

Lecture 4

Deviation from Mendel's genetics and Application in Modern science

Chapter 14

Chromosomal basis of inheritance & its application in Medicine

Chapter 15

Degrees of Dominance

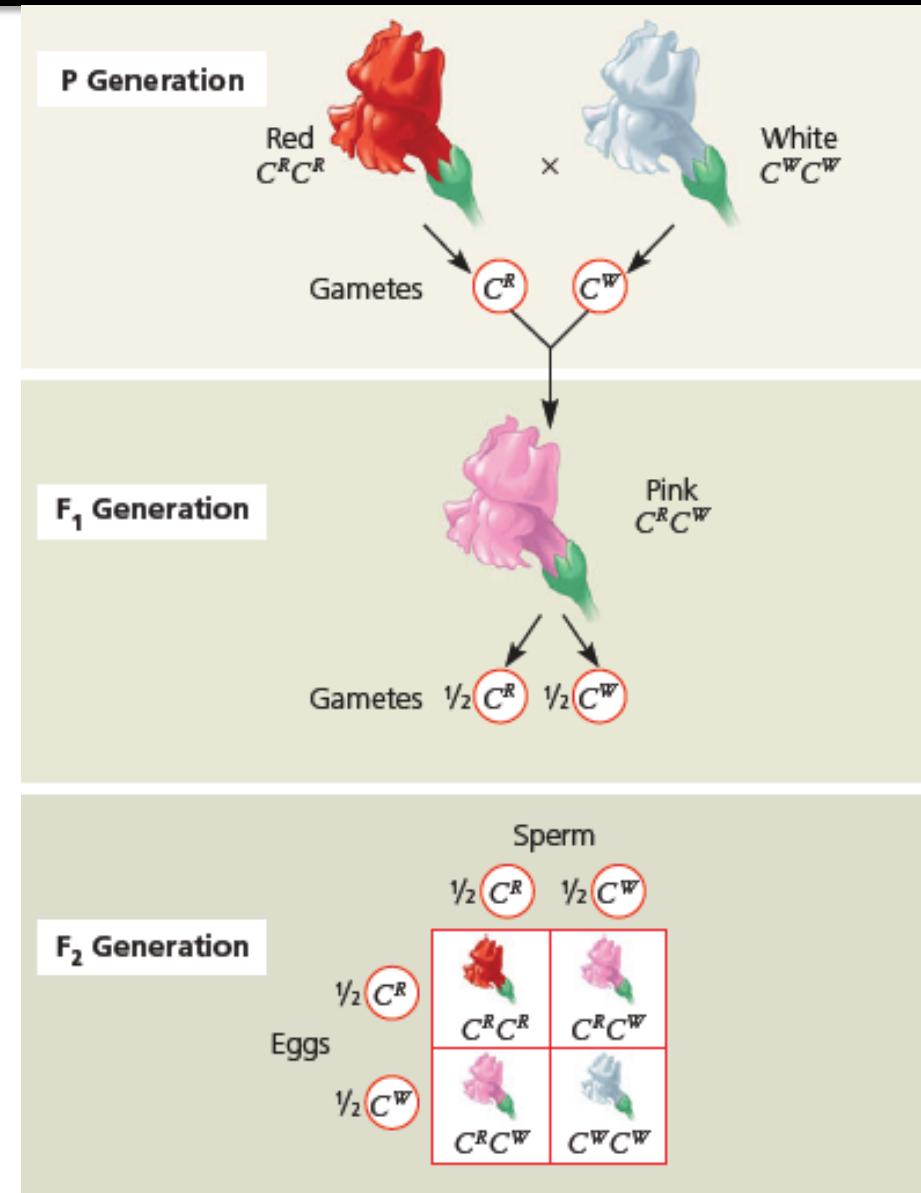
- **Complete dominance** occurs when phenotypes of the heterozygote and dominant homozygote are identical
- **Incomplete dominance** the phenotype of F_1 hybrids is somewhere between the phenotypes of the two parental varieties
- **Codominance** two dominant alleles affect the phenotype in separate, distinguishable ways

Examples of deviation from Mendelian genetics

- **Incomplete dominance** (alleles are not completely dominant or recessive)

Example: Snapdragon color

Heterozygotes always lead to intermediate color



Examples of deviation from Mendelian genetics

- Multiple alleles (when genes exist in more than 2 allelic forms)

(a) The three alleles for the ABO blood groups and their carbohydrates. Each allele codes for an enzyme that may add a specific carbohydrate (designated by the superscript on the allele and shown as a triangle or circle) to red blood cells.

Allele	I^A	I^B	i	
Carbohydrate	A 	B 	none	
Genotype	$I^A I^A$ or $I^A i$	$I^B I^B$ or $I^B i$	$I^A I^B$	ii

I^A and I^B are dominant

i is recessive

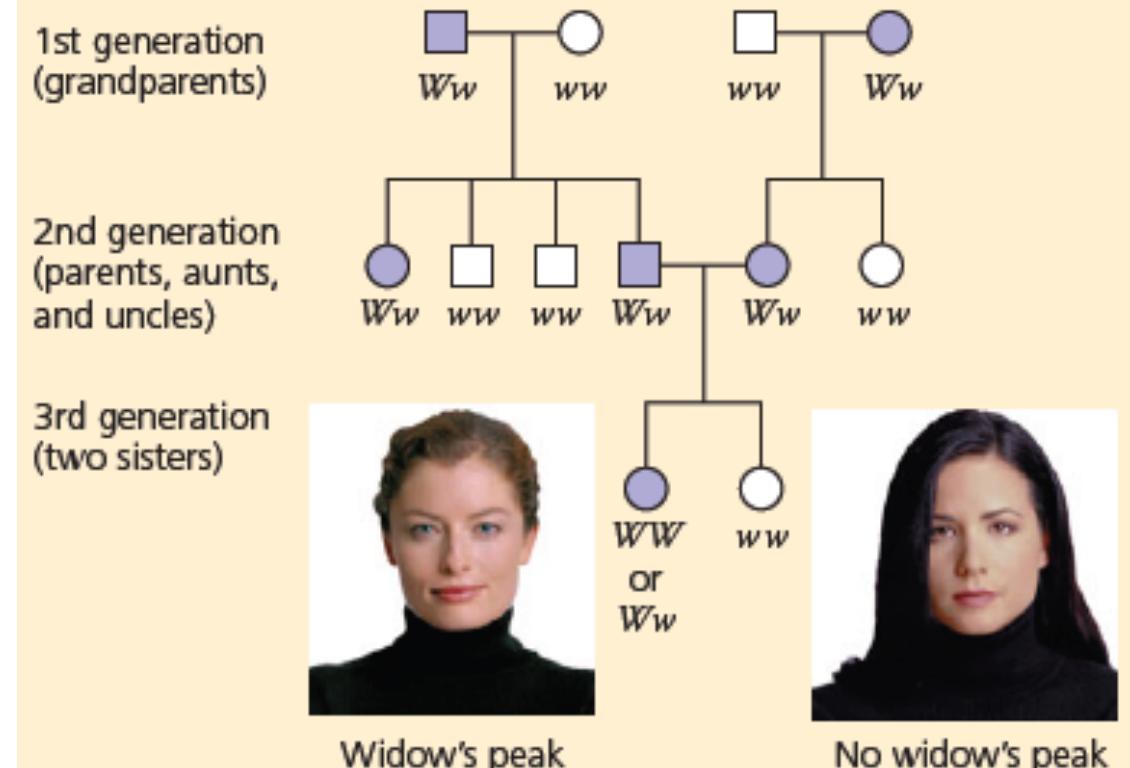
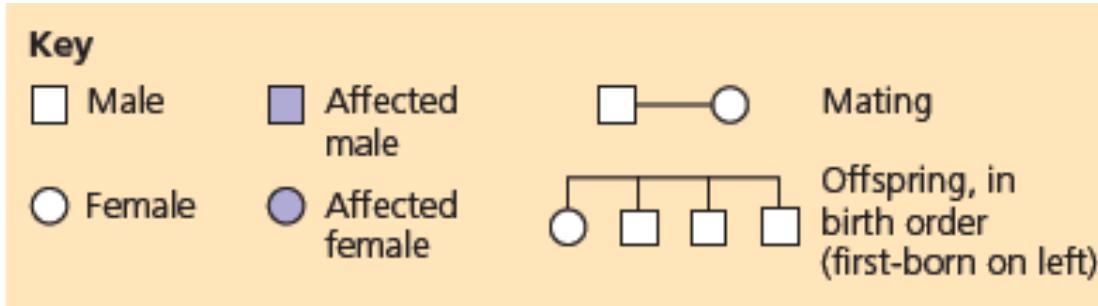
(b) Blood group genotypes and phenotypes. There are six possible genotypes, resulting in four different phenotypes.

Genotype	$I^A I^A$ or $I^A i$	$I^B I^B$ or $I^B i$	$I^A I^B$	ii
Red blood cell appearance				
Phenotype (blood group)	A	B	AB	O

Pleiotropy multiple phenotypic effects

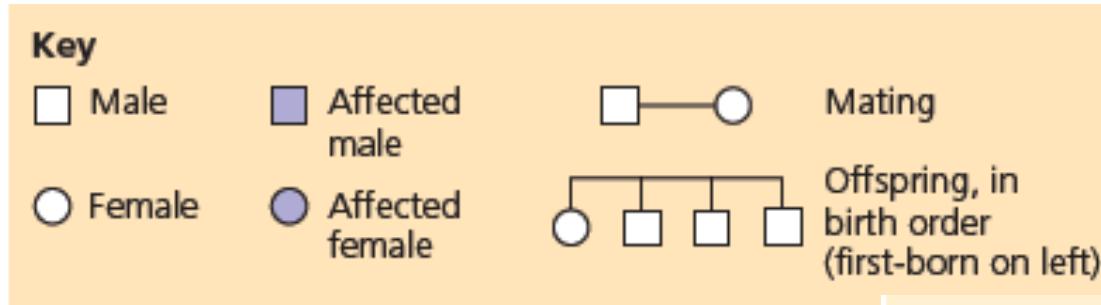
Human traits that follow Mendelian genetics

- Widow's peak (dominant trait)

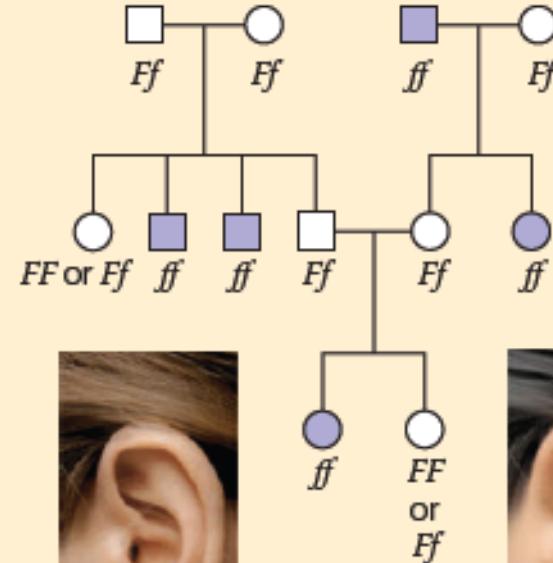


Human traits that follow Mendelian genetics

- Attached earlobe (recessive trait)



1st generation
(grandparents)



2nd generation
(parents, aunts,
and uncles)

3rd generation
(two sisters)



Attached earlobe



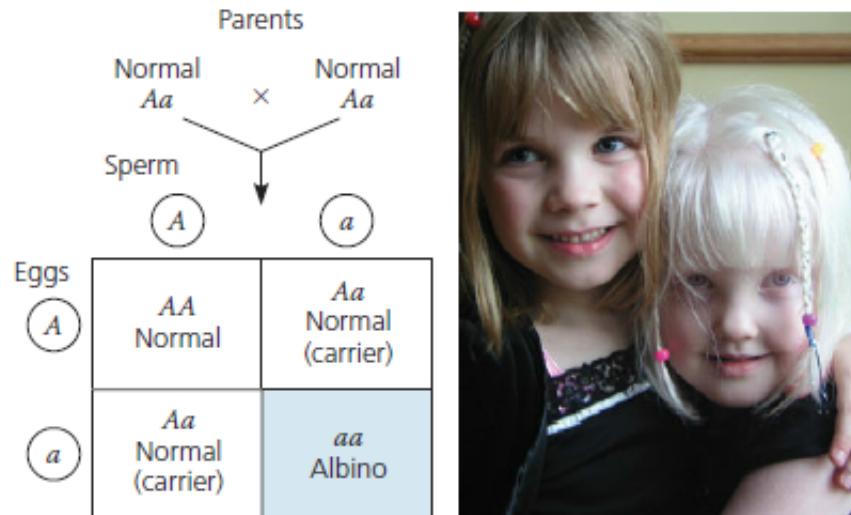
Free earlobe

Human traits that follow Mendelian genetics

- RECESSIVE DISORDERS
 - Cystic Fibrosis
 - Colour blindness
([Christopher Nolan!](#))
 - Haemophilia ([The entire British royal family](#))
- DOMINANT DISORDERS
 - Polydactyly ([Hrithik Roshan](#))
 - ALS ([ice bucket challenge?](#))
 - Huntington's disease

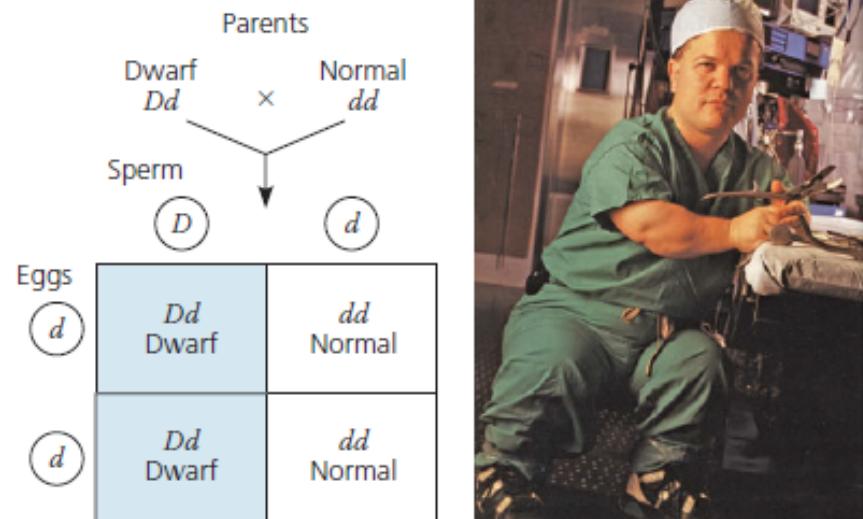
Clinical relevance of Mendelian Genetics

We have seen several harmless traits that follow mendelian genetics. Can diseases also be inherited in this fashion?



▲ **Figure 14.16 Albinism: a recessive trait.** One of the two sisters shown here has normal coloration; the other is albino. Most recessive homozygotes are born to parents who are carriers of the disorder but themselves have a normal phenotype, the case shown in the Punnett square.

Albinism follows
recessive inheritance



▲ **Figure 14.17 Achondroplasia: a dominant trait.**

Achondroplasia follows
dominant inheritance

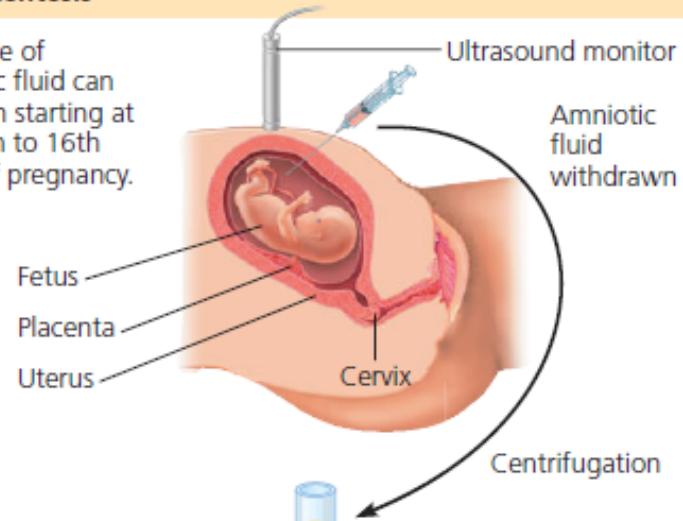
Genetic Testing

- Risk of a particular disorder can be assessed.
- Genetic testing based on familial history
- Fetal testing:
 - Amniocentesis
 - Choriotocentesis
 - Ultrasound
- New born screening:
 - Screening for Phenylketonuria

Biochemical Testing

(a) Amniocentesis

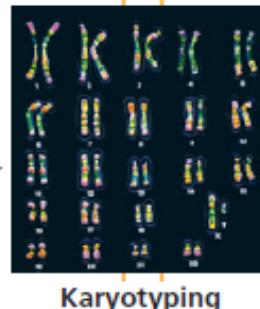
- 1 A sample of amniotic fluid can be taken starting at the 14th to 16th week of pregnancy.



- 2 Biochemical and genetic tests can be performed immediately on the amniotic fluid or later on the cultured cells.

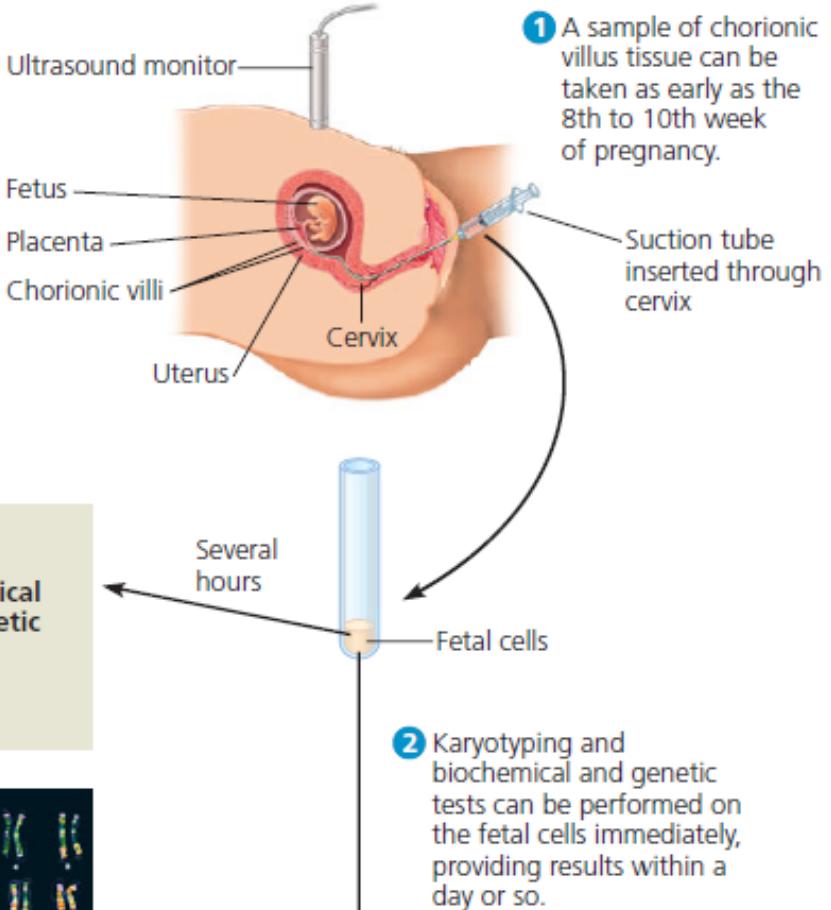
- 3 Fetal cells must be cultured for several weeks to obtain sufficient numbers for karyotyping.

Biochemical and genetic tests



(b) Chorionic villus sampling (CVS)

- 1 A sample of chorionic villus tissue can be taken as early as the 8th to 10th week of pregnancy.



- 2 Karyotyping and biochemical and genetic tests can be performed on the fetal cells immediately, providing results within a day or so.

A modern example of genetic analysis

- Women with a family history of breast and ovarian cancer and mutations in the BRCA1 gene are given a risk assessment of their own chances of getting the disease
- As there is no ‘cure’ for breast cancer once it appears, some women assess their risk and decide to undergo a mastectomy to reduce their risk of getting breast cancer
- BRCA1 mutations are dominant i.e. the presence of the mutations can give rise to breast cancer and we know the following about Angelina Jolie:
 - Her mother died of ovarian cancer and maternal aunt died of breast cancer
 - She has the mutations in BRCA1 that predispose to breast cancer
 - **Assuming Angelina Jolie is heterozygous for BRCA1 mutations and Brad Pitt has no BRCA1 mutations, draw a Punnett square showing the genotypes and phenotypes for breast cancer of their children**
 - By the way, breast cancer genetics are not this simple but it is a good example of the real world consequences of genes



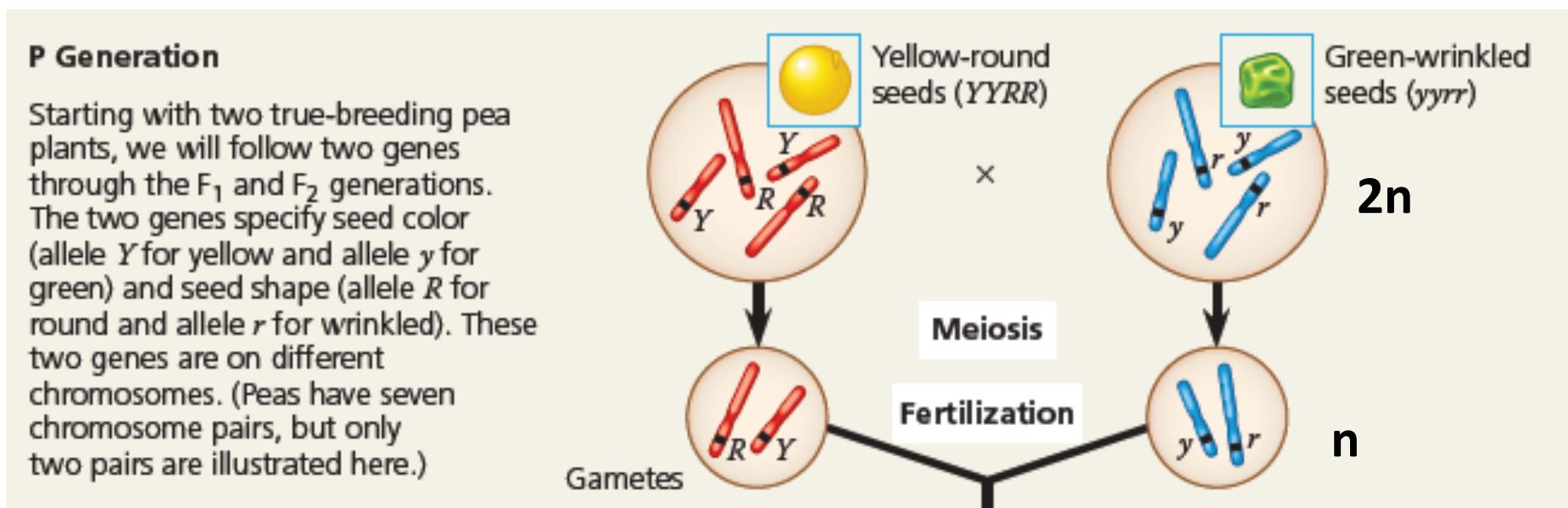
Lecture 4- 5

Chromosomal basis of inheritance & its application in Medicine

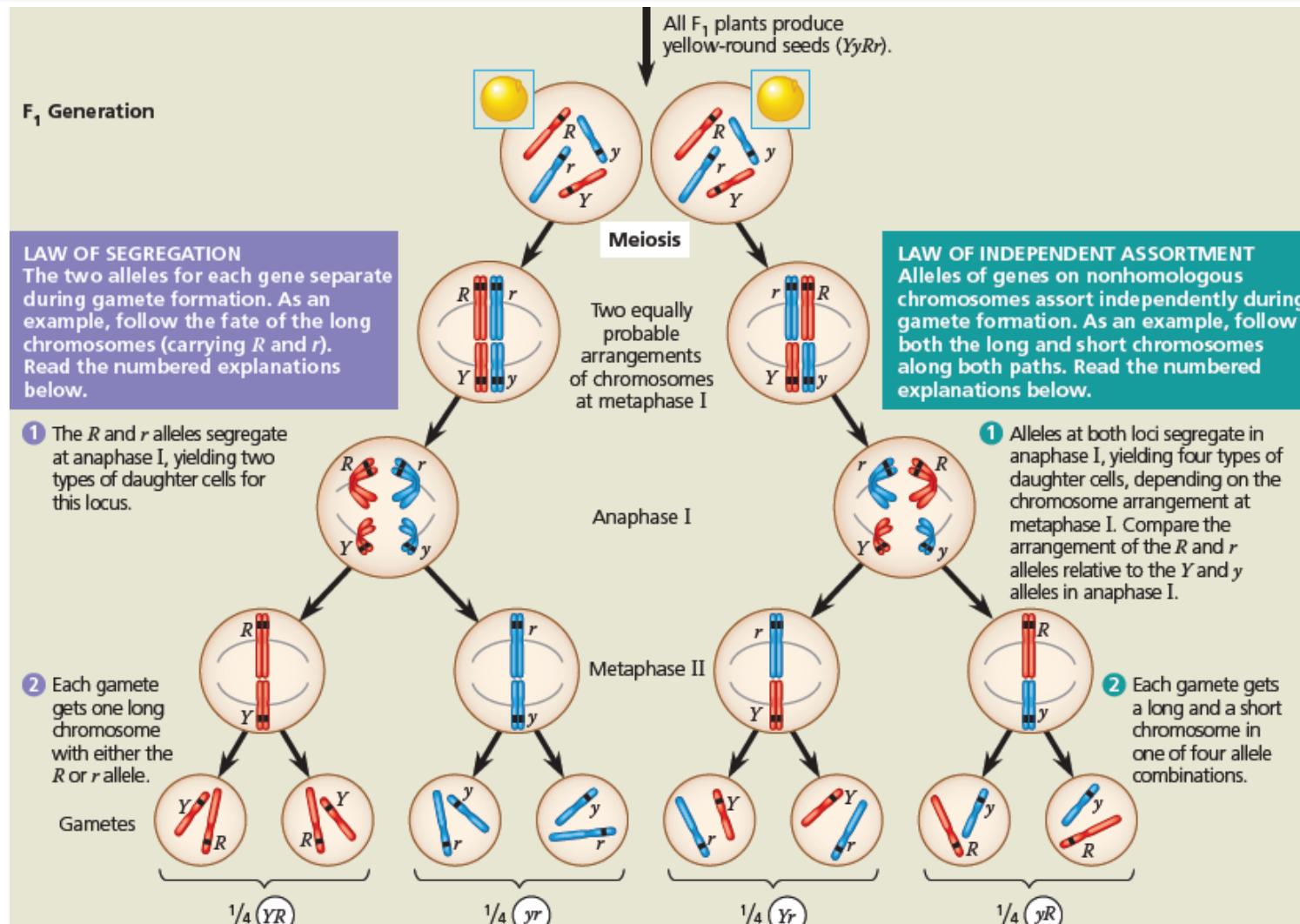
Chapter 15

Chromosomal basis of Mendel's laws

- Chromosomes & genes: present in pairs in diploid cells ($2n$: male 44+XY, female 44+XX)
- Homologous chromosomes separate and alleles segregate during Meiosis.
- ..Genes are located on chromosomes and that the behavior of chromosomes during meiosis accounts for Mendel's laws of segregation and independent assortment



Chromosomal basis of Mendel's laws



F₂ Generation

- ⑤ Fertilization recombines the R and r alleles at random.

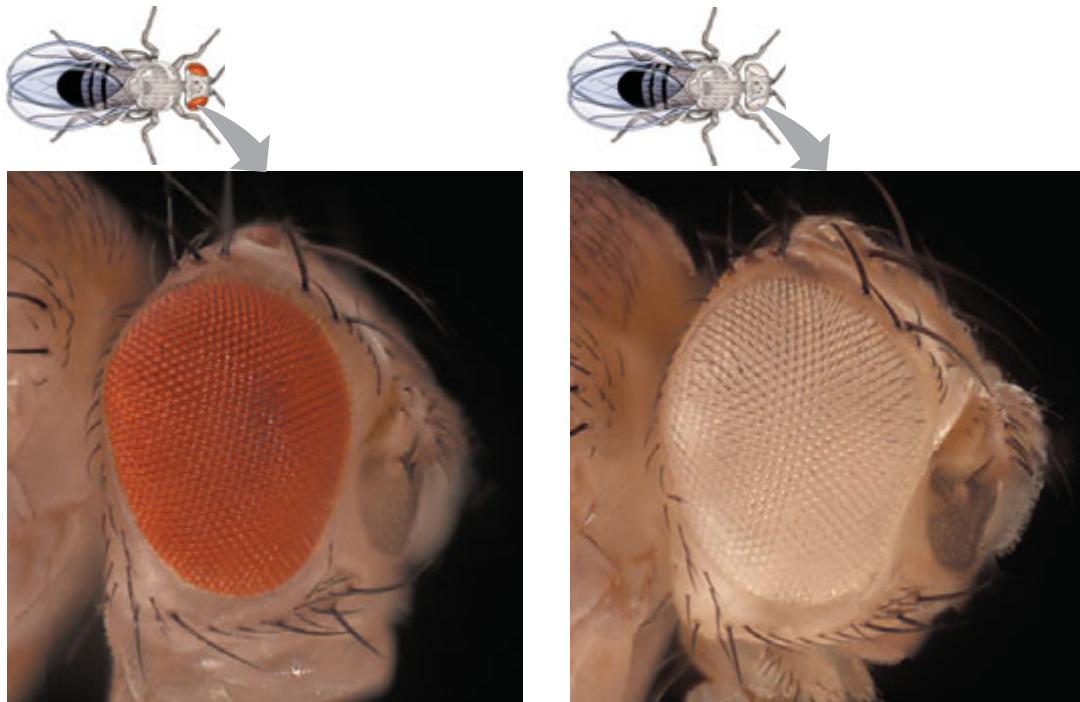
An F₁ × F₁ cross-fertilization

9 : 3 : 3 : 1

- ⑥ Fertilization results in the 9:3:3:1 phenotypic ratio in the F₂ generation.

Experimental evidence: Chromosomal basis of Mendel's laws

Morgan in 1907, provided Solid evidence of a specific gene associated with a specific chromosome



- After two years of hard work,, one male fly with white eye (mating of red eye flies)

Wild type: normal/natural (red eye)
Mutant: alternative form (white eye)

▲ **Figure 15.3 Morgan's first mutant.** Wild-type *Drosophila* flies have red eyes (left). Among his flies, Morgan discovered a mutant male with white eyes (right). This variation made it possible for Morgan to trace a gene for eye color to a specific chromosome (LMs).

Correlating behavior of a gene's alleles with behavior of a chromosome pair

- F₁ and F₂ generation followed Mendel's laws
- One unique observation:
 - White-eye trait in males ONLY

Inferences/Conclusion

- Eye color is linked to its sex/gender and gene is located on the X-chromosome and no corresponding allele on Y-chromosome

▼ Figure 15.4

INQUIRY

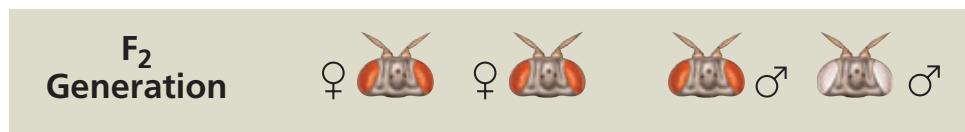
In a cross between a wild-type female fruit fly and a mutant white-eyed male, what color eyes will the F₁ and F₂ offspring have?

EXPERIMENT Thomas Hunt Morgan wanted to analyze the behavior of two alleles of a fruit fly eye-color gene. In crosses similar to those done by Mendel with pea plants, Morgan and his colleagues mated a wild-type (red-eyed) female with a mutant white-eyed male.



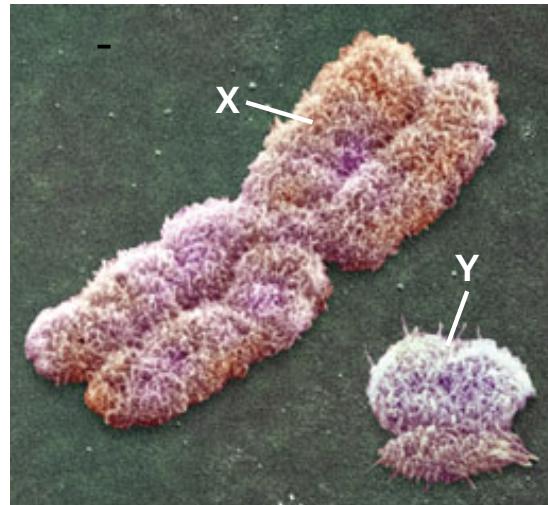
Morgan then bred an F₁ red-eyed female to an F₁ red-eyed male to produce the F₂ generation.

RESULTS The F₂ generation showed a typical Mendelian ratio of 3 red-eyed flies : 1 white-eyed fly. However, no females displayed the white-eye trait; all white-eyed flies were males.

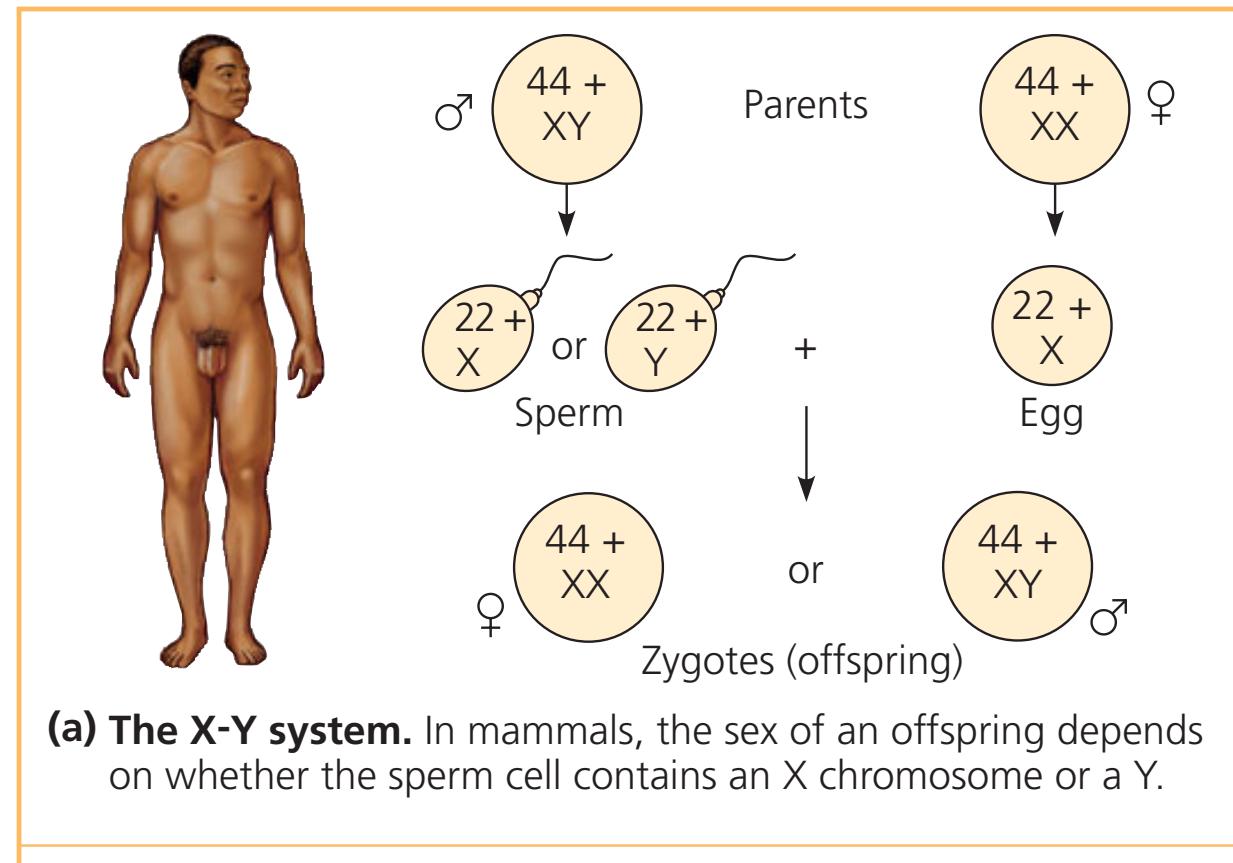


CONCLUSION All F₁ offspring had red eyes, so the mutant white-eye trait (*w*) must be recessive to the wild-type red-eye trait (*w⁺*). Since the recessive trait—white eyes—was expressed only in males in the F₂ generation, Morgan deduced that this eye-color gene is located on the X chromosome and that there is no corresponding locus on the Y chromosome.

Sex linked genes exhibit unique pattern of inheritance



▲ Figure 15.5 Human sex chromosomes.



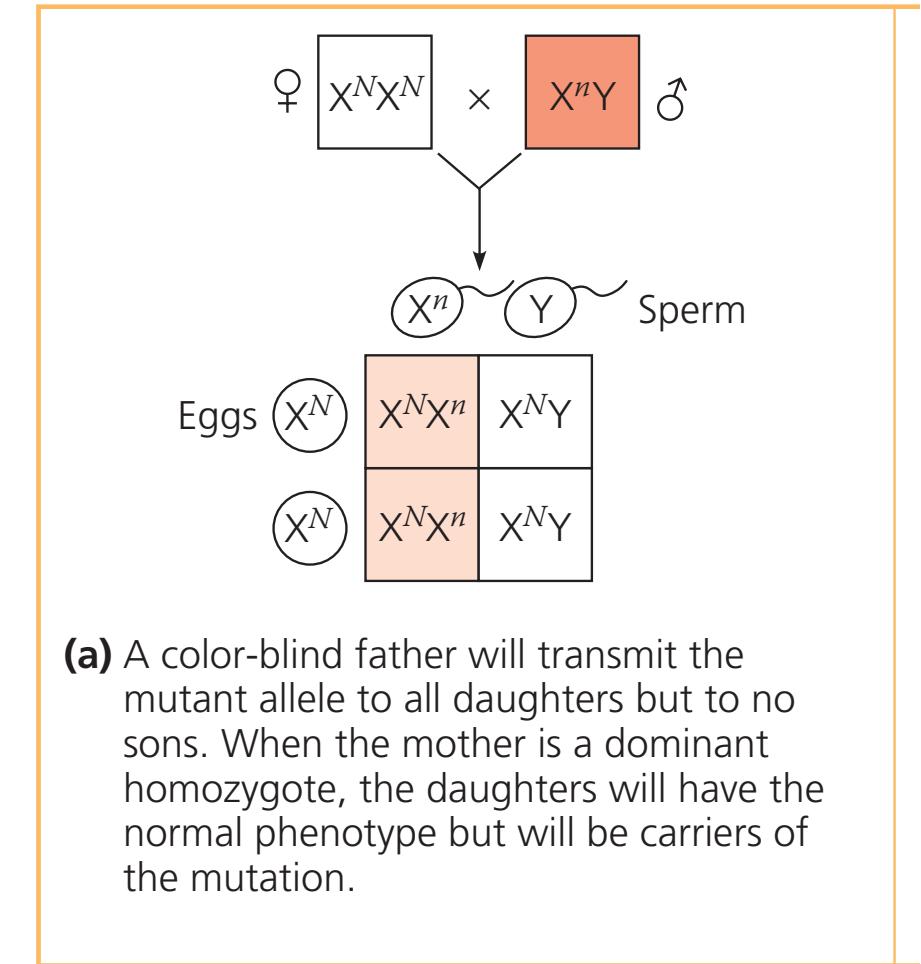
Sex linked genes:

Y chromosome: 78 genes, codes for approx 25 proteins

X chromosome: 1100 genes (x-linked genes), many genes of different character including gender

Inheritance of X-linked genes

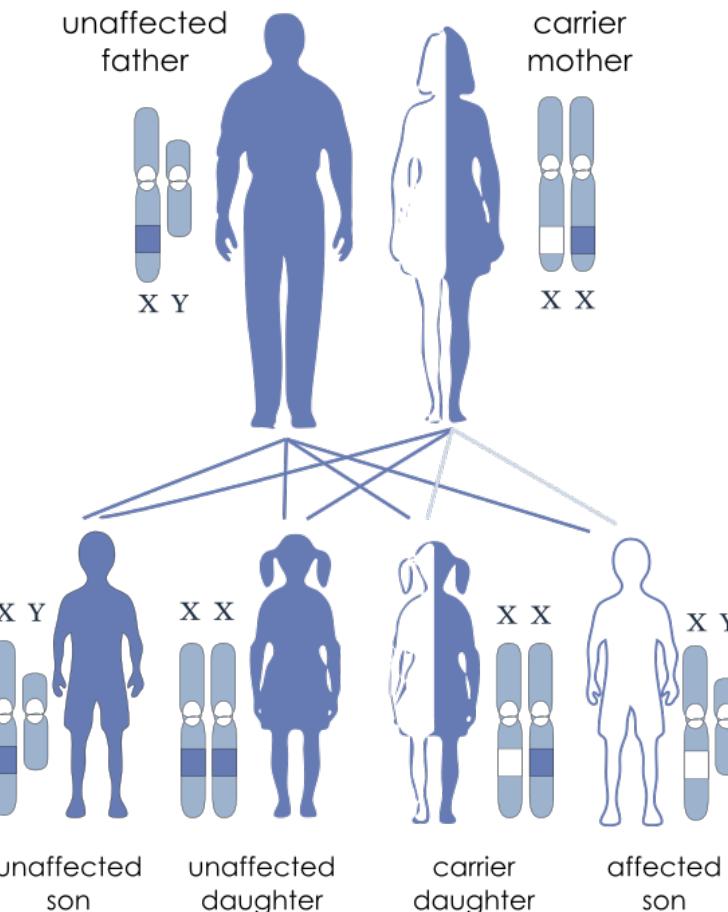
- Male and female: different numbers of X-chromosome
- Father passes X chromosome to daughters, mothers pass to son/daughter
- X-linked trait is due to a recessive allele
 - What genotype in a female and male will express the phenotype?????????
- Higher incidence of males having X-linked recessive disorder than females
- Color blindness, Hemophilia, muscular dystrophy



How an individual inherit Hemophilia?

- Unable to clot the blood: “the royal disease”
- X linked recessive disorder
- Gene is not present on Y-chromosome
- Mainly occur in male due to presence of single sex-linked X-chromosome, however, female needs both copies to develop disease

X-linked recessive inheritance



■ unaffected

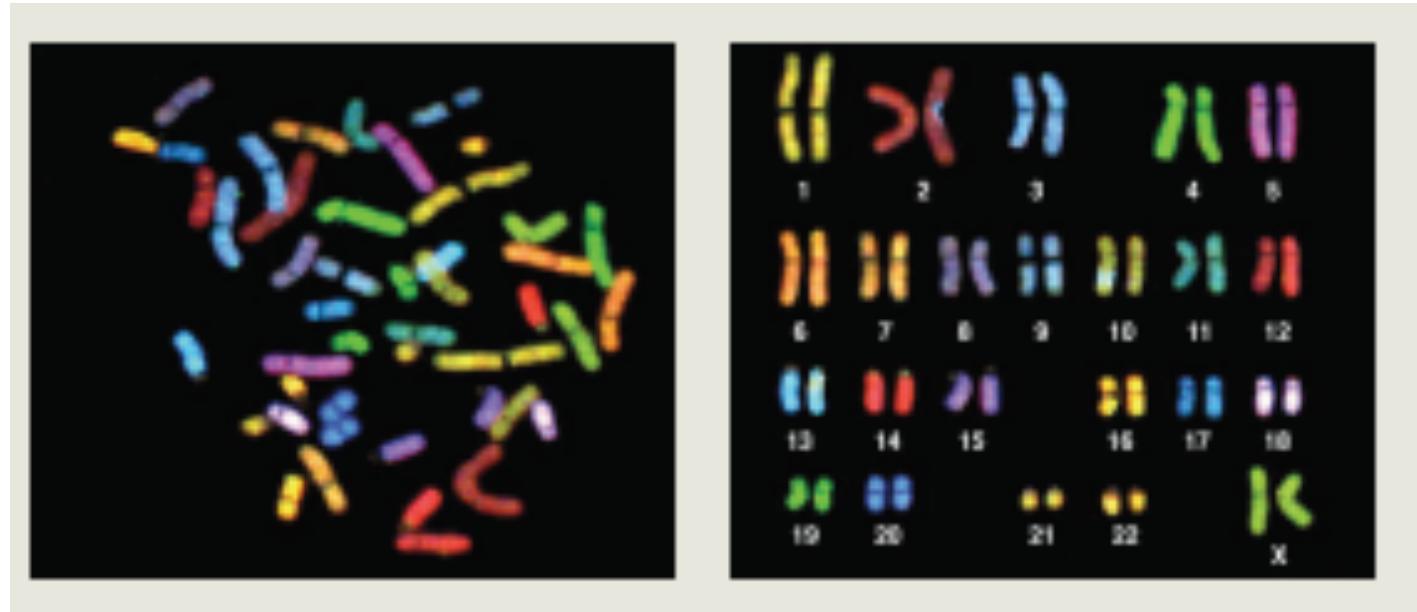
■ carrier

□ affected

Eukaryotic genomes are organized into chromosomes

Humans have 23 pairs of chromosomes: 22 pairs of autosomes and one pair of sex chromosomes (X and Y)

The image below shows a spread of human chromosomes, each ‘painted’ with a different color; on the right these are organized into a karyotype



Karyotypes can tell us about diseases such as cancer (chromosome aberrations/translocations), disorders such as Down’s syndrome (Trisomy 21) and sex determination (XX vs XY)

Chromosomal aberrations

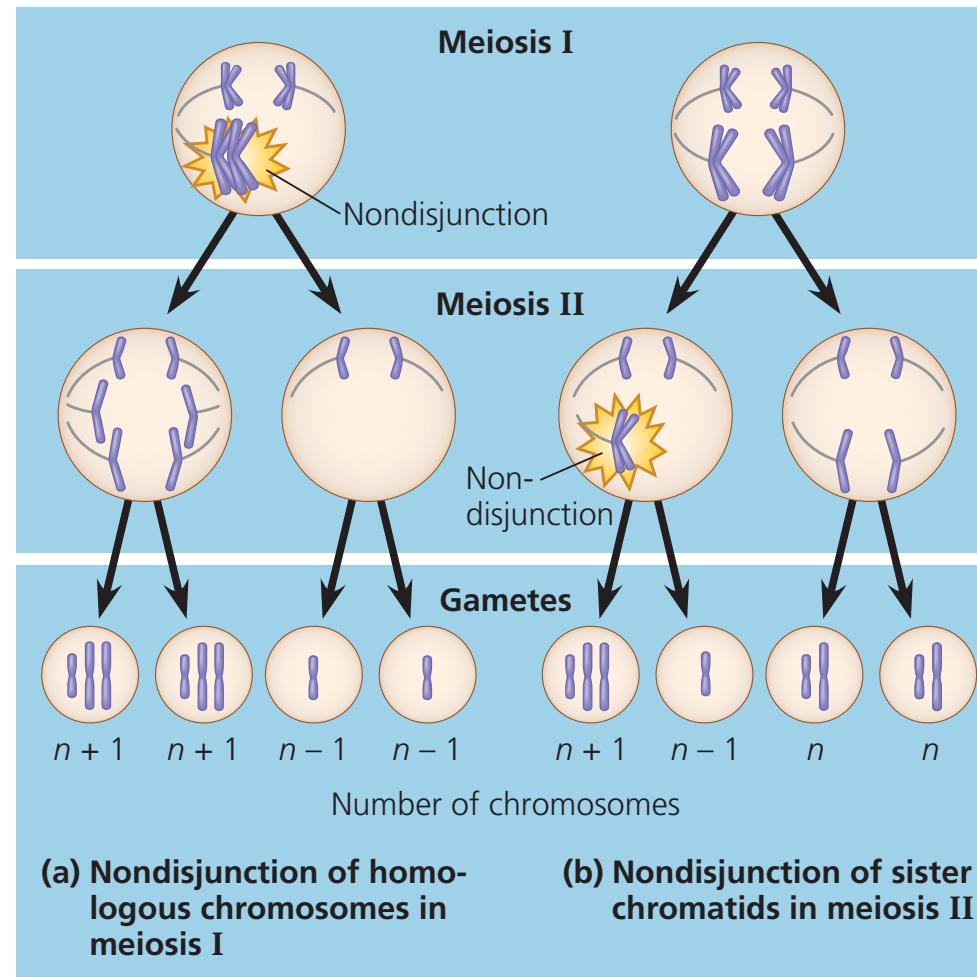
- Abnormal chromosomal number (aneuploidy): nondisjunction

Monosomic: $2n-1$

Trisomic: $2n+1$: trisomy 21

Down syndrome

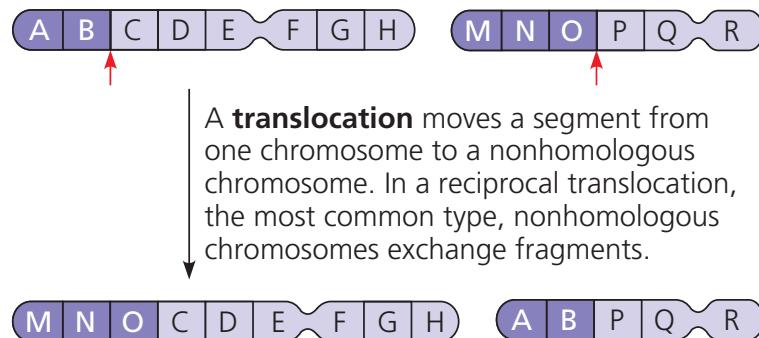
- Risk of having a baby with Down's syndrome increases with maternal age



Chromosomal aberrations

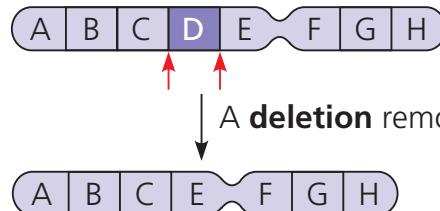
- Alteration in chromosomal structure:

(d) Translocation

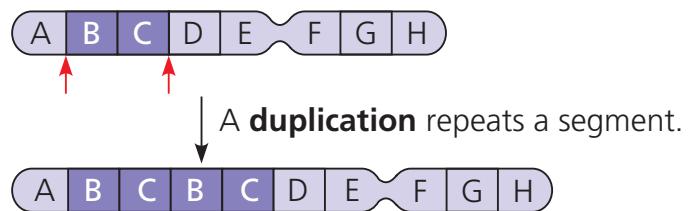


Less often, a nonreciprocal translocation occurs: A chromosome transfers a fragment but receives none in return (not shown).

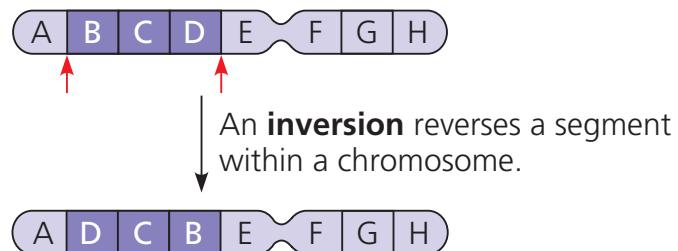
(a) Deletion



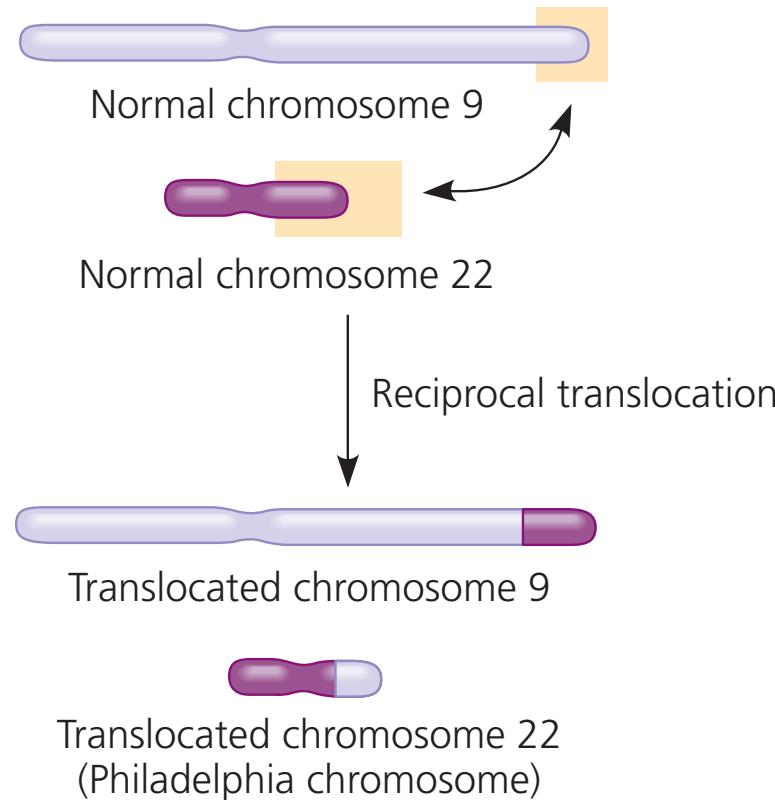
(b) Duplication



(c) Inversion



Chromosomal aberrations: alteration in chromosome structure



▲ **Figure 15.16 Translocation associated with chronic myelogenous leukemia (CML).** The cancerous cells in nearly all CML patients contain an abnormally short chromosome 22, the so-called Philadelphia chromosome, and an abnormally long chromosome 9. These altered chromosomes result from the reciprocal translocation shown here, which presumably occurred in a single white blood cell precursor undergoing mitosis and was then passed along to all descendant cells.