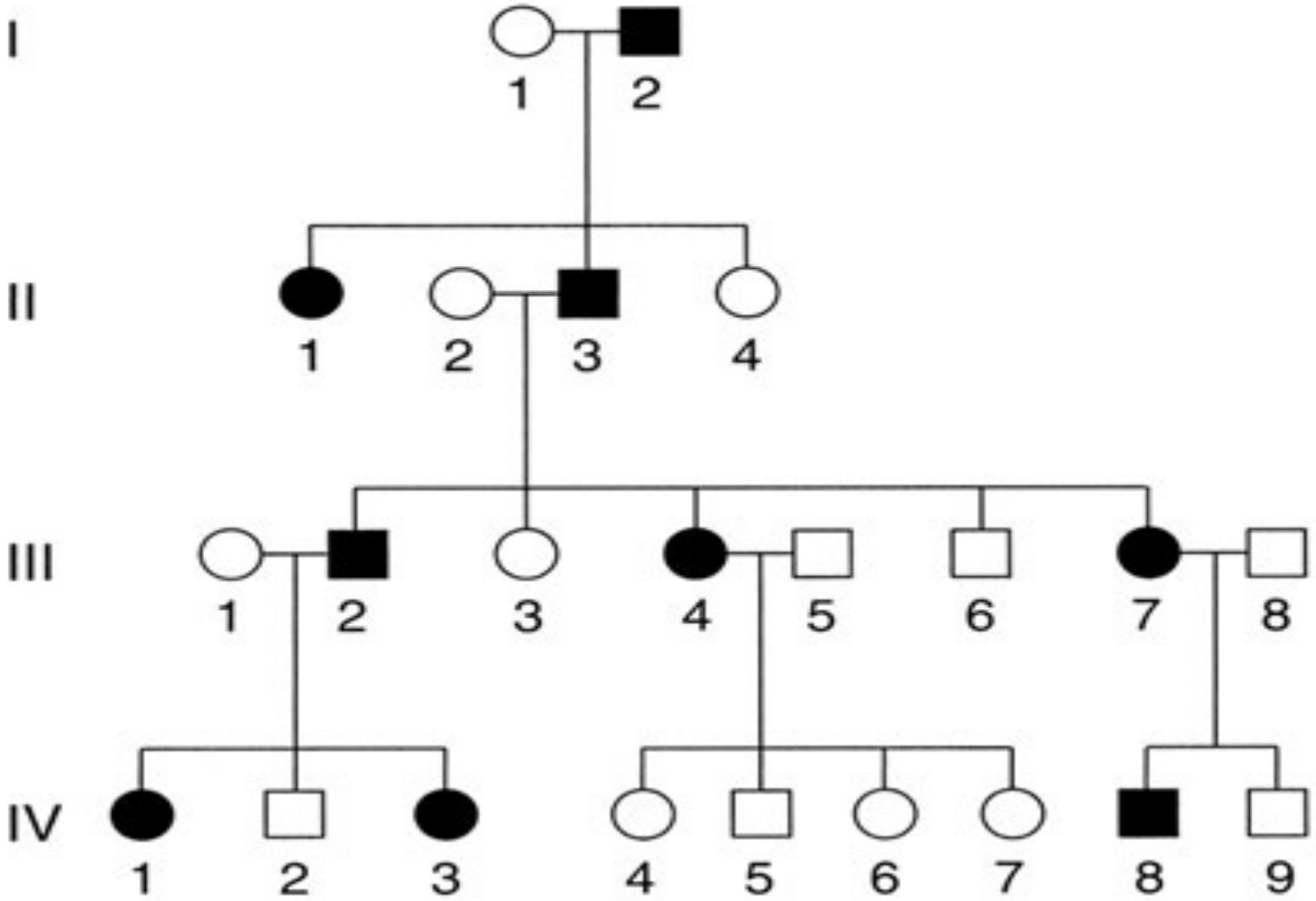


Figure 2-29
Introduction to Genetic Analysis, Ninth Edition

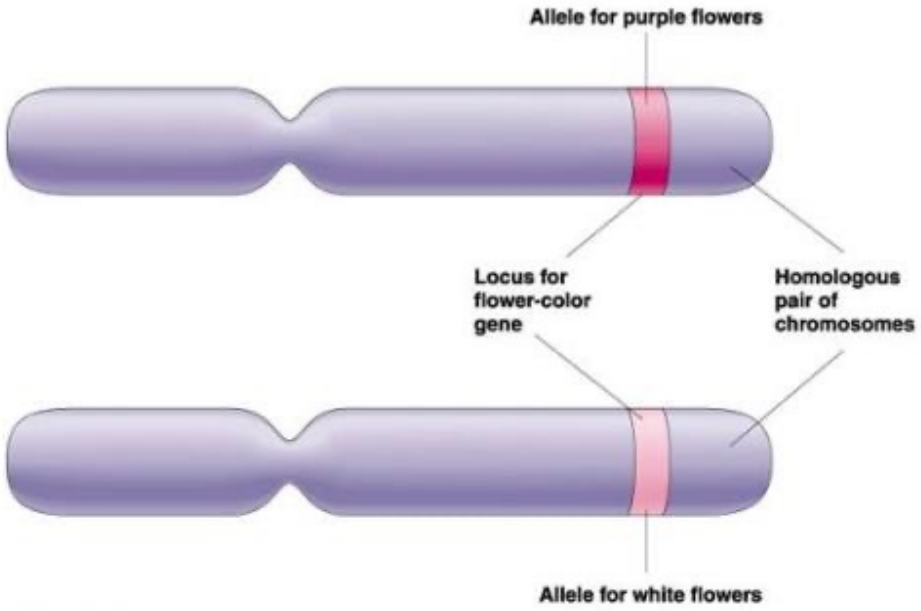

I
1
2
II
1
2
3
4
III
1
2
3
4
5
6
7
8
IV
1
2
3
4
5
6
7
8
9

- **Phenotype**: composite of an organism's observable traits.

- **Genotype**: the genetic makeup of an organism.

Genotype	Set of alleles that an individual possesses
Heterozygote	An individual possessing two different alleles at a locus
Homozygote	An individual possessing two of the same alleles at a locus
Phenotype or trait	The appearance or manifestation of a character

Locus, genes and alleles



Term	Definition
Gene	A genetic factor (region of DNA) that helps determine a characteristic
Allele	One of two or more alternate forms of a gene
Locus	Specific place on a chromosome occupied by an allele

DNA replication is the basis for the perpetuation of life through time

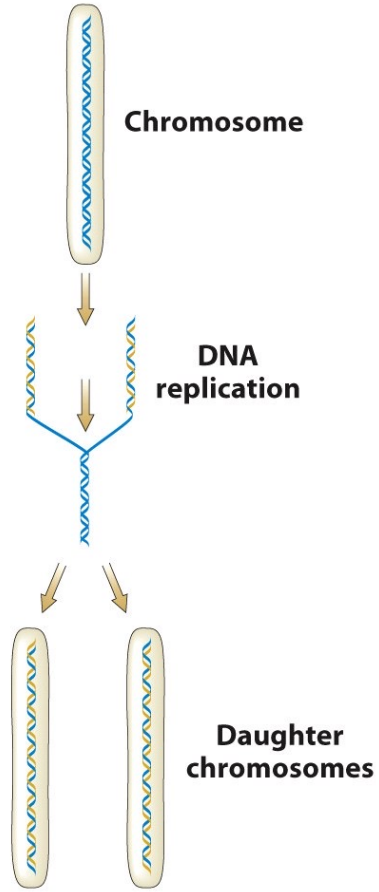


Figure 1-14
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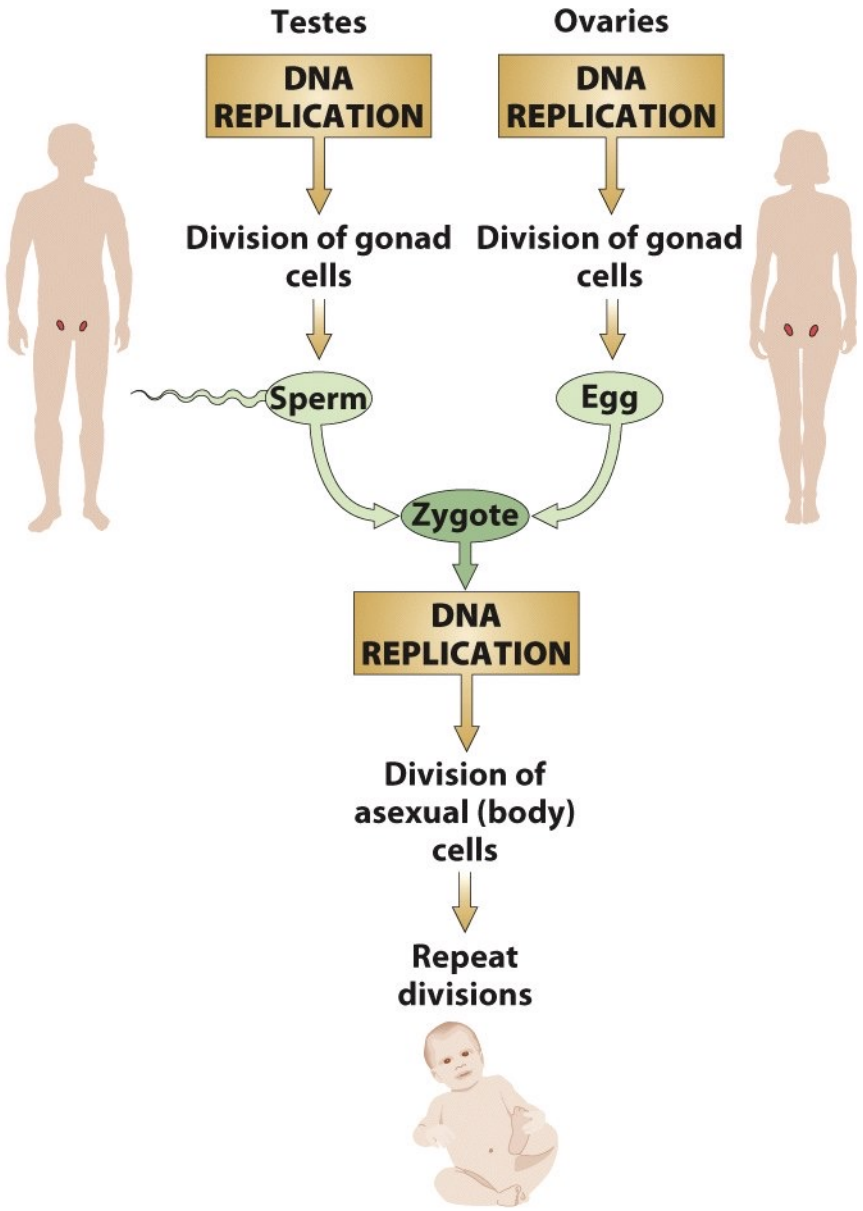

Figure 1-15
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Key stages of meiosis and mitosis

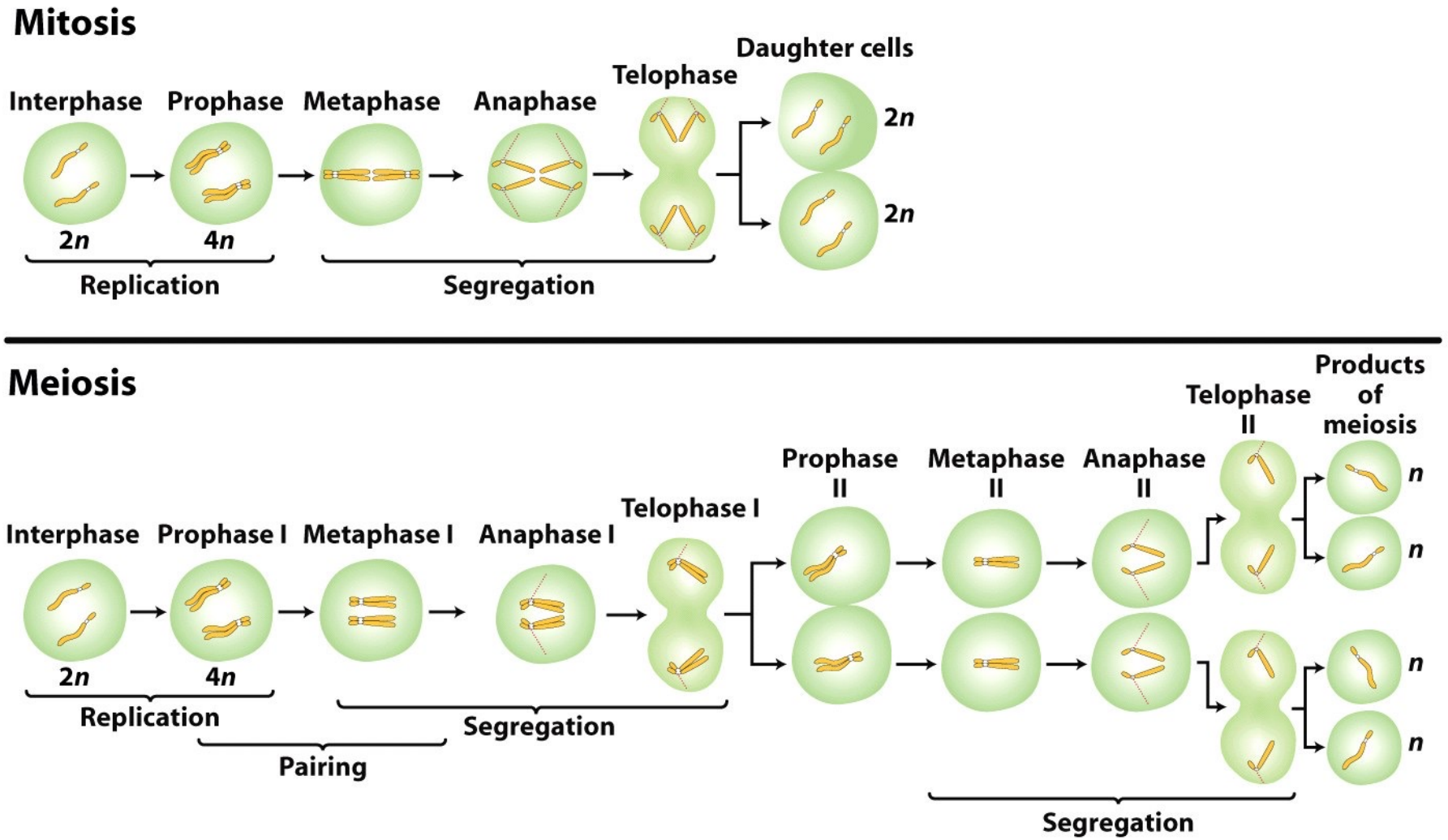

Figure 2-8
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Mendelian Inheritance

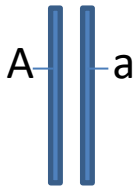
- Law of segregation
  - Every individual contains two alleles for each trait, and during gamete formation this alleles segregate from each other so that each gamete carries only one allele for each gene.

    Offspring receives a pair of alleles for a trait by inheriting homologous chromosomes from the parents.

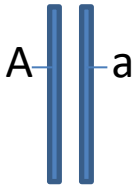
    - Consequence of the chromosomes separation on the first meiotic division.

Law of dominance

- Some alleles are dominant while others are recessive; an organism with at least one dominant allele will display the effect of the dominant allele.



Aa



Aa

Table 5.1 Differences among dominance, incomplete dominance, and codominance

Type of Dominance	Definition
Dominance	Phenotype of the heterozygote is the same as the phenotype of one of the homozygotes
Incomplete dominance	Phenotype of the heterozygote is intermediate (falls within the range) between the phenotypes of the two homozygotes
Codominance	Phenotype of the heterozygote includes the phenotypes of both homozygotes

Genetic disorders with classical Mendelian inheritance

	Dominant	**Recessive**
Autosomal	Autosomal dominant	Autosomal recessive
X-linked	X-linked dominant	X-linked recessive

gametes

	A	a
A	AA	Aa
a	Aa	aa

Autosomal recessive

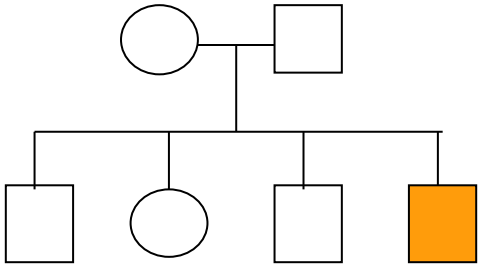
P (healthy) = 3/4
P (affected) = 1/4

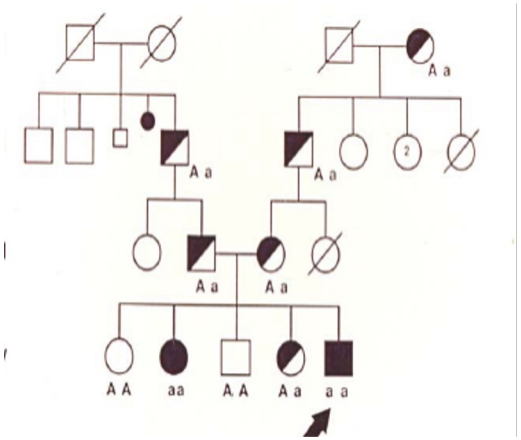
Two possible phenotypes
Three possible genotypes

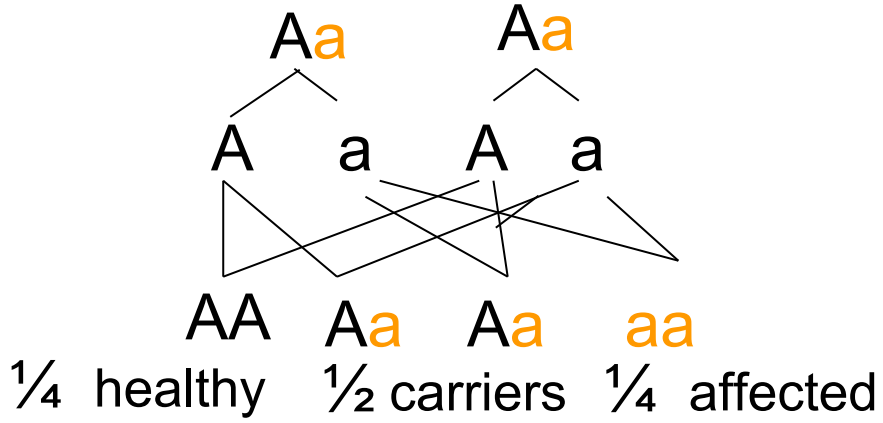
Autosomal recessive inheritance

Two copies of the mutant allele are necessary to produce an increase in risk, or equivalently, one copy of the normal allele is sufficient to provide protection.

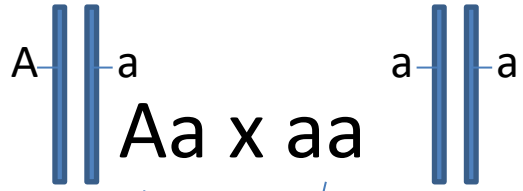
Cystic Fibrosis (Chromosome 17) 1/ 2.000







¼ healthy ½ carriers ¼ affected



gametes

	a	a
A	Aa	Aa
a	aa	aa

Autosomal dominant

P (healthy) = 1/2
P (affected) = 1/2

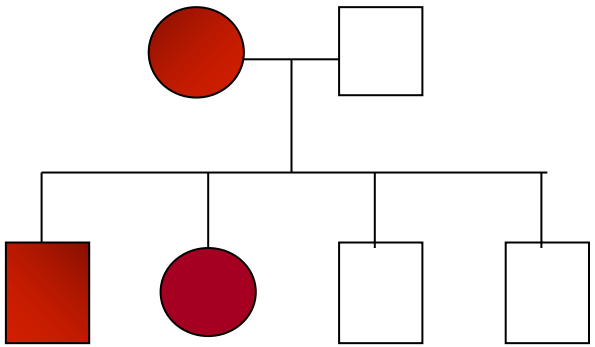
Two possible phenotypes
Two possible genotypes

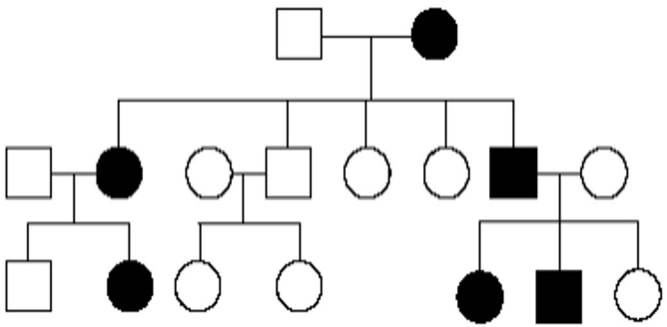
Autosomal dominant inheritance

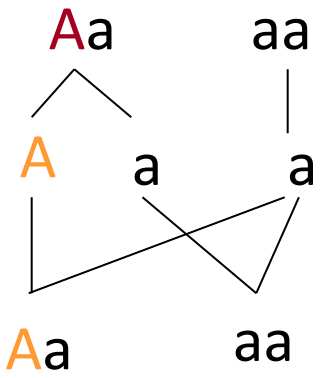
A single copy of the mutant allele is sufficient to produce an increase in risk, and we say A allele is dominant over allele a

Huntington's chorea (Chromosome 4)

1/10.000- 20.000

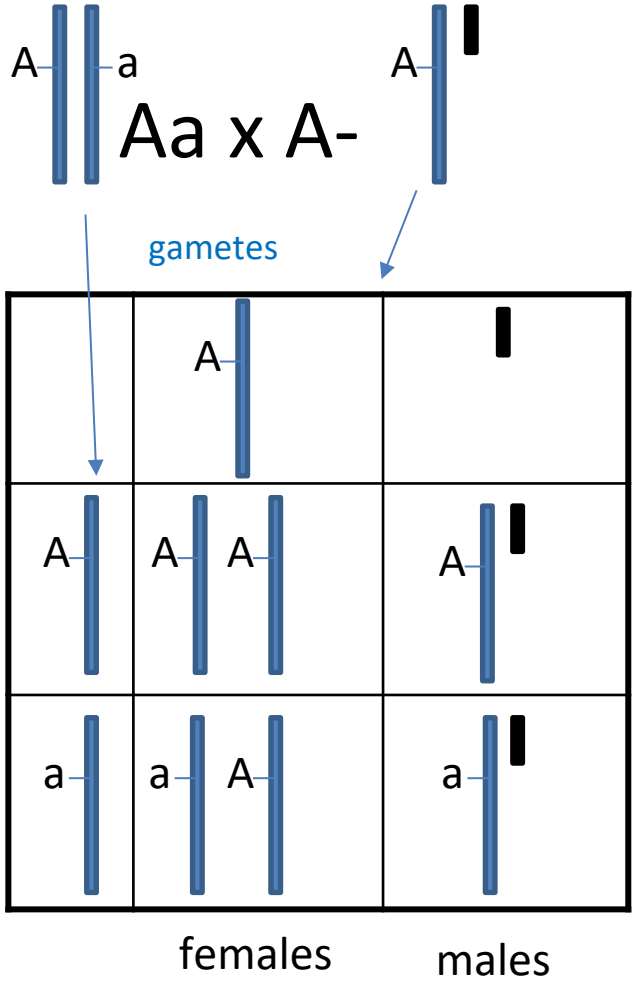






½ affected

½ non-affected



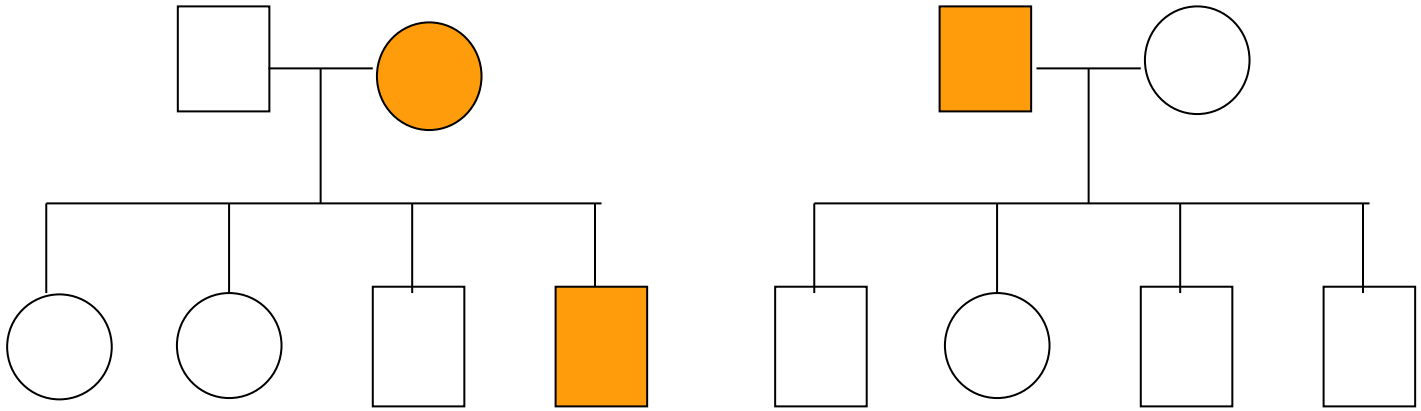
X-linked recessive (carrier female)

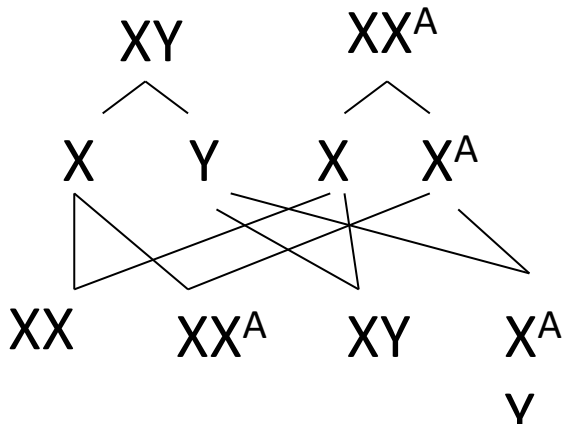
P (healthy, males) = ½
P (affected, males) = ½

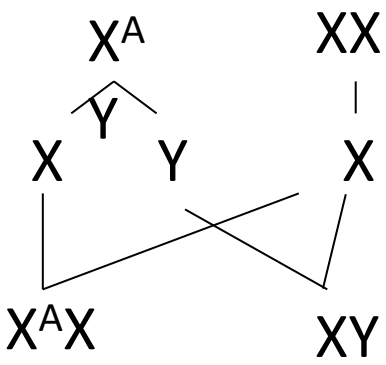
P (healthy, females) = 1
P (affected, females) = 0

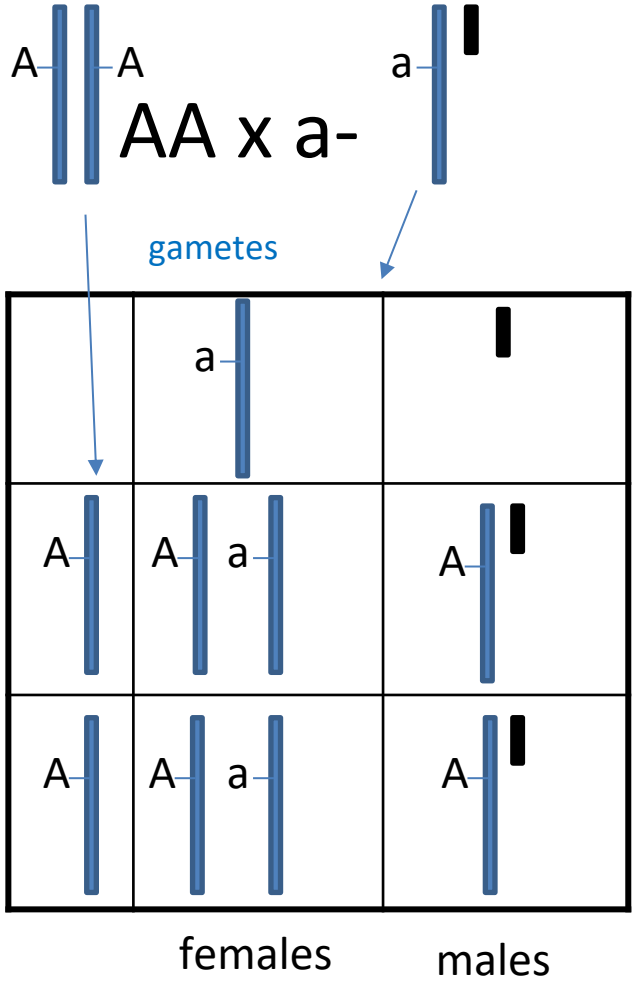
Recessive X-linked inheritance

Duchenne muscular dystrophy (Chromosome X) 1/ 20.000





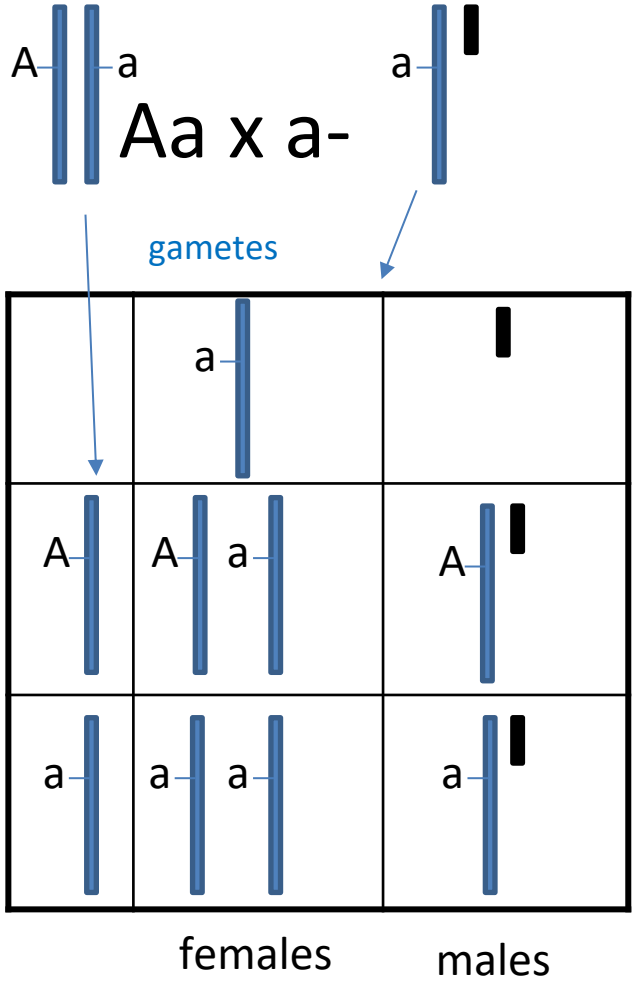




X-linked recessive (affected male)

P (healthy, males) = 1
P (affected, males) = 0

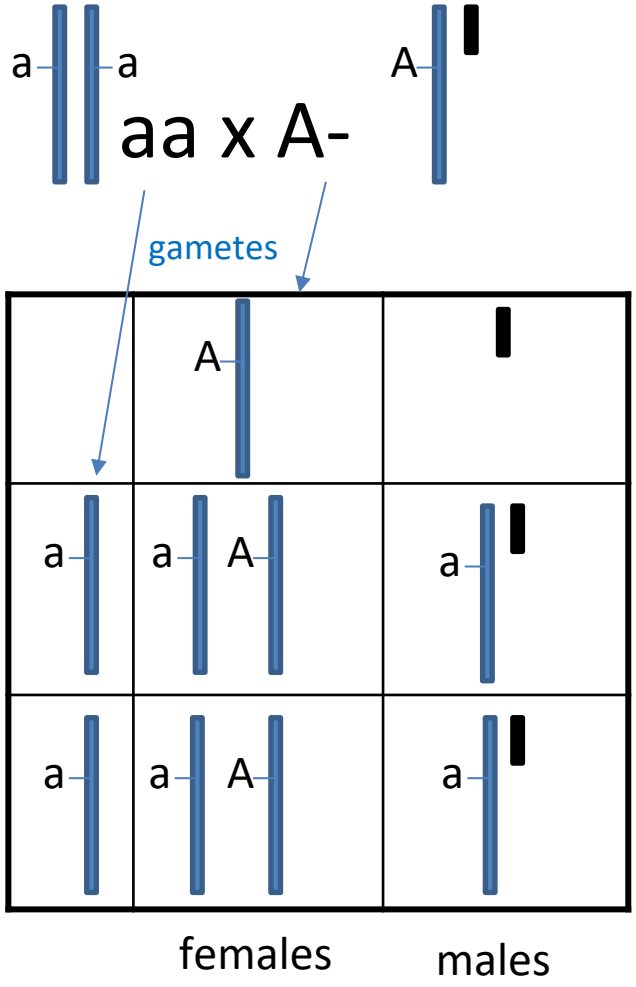
P (healthy, females) = 1
P (affected, females) = 0



X-linked dominant (affected female)

P (healthy, males) = ½
P (affected, males) = ½

P (healthy, females) = ½
P (affected, females) = ½



X-linked dominant (affected male)

P (healthy, males) = 1
P (affected, males) = 0

P (healthy, females) = 0
P (affected, females) = 1

Mendelian pedigree patterns

Autosomal dominant inheritance

An affected person usually has at least one affected parent
Affects either sex.
Transmitted by either sex.
A child of an affected × unaffected mating has a 50% chance of being affected (this assumes the affected parent is heterozygous, which is usually true for rare conditions).

Autosomal recessive inheritanc

Affected people are usually born to unaffected parents.
Parents of affected people are usually asymptomatic carriers.
There is an increased incidence of parental consanguinity.
Affects either sex.
After birth of an affected child, each subsequent child has a 25% chance of being affected.

X-linked recessive inheritance

Affects mainly males.
Affected males are usually born to unaffected parents; the mother is normally an asymptomatic carrier and may have affected male relatives.
Females may be affected if the father is affected and the mother is a carrier, or occasionally as a result of non-random X-inactivation.
There is no male-to-male transmission in the pedigree (but matings of an affected male and carrier female can give the appearance of male to male transmission

X-linked dominant inheritance

Affects either sex, but more females than males.
Females are often more mildly and more variably affected than males.
The child of an affected female, regardless of its sex, has a 50% chance of being affected.
For an affected male, all his daughters but none of his sons are affected.