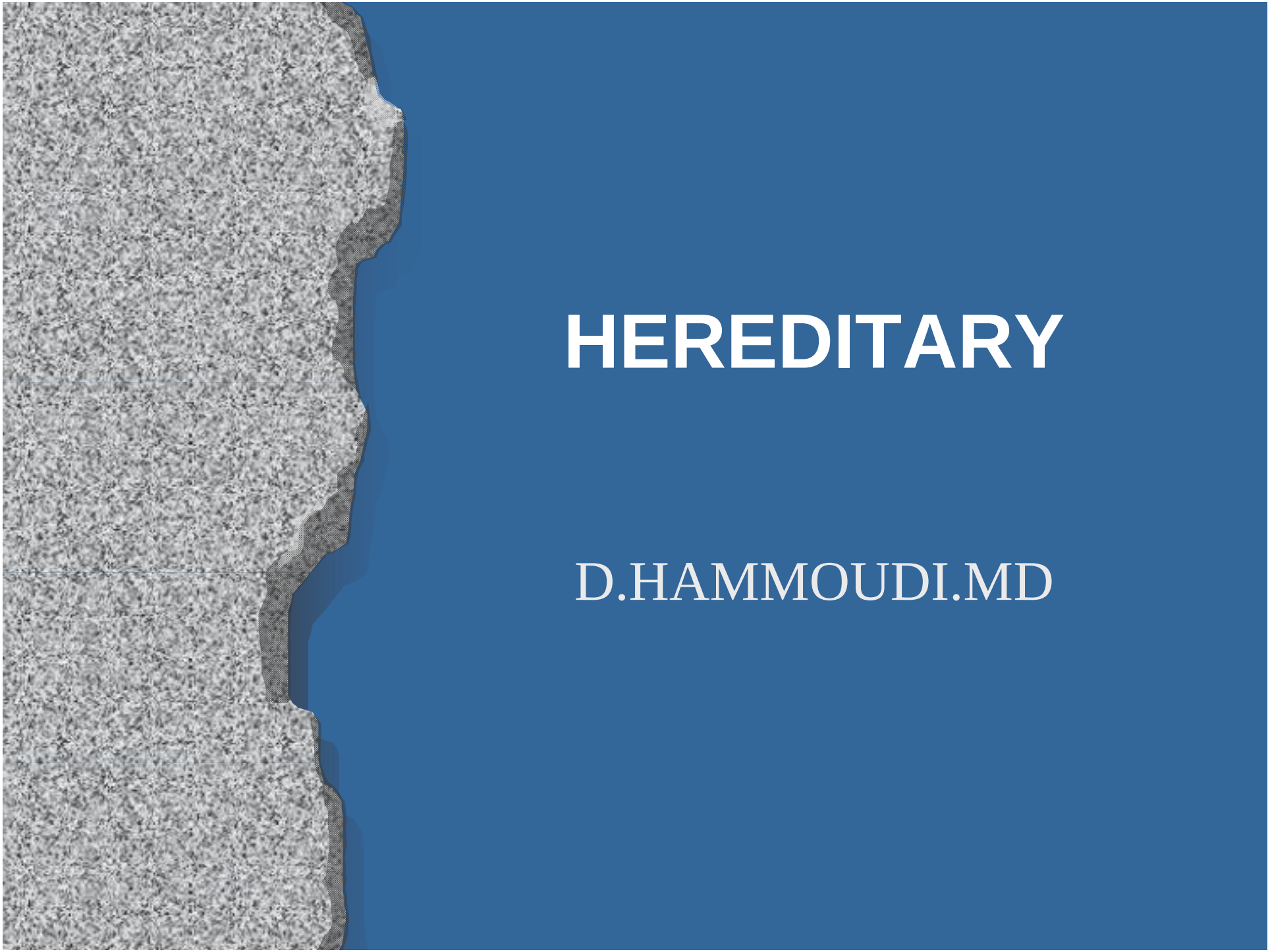
HEREDITARY
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Genetics

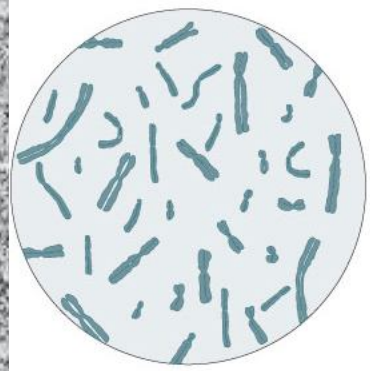
- The study of the mechanism of heredity
- Basic principles proposed by Mendel in the mid-1800s

Genetics

- Diploid number of chromosomes
  - In all cells except gametes
  - Diploid number = 46 (23 pairs of homologous chromosomes)
    - 1 pair of sex chromosomes determines the genetic sex (XX = female, XY = male)
    - 22 pairs of autosomes guide expression of most other traits

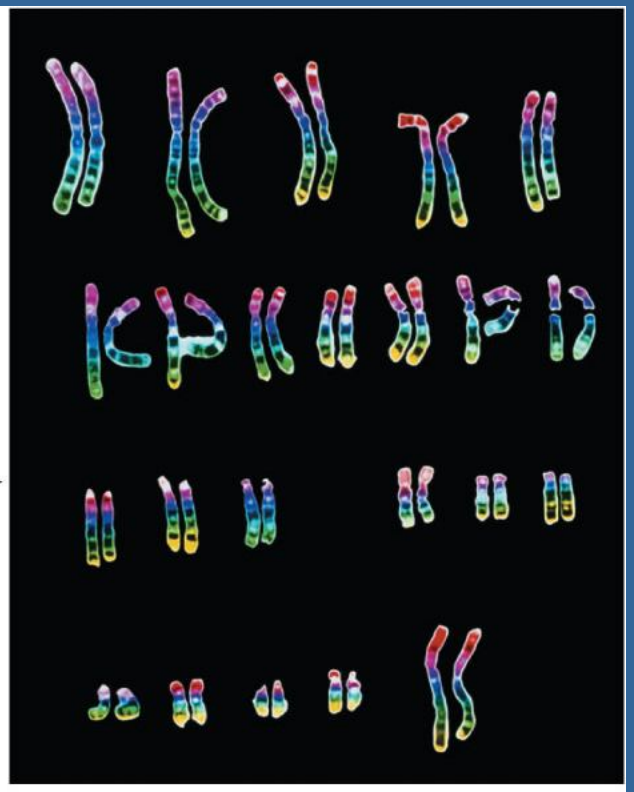
Genetics

- Karyotype: diploid chromosomal complement displayed in homologous pairs
- Genome: genetic (DNA) makeup; two sets of genetic instructions (maternal and paternal)



(a) The slide is viewed with a microscope, and the chromosomes are photographed.

(b) The photograph is entered into a computer, and the chromosomes are electronically rearranged into homologous pairs according to size and structure.



(c) The resulting display is the karyotype, which is examined for chromosome number and structure.

Figure 29.1

Alleles

- Matched genes at the same locus on homologous chromosomes
- Homozygous: alleles controlling a single trait are the same
- Heterozygous: alleles for a trait are different
- Dominant: an allele that masks or suppresses its (recessive) partner

Genotype and Phenotype

- Genotype: the genetic makeup
- Phenotype: the way the genotype is expressed

Sexual Sources of Genetic Variation

- Independent assortment of chromosomes
- Crossover of homologues
- Random fertilization of eggs by sperm

Segregation and Independent Assortment

- During gametogenesis, maternal and paternal chromosomes are randomly distributed to daughter cells
- The two alleles of each pair are segregated during meiosis I
- Alleles on different pairs of homologous chromosomes are distributed independently

Segregation and Independent Assortment

- The number of gamete types = 2^n, where n is the number of homologous pairs
- In a man's testes, $2^n = 22^{23}$ = 8.5 million

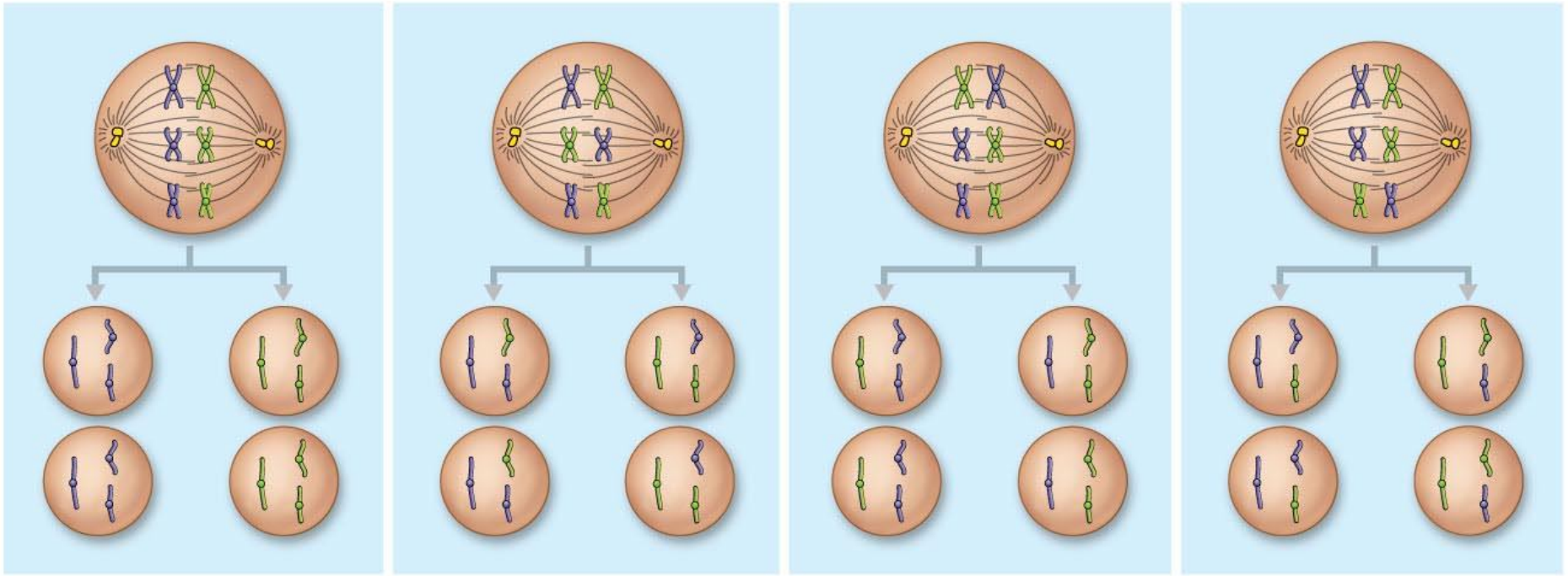
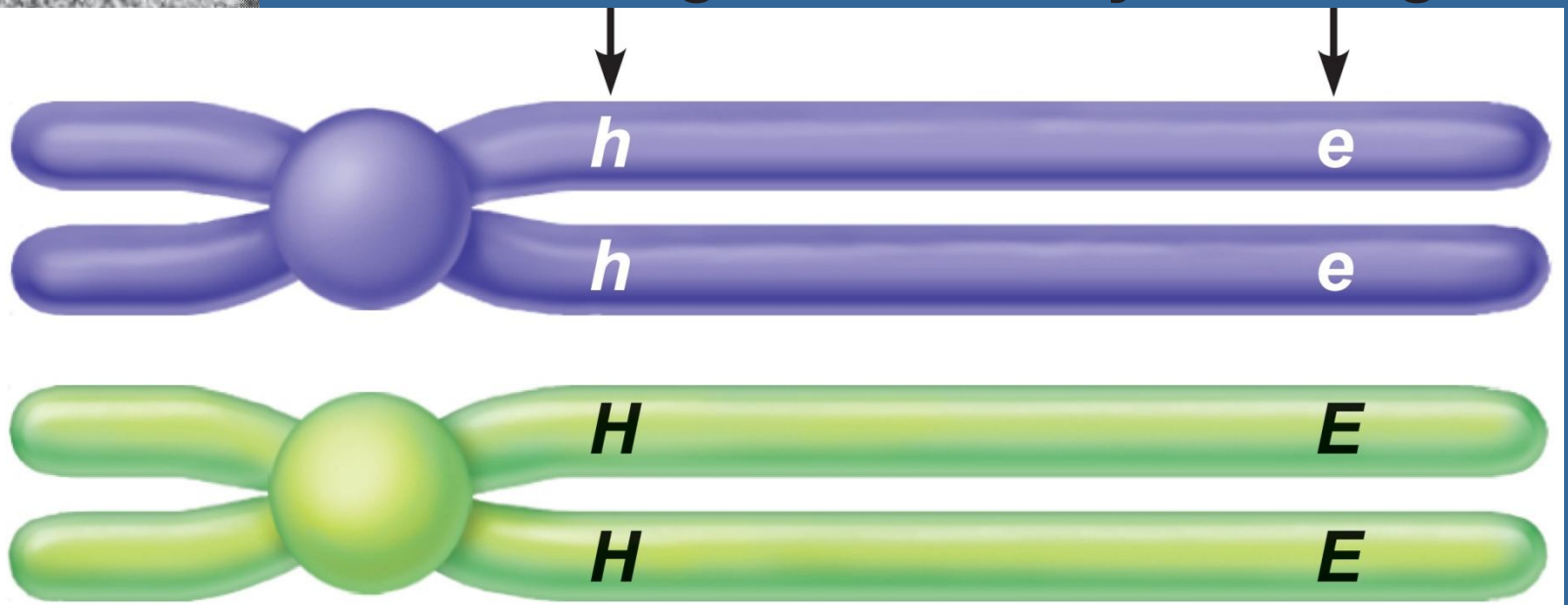


Figure 29.2

Crossover and Genetic Recombination

- Genes on the same chromosome are linked
- Chromosomes can cross over, forming a chiasma, and exchange segments
- Recombinant chromosomes have mixed contributions from each parent



Homologous chromosomes synapse during prophase of meiosis I. Each chromosome consists of two sister chromatids.

H Allele for brown hair
h Allele for blond hair
E Allele for brown eyes
e Allele for blue eyes
Paternal chromosome
Maternal chromosome
Homologous pair

Figure 29.3 (1 of 4)

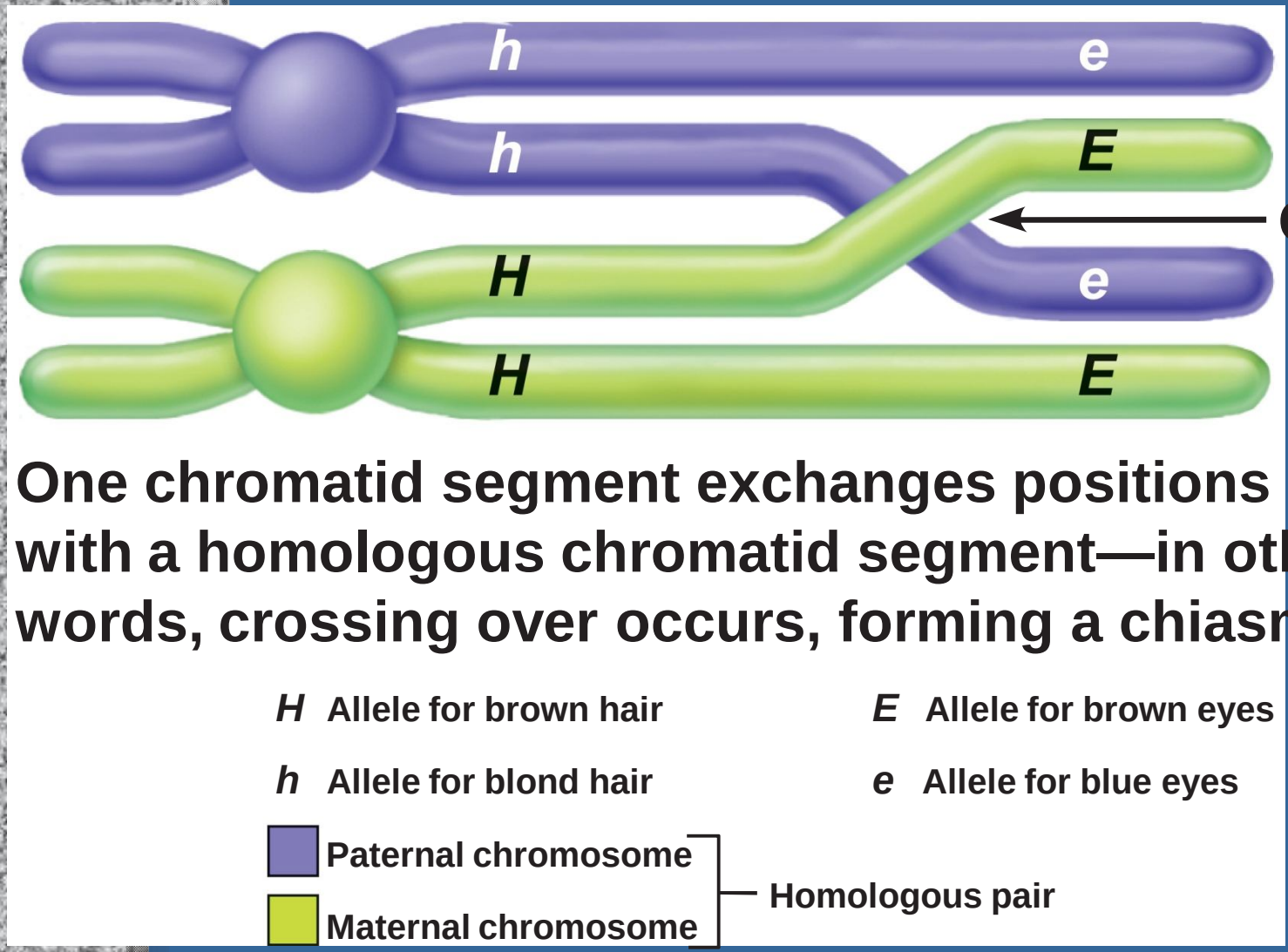


Figure 29.3 (2 of 4)

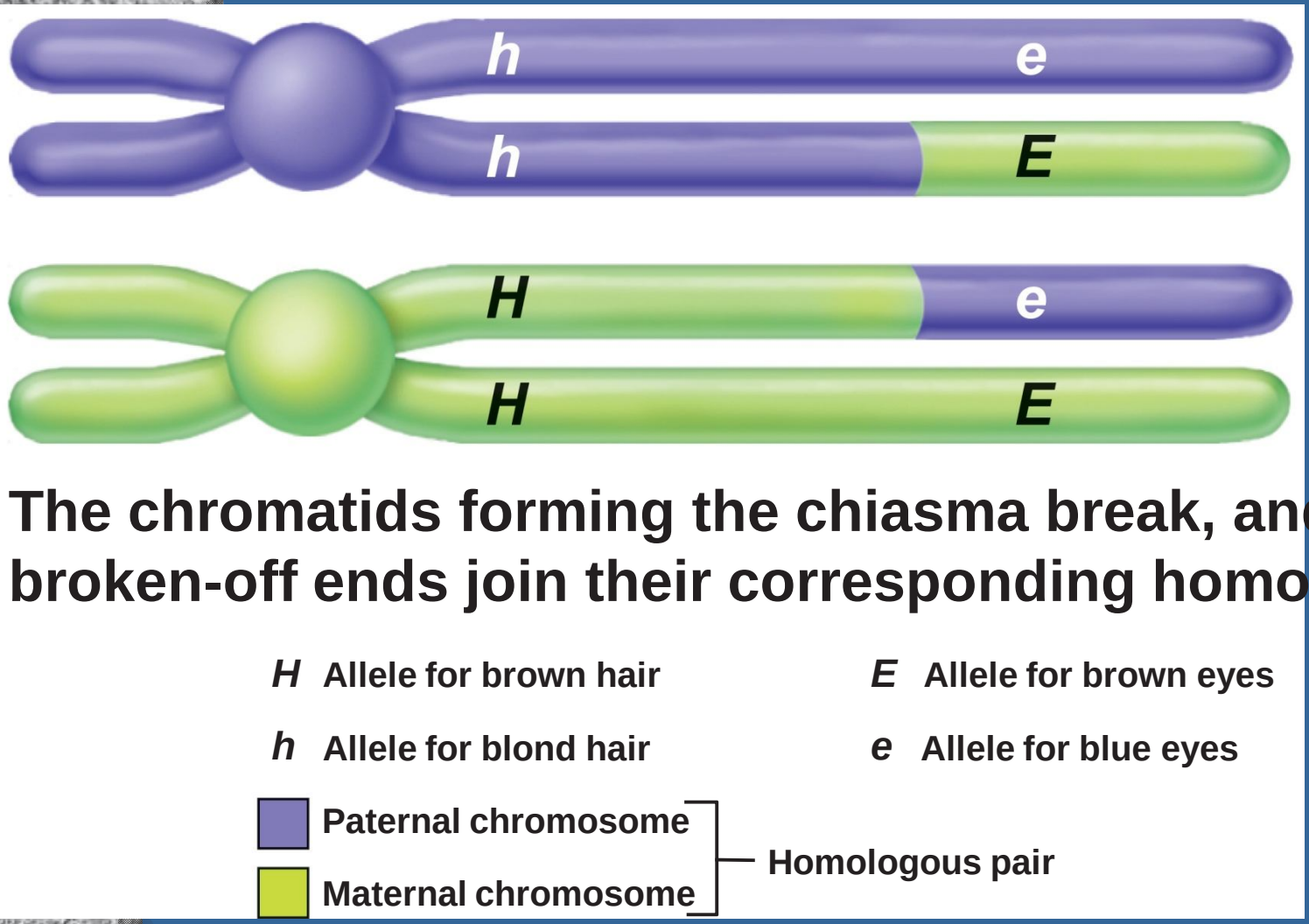


Figure 29.3 (3 of 4)

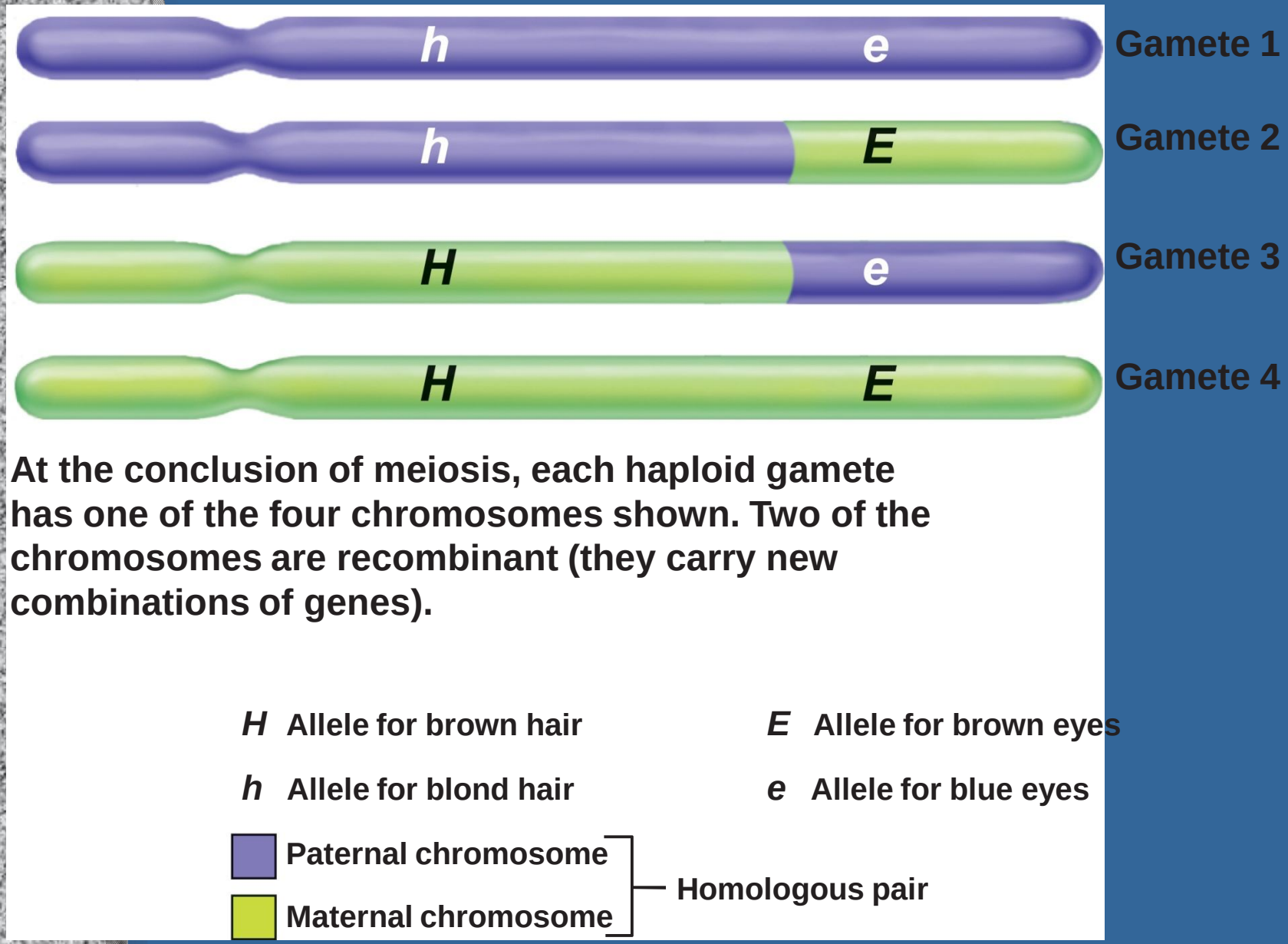


Figure 29.3 (4 of 4)

Random Fertilization

- A single egg is fertilized by a single sperm in a random manner
- Because of independent assortment and random fertilization, an offspring represents one out of 72 trillion (8.5 million × 8.5 million) zygote possibilities

Types of Inheritance

- Most traits are determined by multiple alleles or by the interaction of several gene pairs

Dominant-Recessive Inheritance

- Reflects the interaction of dominant and recessive alleles
- Punnett square: predicts the possible gene combinations resulting from the mating of parents of known genotypes

Dominant-Recessive Inheritance

- Example: probability of genotypes from mating two heterozygous parents
  - Dominant allele—capital letter; recessive allele—lowercase letter
  - *T* = tongue roller and *t* = cannot roll tongue
  - *TT* and *tt* are homozygous; *Tt* is heterozygous

Dominant-Recessive Inheritance

- Offspring: 25% *TT*, 50% *Tt*, 25% *tt*
- The larger the number of offspring, the greater the likelihood that the ratios will conform to the predicted values

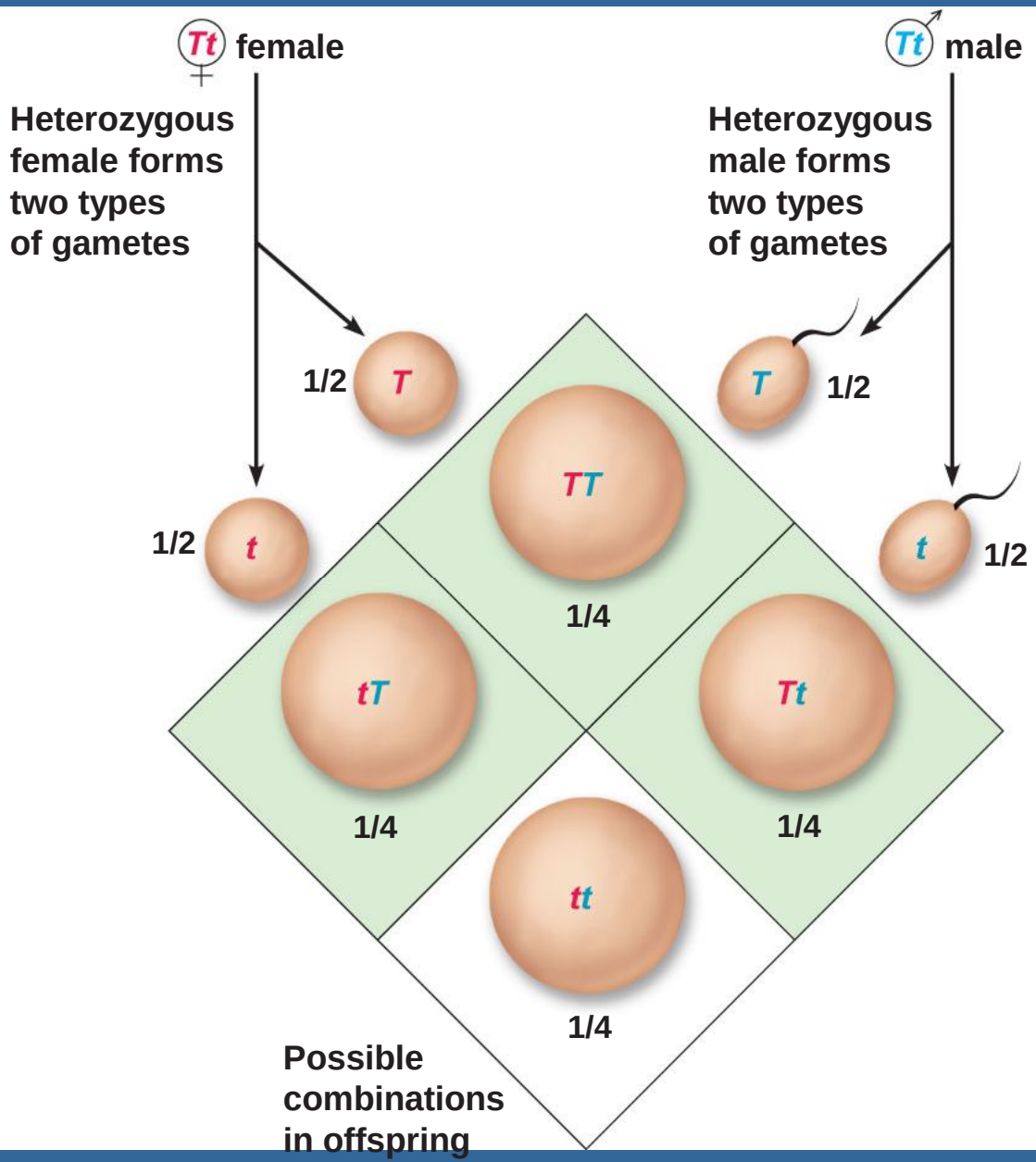

Tt female
Heterozygous female forms two types of gametes
1/2 T
1/2 t
Tt male
Heterozygous male forms two types of gametes
T 1/2
t 1/2
TT
1/4
tT
1/4
Tt
1/4
tt
1/4
Possible combinations in offspring

Figure 29.4

Dominant-Recessive Inheritance

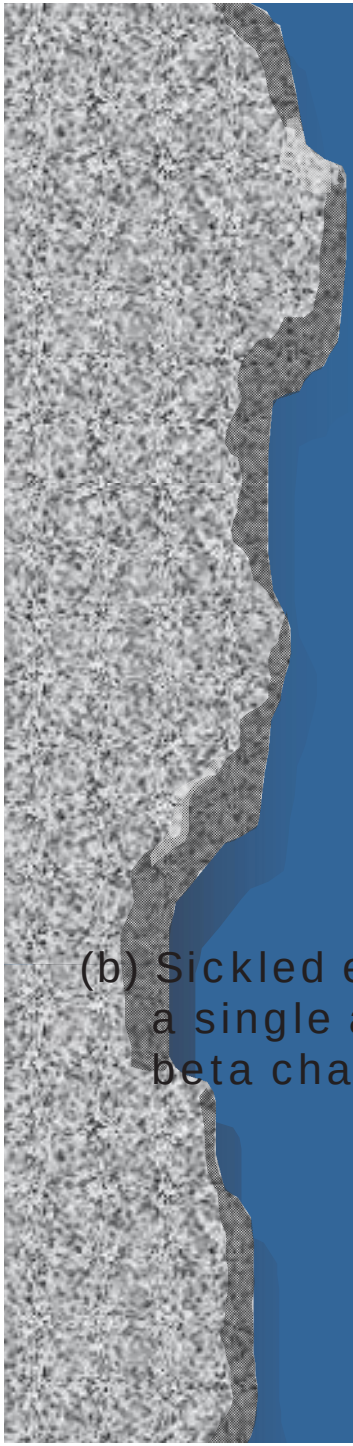
- Dominant traits (for example, widow's peaks, freckles, dimples)
- Dominant disorders are uncommon because many are lethal and result in death before reproductive age
- Huntington's disease is caused by a delayed-action gene

Dominant-Recessive Inheritance

- Most genetic disorders are inherited as simple recessive traits
  - Albinism, cystic fibrosis, and Tay-Sachs disease
- Heterozygotes are carriers who do not express the trait but can pass it on to their offspring

Incomplete Dominance

- Heterozygous individuals have an intermediate phenotype
- Example: Sickling gene
  - *SS* = normal Hb is made
  - *Ss* = sickle-cell trait (both aberrant and normal Hb are made); can suffer a sickle-cell crisis under prolonged reduction in blood O2)
  - *ss* = sickle-cell anemia (only aberrant Hb is made; more susceptible to sickle-cell crisis)



(b) Sickled erythrocyte results from a single amino acid change in the beta chain of hemoglobin.

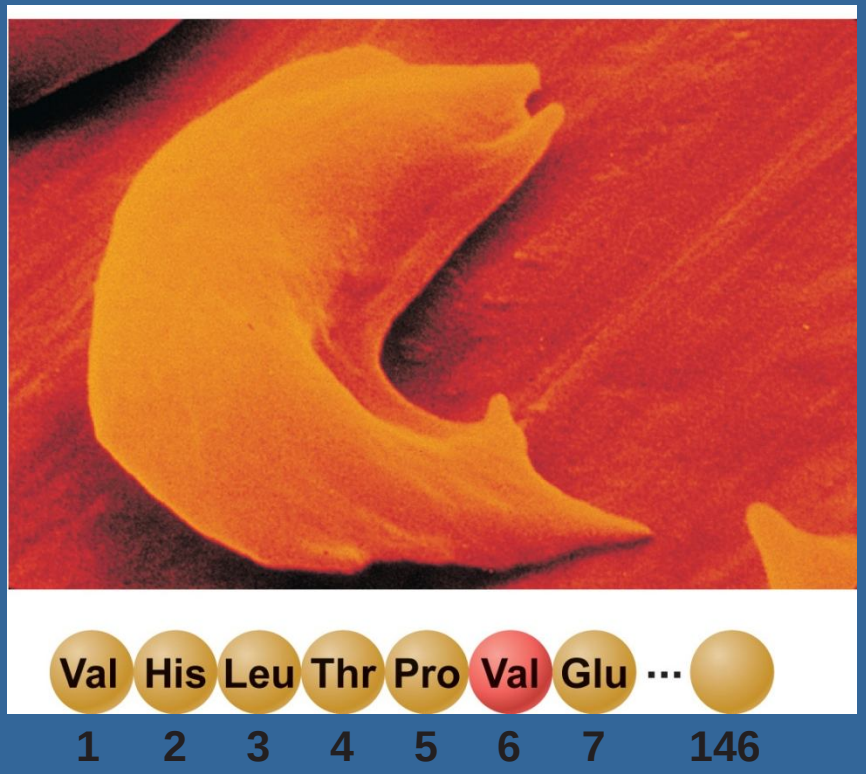


Figure 17.8b

Multiple-Allele Inheritance

- Genes that exhibit more than two allele forms
- ABO blood grouping is an example
- Three alleles (I^A, I^B, i) determine the ABO blood type in humans
- I^A and I^B are codominant (both are expressed if present), and i is recessive

TABLE 29.2 ABO Blood Groups

BLOOD GROUP (PHENOTYPE)	FREQUENCY (% OF U.S. POPULATION)			
	GENOTYPE	WHITE	BLACK	ASIAN
O	ii	45	49	40
A	$I^A I^A$ or $I^A i$	40	27	28
B	$I^B I^B$ or $I^B i$	11	20	27
AB	$I^A I^B$	4	4	5

Table 29.2

Sex-Linked Inheritance

- Inherited traits determined by genes on the sex chromosomes
- X chromosomes bear over 2500 genes (many for brain function); Y chromosomes carry about 78 genes

Sex-Linked Inheritance

- X-linked genes are
  - Found only on the X chromosome
  - Typically passed from mothers to sons (e.g., hemophilia or red-green color blindness)
  - Never masked or damped in males (no Y counterpart)

Polygene Inheritance

- Depends on several different gene pairs at different locations acting in tandem
- Results in continuous phenotypic variation between two extremes
- Examples: skin color, eye color, height

Polygene Inheritance of Skin Color

- Alleles for dark skin (*ABC*) are incompletely dominant over those for light skin (*abc*)
- The first-generation offspring each have three “units” of darkness (intermediate pigmentation)
- The second-generation offspring have a wide variation in possible pigmentations

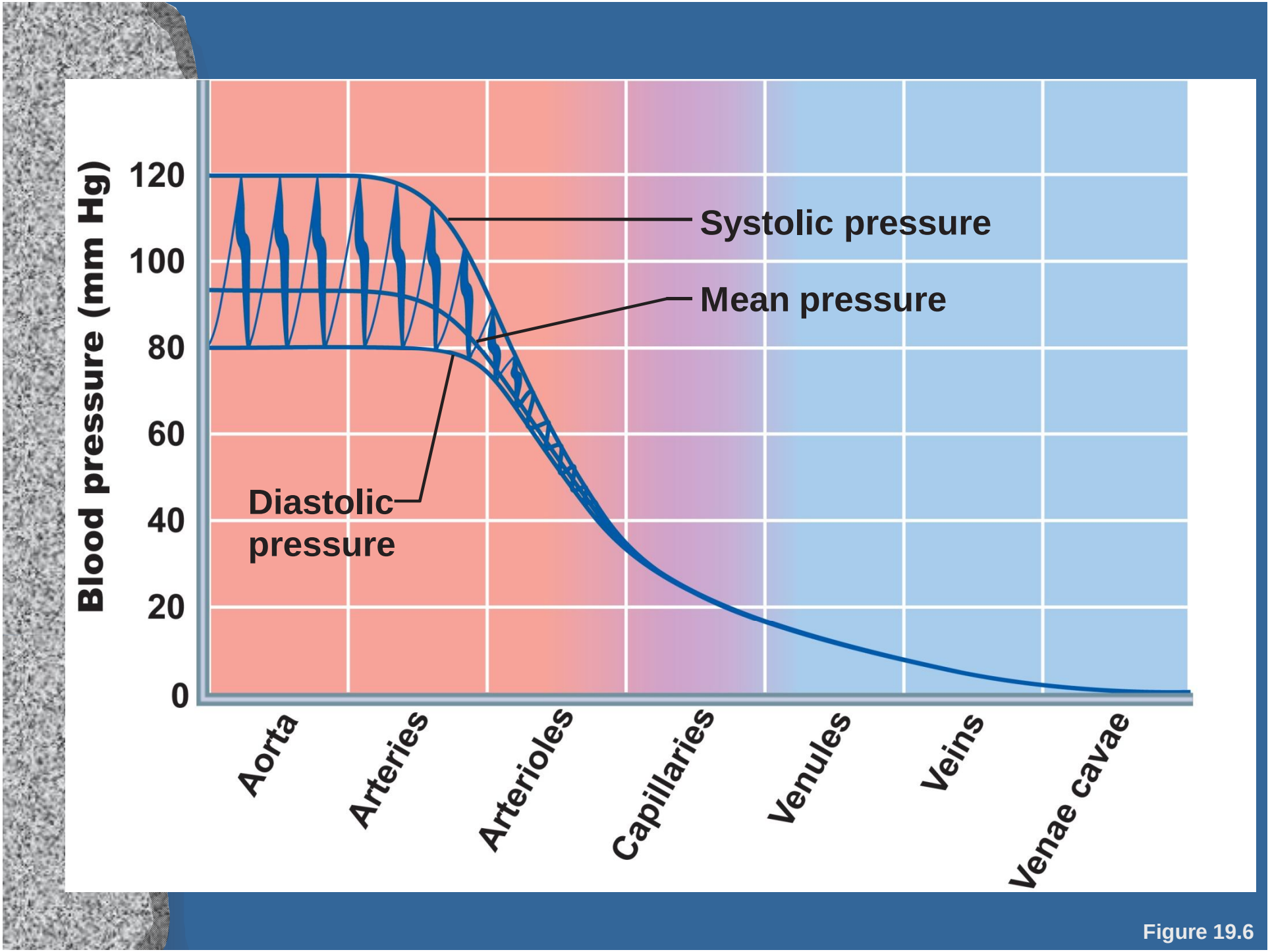

Blood pressure (mm Hg)
120
100
80
60
40
20
0
Systolic pressure
Mean pressure
Diastolic pressure
Aorta
Arteries
Arterioles
Capillaries
Venules
Veins
Venae cavae

Figure 19.6

Environmental Factors in Gene Expression

- Phenocopies: environmentally produced phenotypes that mimic conditions caused by genetic mutations
- Environmental factors can influence genetic expression after birth
  - Poor nutrition can affect brain growth, body development, and height
  - Childhood hormonal deficits can lead to abnormal skeletal growth and proportions

Nontraditional Inheritance

- Influences due to
  - Genes of small RNAs
  - Epigenetic marks (chemical groups attached to DNA)
  - Extranuclear (mitochondrial) inheritance

Small RNAs

- MicroRNAs (miRNAs) and short interfering RNAs (siRNAs)
  - Act directly on DNA, other RNAs, or proteins
  - Inactivate transposons, genes that tend to replicate themselves and disable or hyperactivate other genes
  - Control timing of apoptosis during development
- In future, RNA-interfering drugs may treat diseases such as age-related macular degeneration and Parkinson's disease

Epigenetic Marks

- Information stored in the proteins and chemical groups bound to DNA
- Determine whether DNA is available for transcription or silenced
- May predispose a cell to cancer or other devastating illness

Epigenetic Marks

- Genomic imprinting tags genes as maternal or paternal and is essential for normal development
- Allows the embryo to express only the mother's gene or the father's gene

Epigenetic Marks

- The same allele can have different effects depending on which parent it comes from
- For example, deletions in chromosome 15 result in
  - Prader-Willi syndrome if inherited from the father
  - Angelman syndrome if inherited from the mother

Extranuclear (Mitochondrial) Inheritance

- Some genes (37) are in the mitochondrial DNA (mtDNA)
- Transmitted by the mother in the cytoplasm of the egg
- Errors in mtDNA are linked to rare disorders: muscle disorders and neurological problems, possibly Alzheimer's and Parkinson's diseases

Genetic Screening, Counseling, and Therapy

- Newborn infants are routinely screened for a number of genetic disorders: congenital hip dysplasia, imperforate anus, PKU and other metabolic disorders
- Other examples: screening adult children of parents with Huntington's disease: for testing a woman pregnant for the first time after age 35 to see if the baby has trisomy-21 (Down syndrome)

Carrier Recognition

- Two major avenues for identifying carriers of genes: pedigrees and blood tests
- Pedigrees trace a particular genetic trait through several generations; helps to predict the future

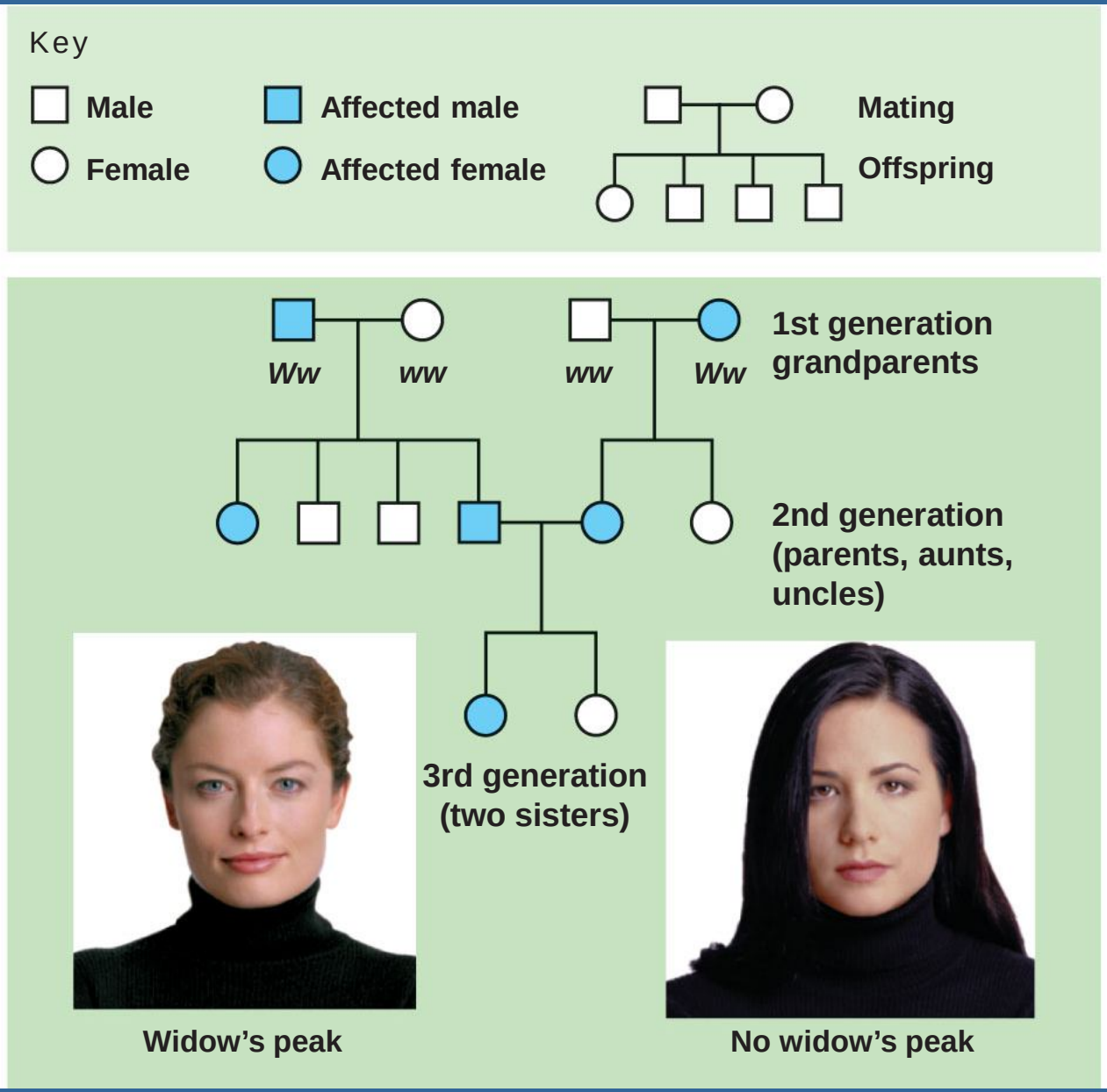

Key
Male
Female
Affected male
Affected female
Mating
Offspring
Ww
ww
ww
Ww
1st generation grandparents
2nd generation (parents, aunts, uncles)
3rd generation (two sisters)
Widow's peak
No widow's peak

Figure 29.7

Carrier Recognition

- Blood tests and DNA probes can detect the presence of unexpressed recessive genes
- Tay-Sachs and cystic fibrosis genes can be identified by such tests

Fetal Testing

- Used when there is a known risk of a genetic disorder
- Amniocentesis: amniotic fluid is withdrawn after the 14th week and fluid and cells are examined for genetic abnormalities
- Chorionic villus sampling (CVS): chorionic villi are sampled and karyotyped for genetic abnormalities

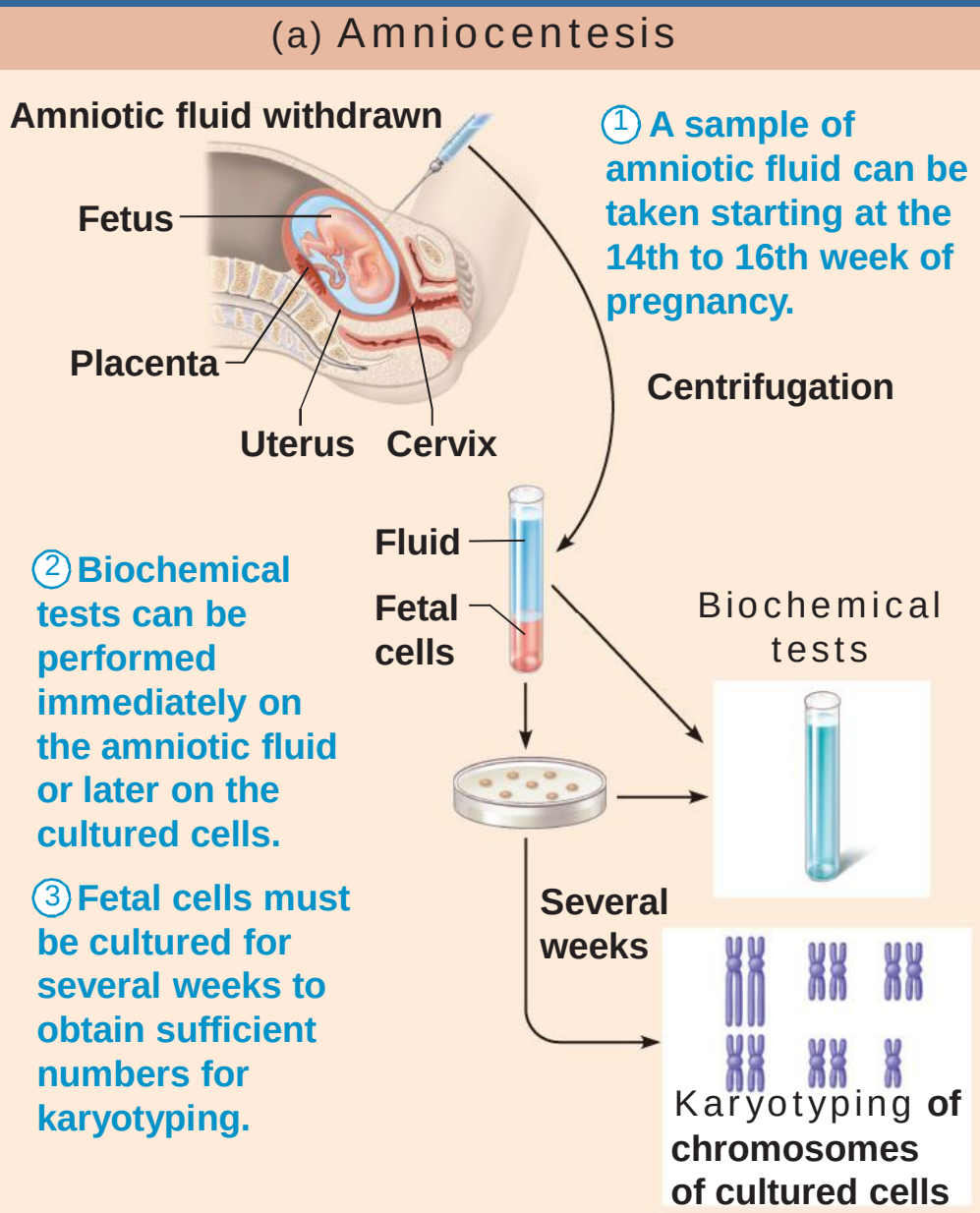

(a) Amniocentesis
Amniotic fluid withdrawn
Fetus
Placenta
Uterus
Cervix
1 A sample of amniotic fluid can be taken starting at the 14th to 16th week of pregnancy.
Centrifugation
Fluid
Fetal cells
2 Biochemical tests can be performed immediately on the amniotic fluid or later on the cultured cells.
3 Fetal cells must be cultured for several weeks to obtain sufficient numbers for karyotyping.
Biochemical tests
Several weeks
Karyotyping of chromosomes of cultured cells

Figure 29.8

Human Gene Therapy

- Genetic engineering has the potential to replace a defective gene
- Defective cells can be infected with a genetically engineered virus containing a functional gene
- The patient's cells can be directly injected with "corrected" DNA