

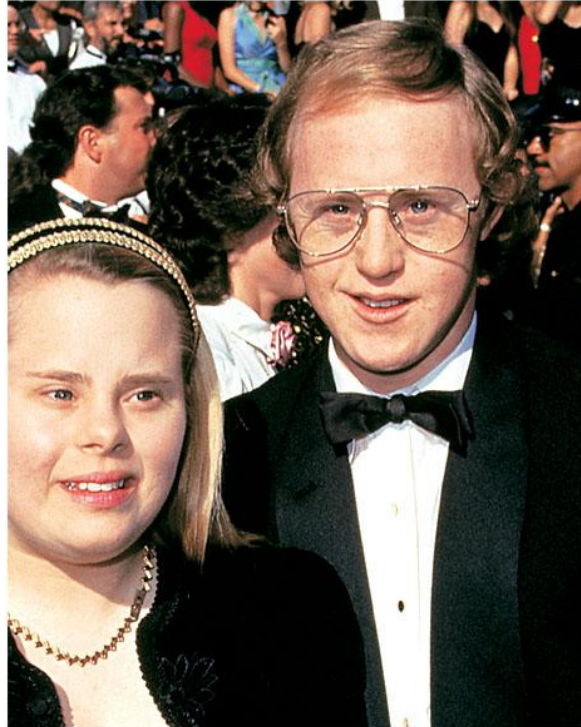
# *Inquiry into Life*

*Eleventh Edition*  
**Sylvia S. Mader**

## Chapter 26 Lecture Outline

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# 26.1 Counseling for chromosomal disorders

- Genetic counseling
  - Determines risk of chromosomal or genetic mutation in a family
  - Allows couples to understand mode of inheritance, medical consequences, and possible decisions
- Counseling for chromosomal disorders
  - Disorders result in **syndromes**-groups of symptoms
  - **Karyotyping**- visual display of chromosomes
    - **Amniocentesis**-14-17<sup>th</sup> week of pregnancy
      - Samples amniotic fluid for baby's cells
    - **Chorionic villi sampling**- 5<sup>th</sup> week of pregnancy
      - Samples cells from chorionic villi of placenta

# Syndromes from abnormal chromosome numbers

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**TABLE 26.1** SYNDROMES FROM ABNORMAL CHROMOSOME NUMBERS

Syndrome	Sex	Chromosomes	Chromosome Number	Frequency	
				<i>Spontaneous Abortions</i>	<i>Live Births</i>
Down	M or F	Trisomy 21	47	1/40	1/800
Poly-X	F	XXX (or XXXX)	47 or 48	0	1/1,500
Klinefelter	M	XXY (or XXXY)	47 or 48	1/300	1/800
Jacobs	M	XYY	47	?	1/1,000
Turner	F	X	45	1/18	1/2,500

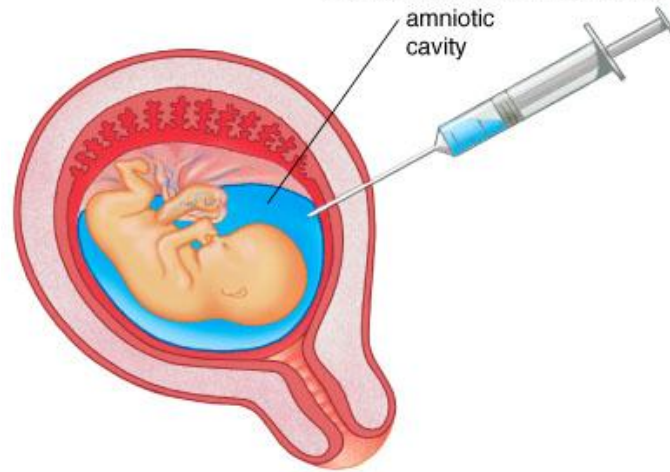
- Table 26.1

# Counseling for chromosomal disorders cont'd.

- The karyotype
  - Cells stimulated to divide in culture medium
  - Chemical stops division in metaphase when chromosomes are most dense
  - Cells are killed, stained, and viewed under a microscope
  - Computer can be used to organize pairs according to size, shape, and banding pattern
  - There should be 23 pairs of chromosomes
    - 22 homologous pairs of autosomes
    - 1 pair of sex chromosomes

# Human karyotype preparation

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a. During amniocentesis, a long needle is used to withdraw amniotic fluid containing fetal cells.



b. During chorionic villi sampling, a suction tube is used to remove cells from the chorion, where the placenta will develop.

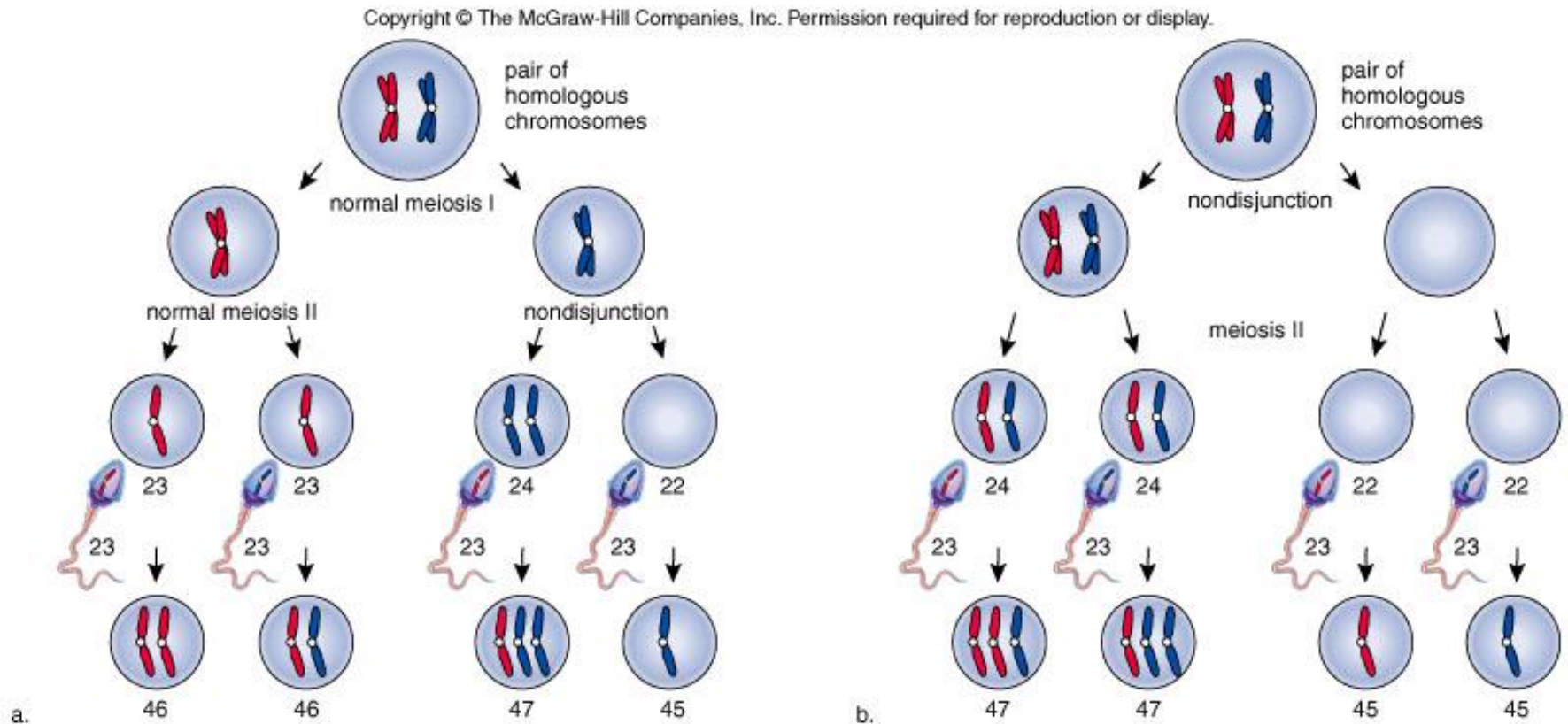


c. Cells are microscopically examined and photographed. Computer arranges the chromosomes into pairs.

# Counseling for chromosomal disorders cont'd.

- Changes in chromosome number
  - Abnormalities in chromosome number may be due to **nondysjunction**
    - When it occurs during meiosis I both members of a homologous pair migrate into the same daughter cell
    - When it occurs in meiosis II, the centromere fails to divide and both daughter chromatids enter the same gamete
      - Egg with 24 chromosomes fertilized by sperm with 23- **trisomy**
      - Egg with 22 chromosomes fertilized by sperm with 23 chromosomes- **monosomy**
  - Normal development depends on the presence of exactly 2 of each kind of chromosome

# Nondysjunction of chromosomes during oogenesis followed by fertilization with normal sperm



• Fig. 26.2

# Counseling for chromosomal disorders cont'd.

- Changes in chromosome number cont'd.
  - Trisomy
    - Three copies of one kind of chromosome
    - The only one compatible with a reasonable chance of survival is trisomy 21 Down Syndrome
  - Monosomy
    - One copy of one kind of chromosome
    - Most are incompatible with life

# Counseling for chromosomal disorders cont'd.

- Chances of survival are greatest if monosomy or trisomy involves the sex chromosomes
  - **Turner's syndrome**-monosomy X (XO), zygote has one X chromosome and no other X or Y
    - Capable of survival, phenotypically female, infertile
  - In normal females, only 1 X is active and the other becomes a **Barr body**- only 1 active X is needed for survival
    - Y chromosome is not needed for survival-how do we know?
    - XXX and XXY are fairly common trisomies-additional X's become Barr bodies
  - **Jacob's syndrome** (XYY) is due to nondysjunction in meiosis II

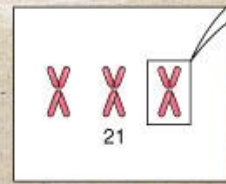
# Counseling for chromosomal disorders cont'd.

- Down Syndrome

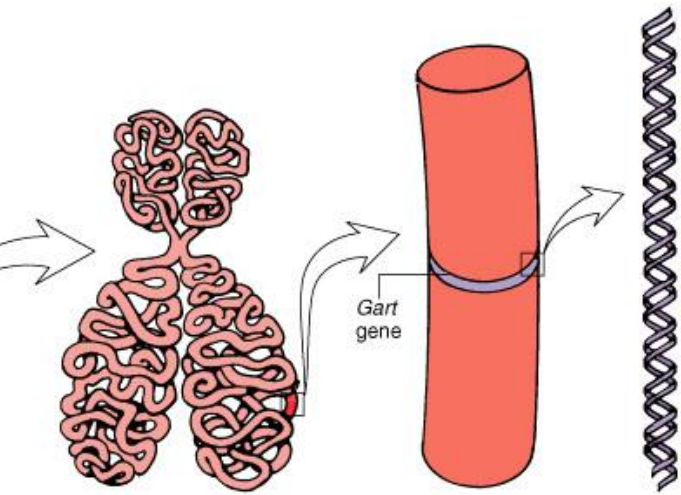
- Most common trisomy in humans
- Short stature, eyelid fold, flat face, stubby fingers, a wide gap between the first and second toes, large fissured tongue, round head, palm crease, simian line, mental retardation
- 3 copies of chromosome 21
  - 75% of cases- egg has 2 copies, sperm has 1
- Can be detected by a karyotype

# Abnormal chromosomal number

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a.



b.

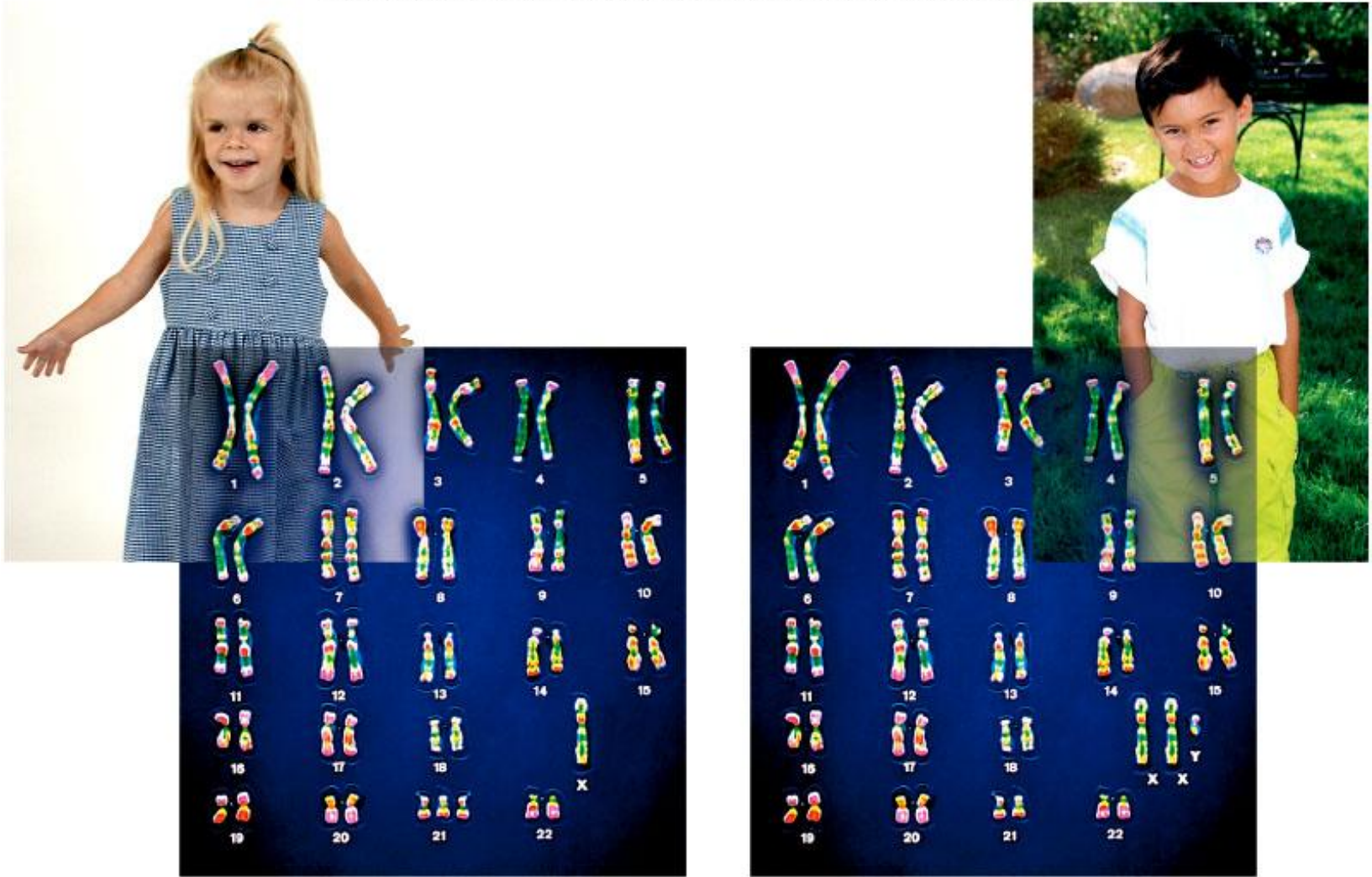
- Fig. 26.3

# Counseling for chromosomal disorders cont'd.

- Changes in sex chromosome number
  - Turner syndrome
    - Short, may have malformed features-webbed neck, high palate, small jaw, congenital heart and kidney defects, ovarian failure, infertility
    - Generally have normal intelligence, may have learning disabilities
  - Klinefelter syndrome
    - XXY
    - Underdeveloped testes and prostate gland, no facial hair
    - Phenotypically male, infertile
    - Generally have normal intelligence, but may be slow learners

# Two sex chromosome abnormalities

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a. Turner syndrome

b. Klinefelter syndrome

# Counseling for chromosomal disorders cont'd.

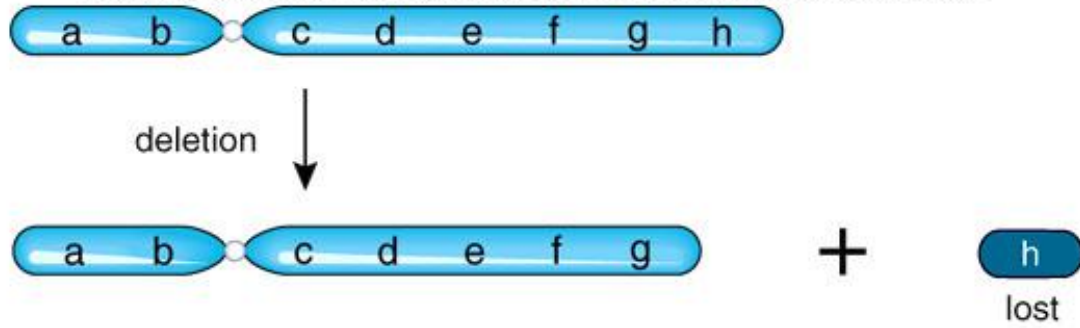
- Changes in sex chromosome number cont'd.
  - Poly-X females
    - More than 2 X chromosomes
    - XXX females may be unusually tall, with delayed language and motor skills but normal cognitive abilities
    - XXXX females are usually severely retarded
  - Jacobs syndrome
    - XYY genotype can only result from nondysjunction in spermatogenesis
    - Taller than average, persistent acne, speech and reading problems

# Counseling for chromosomal disorders cont'd.

- Disorders from changes in chromosomal structure
  - Deletions and mutations
    - **Deletion**- breaks in a chromosome which result in loss of genes
    - **Williams syndrome**
      - Chromosome 7 loses an end piece
        - » Turned up nose
        - » Wide mouth with small chin
        - » Poor academic skills but well-developed verbal and musical skills
    - **Cri du chat syndrome**
      - Chromosome 5 loses an end piece
      - Small head, mental retardation, cat-like cry

# Deletion

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a.



b.

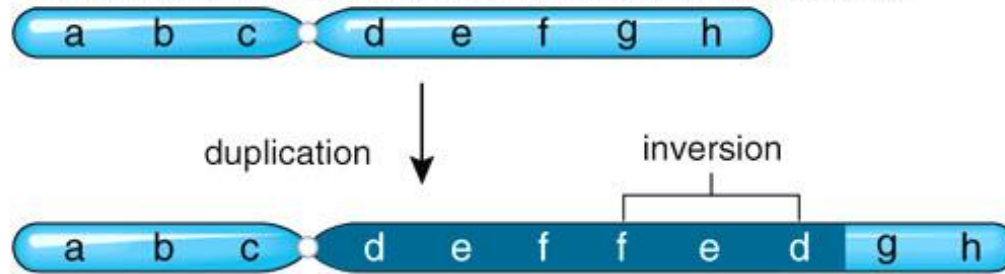
• Fig. 26.5

# Counseling for chromosomal disorders cont'd.

- Disorders from changes in chromosomal structure cont'd.
  - **Duplications**-may have more than 2 alleles for certain traits
    - Inverted duplication of chromosome 15-segment joins in direction opposite from normal
      - Poor muscle tone
      - Mental retardation
      - Seizures, autism
  - **Translocation**-exchange between 2 non-homologues
    - Person with both involved chromosomes is normal
    - Person who inherits only 1 will have various syndromes
      - Depends on which chromosomes are affected

# Duplication

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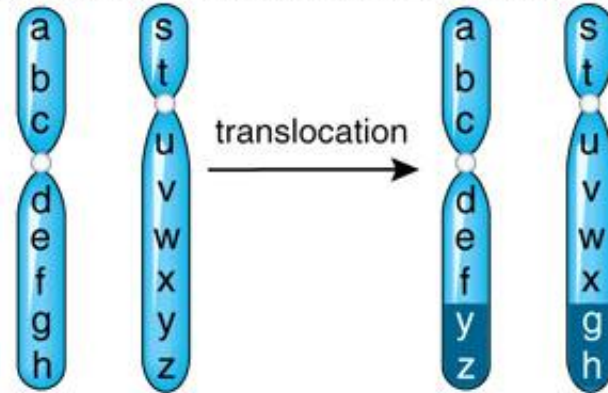
a.



b.

# Translocation

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a.



b.

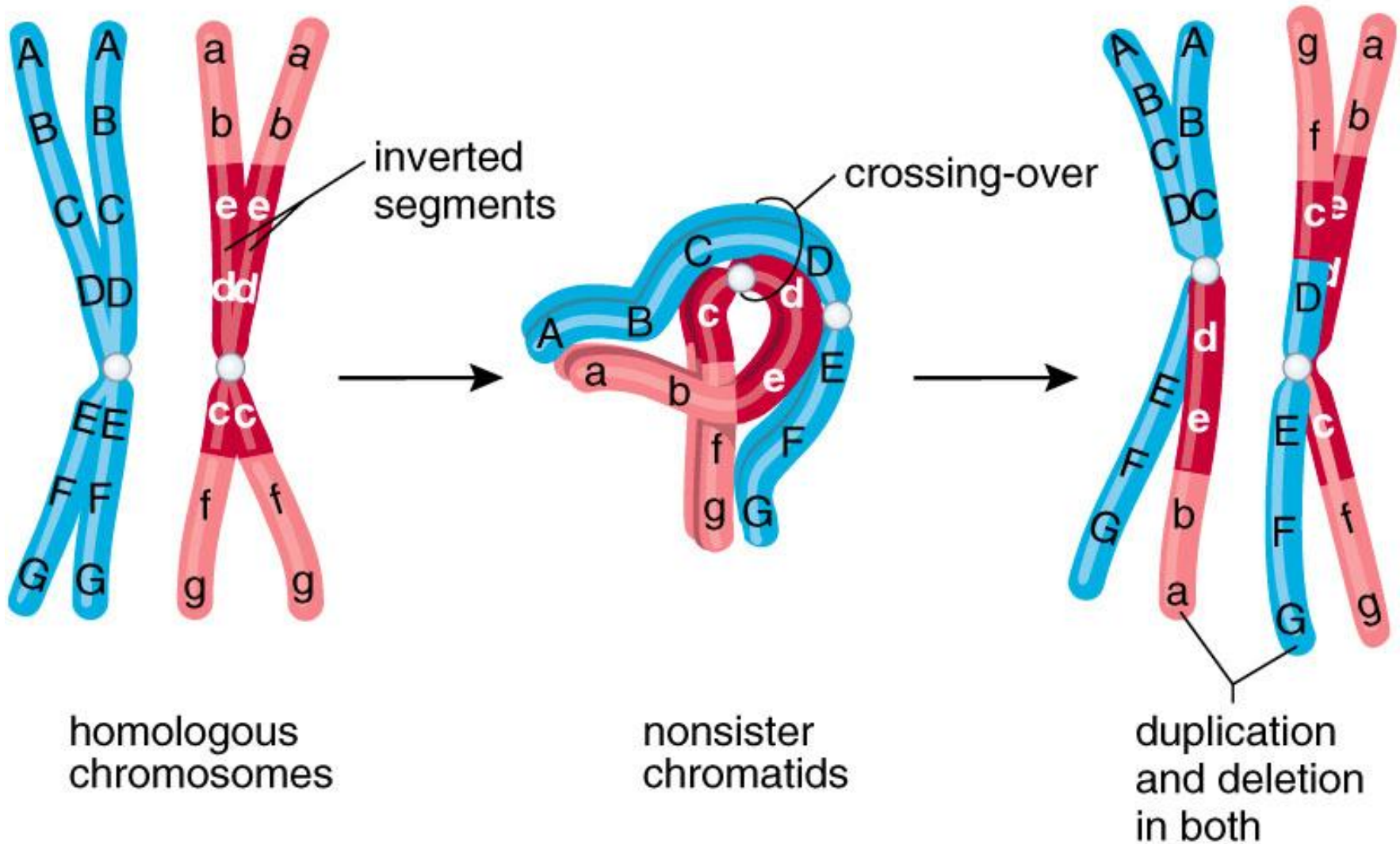
- Fig. 26.7

# Counseling for chromosomal disorders cont'd.

- Disorders from changes in chromosomal structure  
cont'd.
  - Inversion
    - Segment is turned 180 degrees
    - Leads to altered gene activity

# Inversion

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# 26.2 Counseling for genetic disorders: the present

- Family pedigrees

- Chart of family's history

- Key

- Males-squares, females-circles

- Shaded means individual is affected by disorder

- Line between square and circle indicates a union

- Vertical line downward indicates child

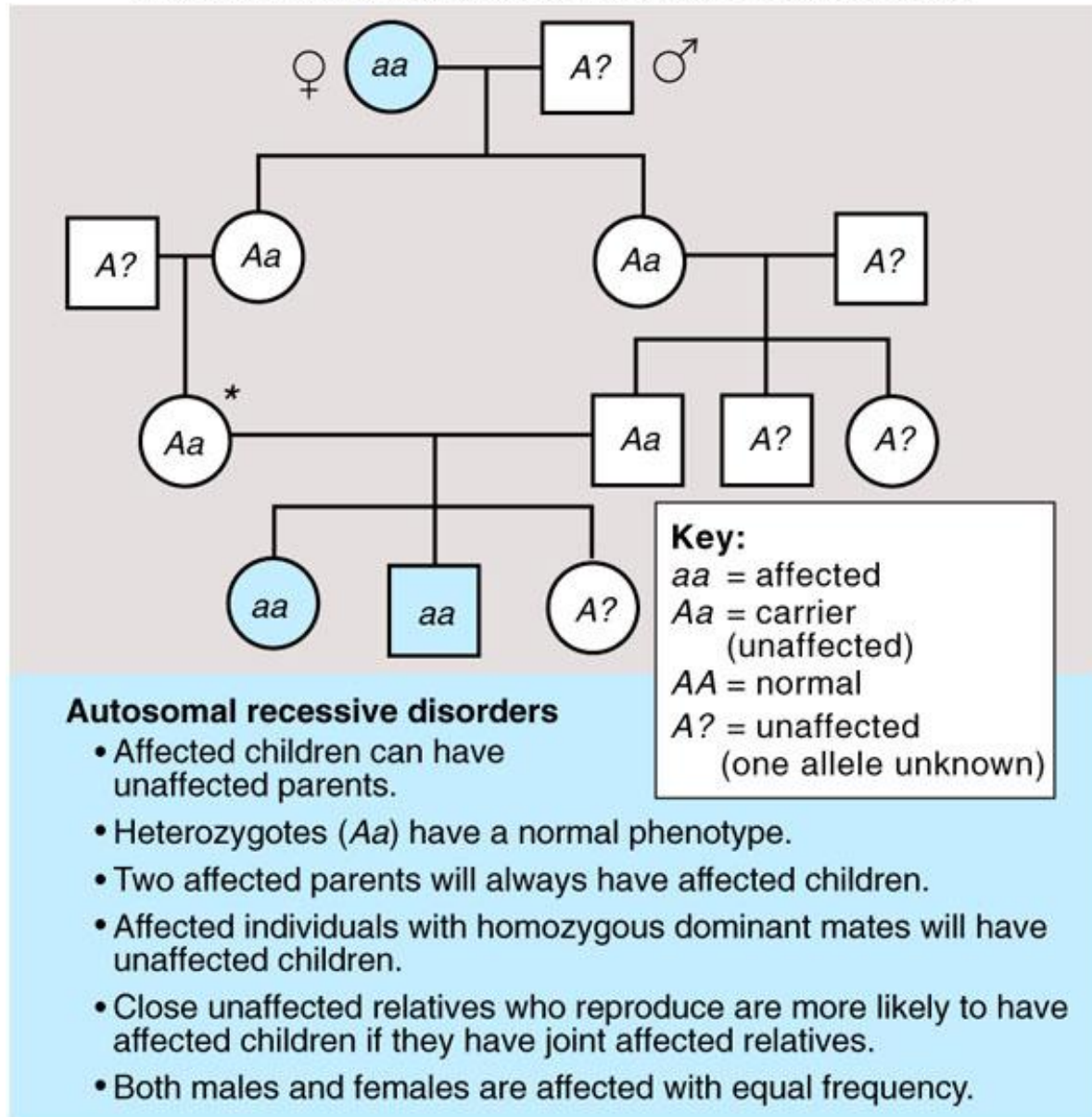
- » Multiple children are drawn off a horizontal line

# Counseling for genetic disorders: the present cont'

- Pedigrees for autosomal disorders
  - An affected child from 2 unaffected parents indicates an autosomal recessive trait
    - Counselor can suggest genetic testing
  - Two affected parents produce an unaffected child
    - Indicates both parents are heterozygous for an autosomal dominant trait
    - Another indicator- when both parents are unaffected, none of their children are either
  - Study the two pedigrees on the following slides

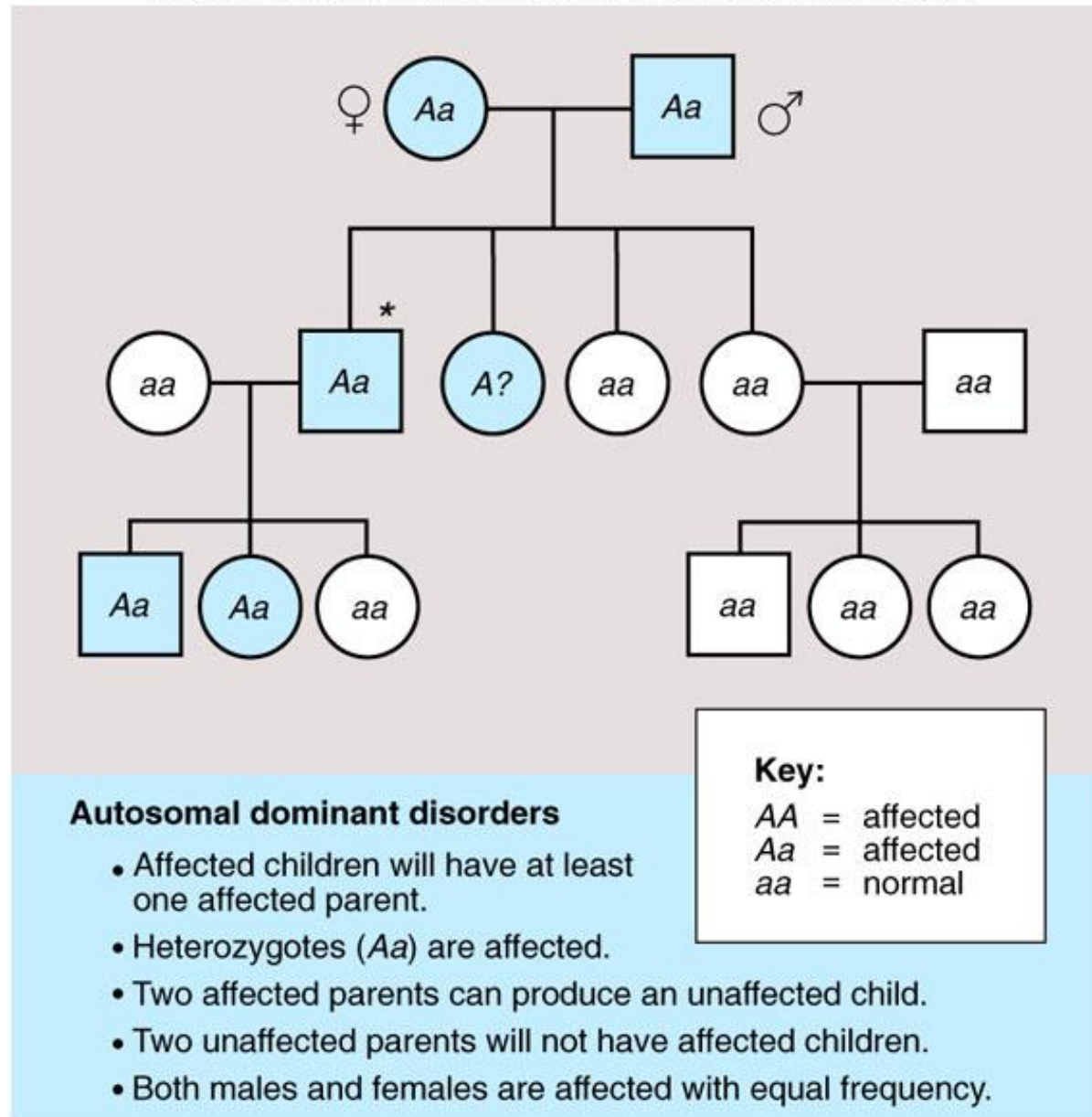
# Autosomal recessive pedigree chart

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# Autosomal dominant pedigree chart

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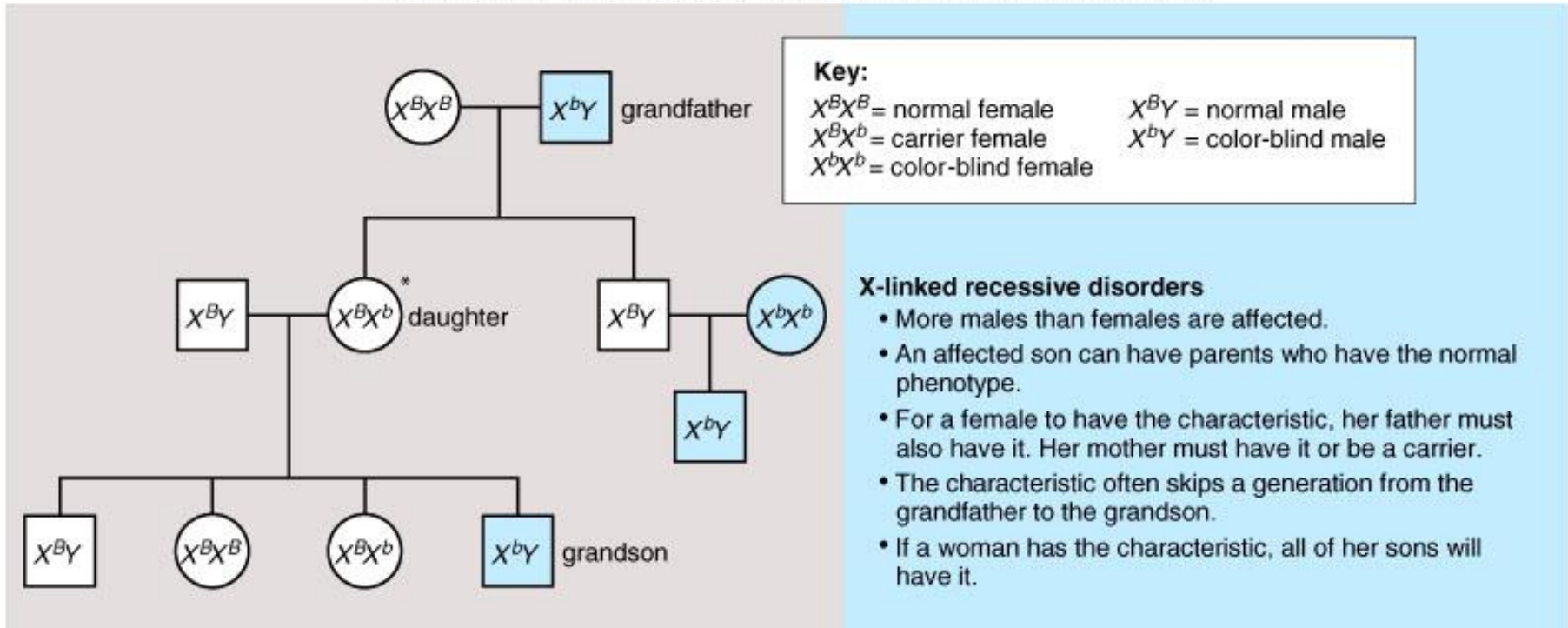
• Fig. 26.10

# Counseling for genetic disorders: the present cont'd.

- Pedigrees for sex-linked disorders
  - X-linked disorders
    - X-linked recessive disorders
      - To be affected, daughters must inherit it from both parents
      - Sons can only inherit it from mother, therefore more males affected than females
    - X-linked dominant disorders
      - Affected males pass the trait only to daughters
      - Females can pass trait to both daughters and sons
  - Y-linked disorders
    - Present only in males
    - Fathers pass trait to all sons
  - Study the pedigree on the following slide

# X-linked recessive pedigree chart

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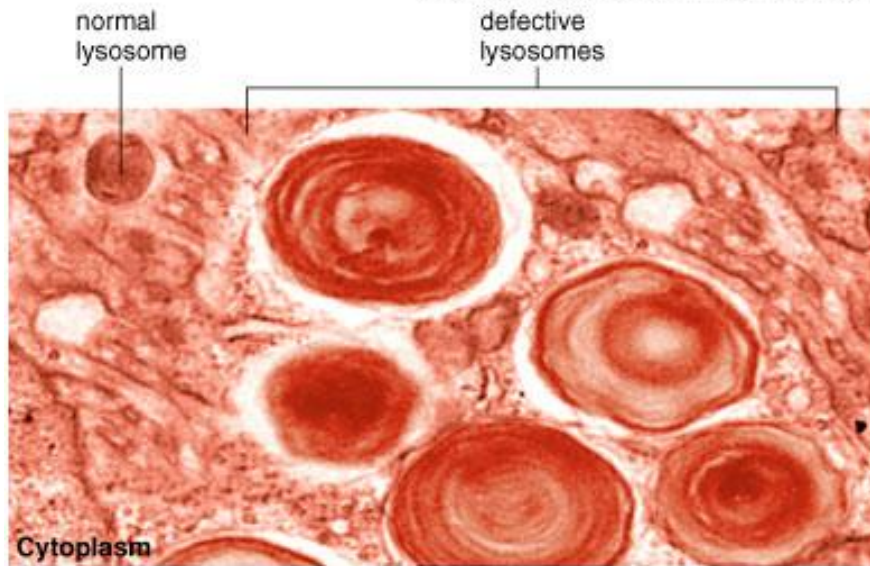
• Fig. 26.11

# Counseling for genetic disorders: the present cont'd.

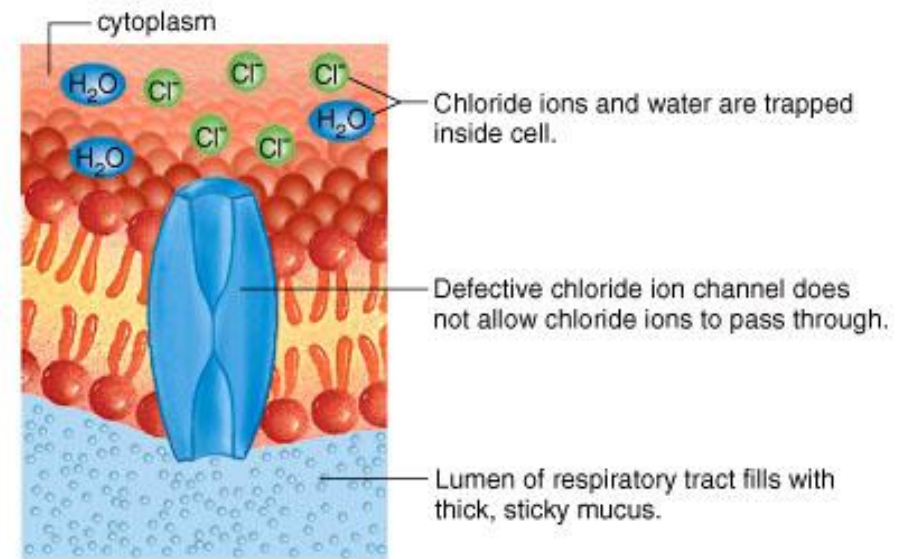
- Genetic disorders of interest
  - Autosomal recessive disorders
    - Tay-sachs disease
      - Jewish people in U.S. of central and eastern European descent
      - Lack of hexosaminidase A
        - » Glycosphingolipid stored in lysosomes
        - » Build up in brain cells-loss of function
      - Symptoms appear in infancy
    - Cystic fibrosis
      - Most common genetic disorder in Caucasians in U.S.
      - Defect in chloride channel proteins in cells
      - Thick, abnormal mucus production
        - » Lungs, bronchial tubes, pancreatic ducts affected

# Genetic disorders

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a. Malfunctioning lysosomes in Tay-Sachs disease.



b. Malfunctioning channel protein in cystic fibrosis.

- Fig. 26.12

# Counseling for genetic disorders: the present cont'd.

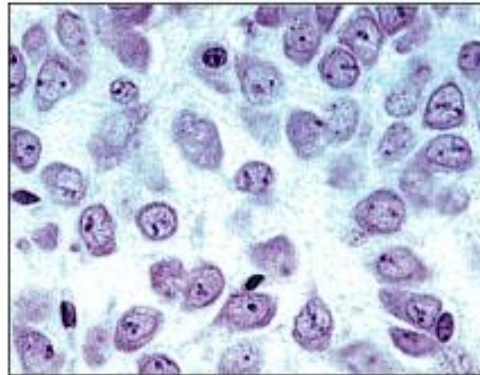
- Autosomal recessive disorders cont'd.
  - Phenylketonuria
    - Lack enzyme for phenylalanine metabolism
    - Affects nervous system development
  - Sickle-cell anemia
    - Irregular red blood cells caused by abnormal hemoglobin
      - Clog vessels- poor circulation
      - Internal hemorrhaging
    - Heterozygous individuals are normal unless dehydrated or experience mild oxygen deprivation

# Genetic disorders

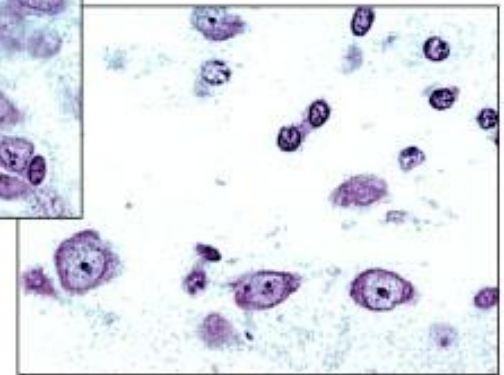
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a. Abnormally shaped red blood cells in sickle-cell disease.



Many neurons in normal brain.



Loss of neurons in Huntington brain.

- Fig. 26.13

# Counseling for genetic disorders: the present cont'd.

- Autosomal dominant disorders
  - Marfan syndrome
    - Defect in fibrillin-protein in elastic connective tissue
      - Long limbs and fingers, weakened arteries, dislocated lenses in the eyes
  - Huntington disease
    - Progressive degeneration of brain cells
    - Gene for defective protein called Huntington
      - Too many copies of the amino acid glutamine

# Counseling for genetic disorders: the present cont'd.

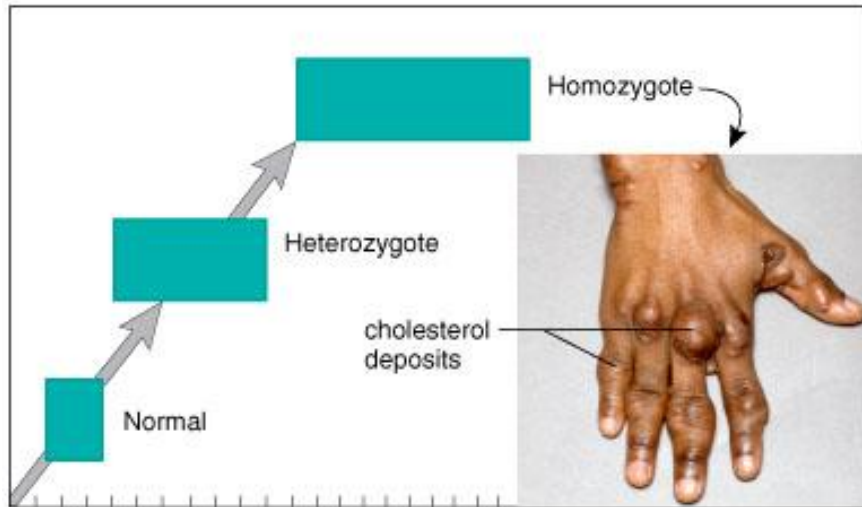
- Incompletely dominant disorders
  - Familial hypercholesterolemia
    - Affects the number of LDL-cholesterol receptors on cells
      - Homozygous for defective gene- has no receptors and develops cardiovascular disease in teenage years
      - Heterozygous individual has half the normal number of receptors

# Counseling for genetic disorders: the present cont'd.

- X-linked recessive disorders
  - Color blindness
    - About 8% of Caucasian males have red-green colorblindness
  - Duchene's muscular dystrophy
    - Absence of a protein called dystrophin
      - Causes calcium to leak into muscle cells which activates enzymes that break down the cells
  - Hemophilia
    - Hemophilia A is due to a lack of clotting factor VIII
    - Hemophilia B is due to a lack of clotting factor IX
    - Blood clots slowly or not at all

# Genetic disorders

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a. Cholesterol levels in familial hypercholesterolemia (FH).



b. Abnormal muscle in muscular dystrophy

# Counseling for genetic disorders: the present cont'd.

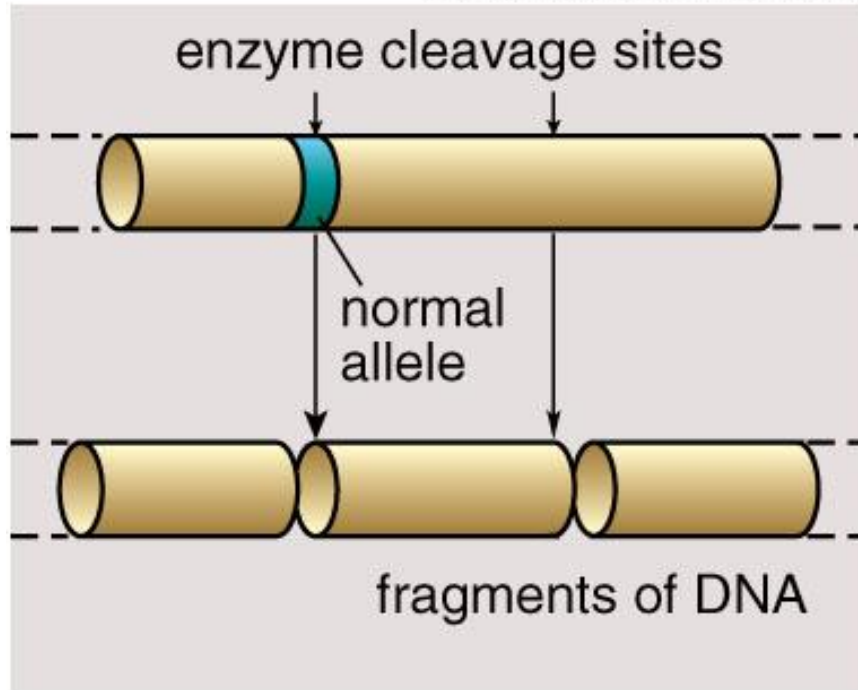
- Testing for genetic disorders
  - Testing for a protein
    - Some mutations lead to disorders caused by a missing enzyme
      - Tay-sachs disease-test for quantity of hex A enzyme present in a sample of cells
        - » can determine if individual is homozygous normal, a carrier, or has Tay-sachs
      - PKU-blood test done on all newborns to detect the presence of phenylalanine

# Counseling for genetic disorders: the present cont'd.

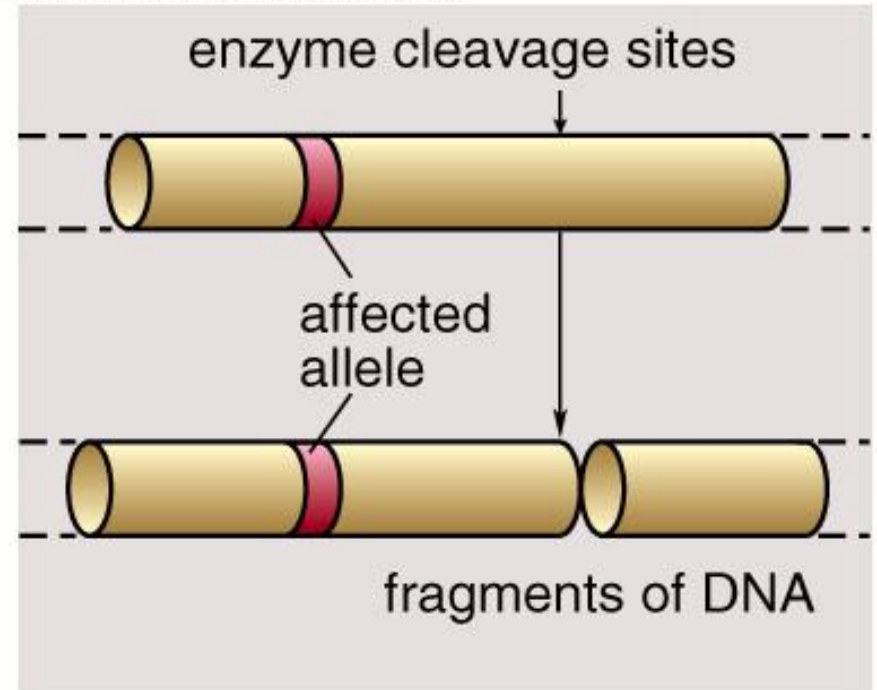
- Testing for genetic disorders cont'd.
  - Testing the DNA
    - Testing for genetic markers-similar to DNA fingerprinting
      - Restriction enzymes cleave DNA
      - Used to test for Huntington disease
    - Testing with DNA probes
      - DNA probe-single stranded piece of DNA that binds to complementary DNA
        - » For genetic testing, the probe has a mutation of interest
      - DNA chip can test for many abnormalities at once
        - » Has many DNA segments
        - » mutated genes bind if present and are detected by laser scanner

# Use of genetic marker to test for a genetic mutation

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a. Normal fragmentation pattern

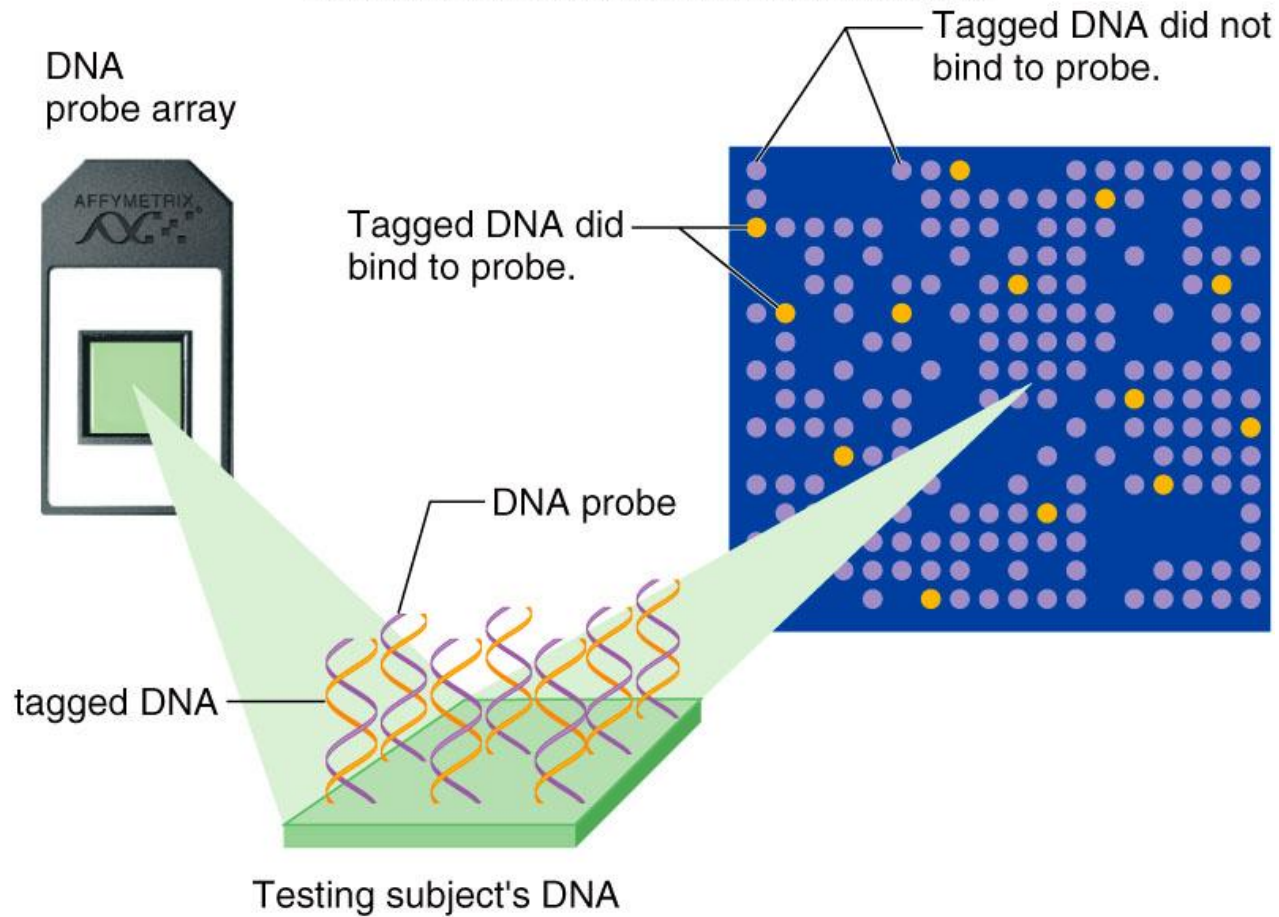


b. Genetic disorder fragmentation pattern

- Fig. 26.15

# Use of a DNA chip to test for mutated genes

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# Counseling for genetic disorders: the present cont'd.

- Testing for genetic disorders cont'd.
  - Testing the fetus, embryo, or egg
    - Ultrasound-can detect severe disorders like spina bifida
  - Testing fetal cells
    - Amniocentesis-performed at 12 weeks of gestation; carries a risk of miscarriage; because amniotic fluid is sampled, can also test for alpha fetoprotein which can indicate neural tube defects
    - Chorionic villi sampling- performed at 7 weeks of gestation; no amniotic fluid taken so cannot test for AFP; shorter wait for results than amniocentesis but slightly higher risk of miscarriage
    - Fetal cells in mother's blood-at 9 weeks of gestation 1/70,000 RBC's in mother's bloodstream are nucleated fetal cells
      - Must use PCR to amplify

# Ultrasound

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• Fig. 26.17

# Counseling for genetic disorders: the present cont'd.

- Testing for genetic disorders cont'd.
  - Testing the embryo
    - If both parents are carrier, they may want assurance that embryo is normal
      - Following in vitro fertilization, can remove a cell at 6-cell stage and test for defect, then implant only those embryos that are normal
  - Testing the egg
    - Test the polar bodies of women who are heterozygous prior to in vitro fertilization
      - If the polar body has the defect, then the ovum is normal

# 26.3 Counseling for genetic disorders: the future

- The human genome project
  - Goals
    - To construct a base sequence map
    - To construct a genetic map of each chromosome
  - The base sequence map
    - 3 million base pairs now known
    - Humans share many genes in common with all other living organisms
  - The genetic map
    - Exact number of genes is unknown at this time
    - Researchers only need to know a short sequence of bases in a gene, and a computer searches the genome for a match

# Genetic map of chromosome 17

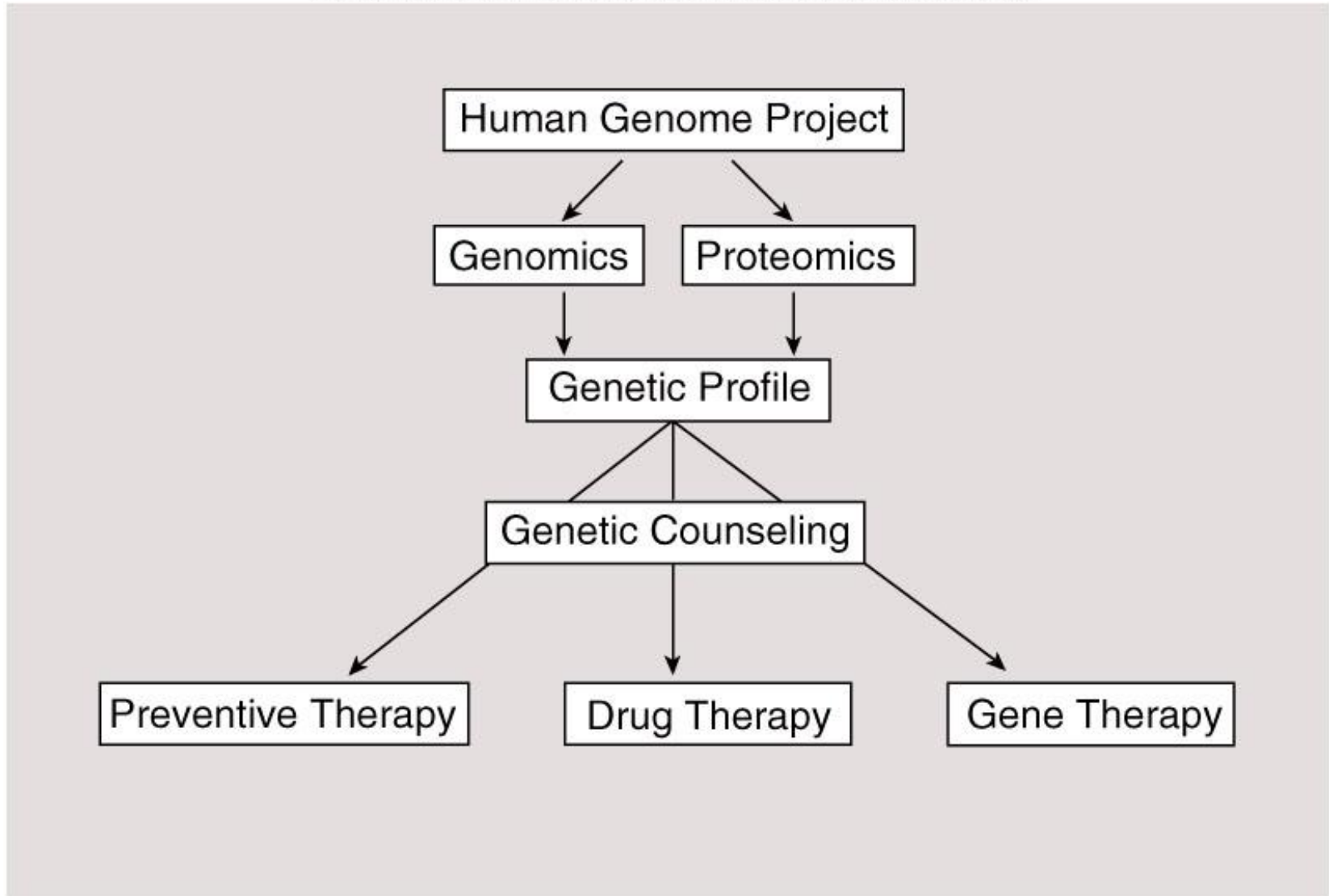
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- Fig. 26.18

# Human genome project

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• Fig. 26.19

# Counseling for genetic disorders: the present cont'd.

- Genomics
  - The study of the human genome
  - Determines how all genes in the genome interact to produce a phenotype
- The genetic profile
  - DNA chips will be available with a person's entire genome, including mutations
  - Can be obtained by using cheek cells
  - DNA is then amplified by PCR, cleaved, and tagged with a fluorescent dye

# Counseling for genetic disorders: the present cont'd.

- **Benefits of genetic profiling**
  - Individuals can be educated by a counselor about their profiles
  - Risk information can then be used to formulate medical surveillance
  - May also provide information about which drug therapies will be most effective against disease
- **Proteomics**
  - Study of structure, function, and interaction of cellular proteins
  - Translation of all human genes results in a collection of proteins called the proteome
  - Computer modeling provides information about the three-dimensional shape of protein molecules
    - May be possible to correlate drug treatment to genetic profiles

# Counseling for genetic disorders: the present cont'd.

- **Bioinformatics**

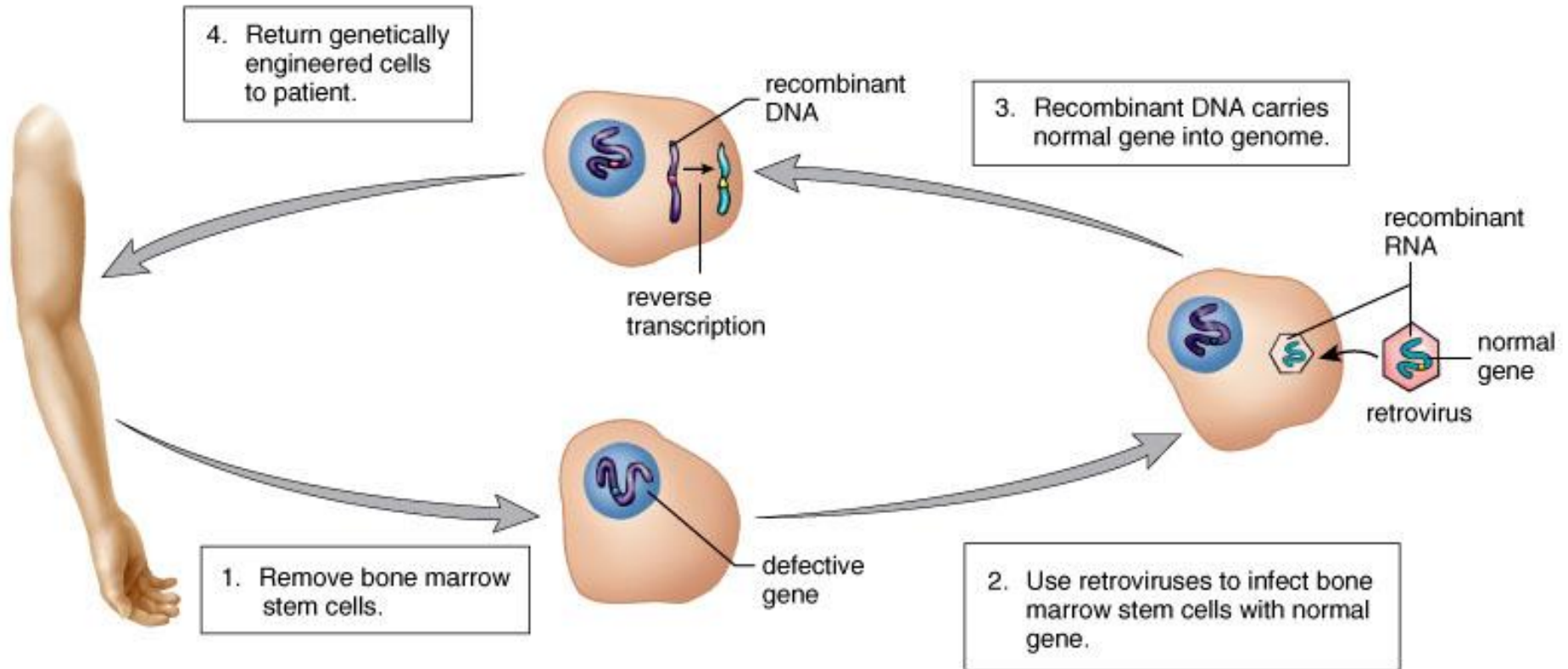
- Application of computer technologies to the study of the genome
- Analysis of data produced by genomics and proteomics
- Cause and effect relationships between various genetic profiles and genetic disorders caused by polygenes
- Current genome includes 82 gene “deserts” with no known function
  - Bioinformatics may discover functions of these regions

# Counseling for genetic disorders: the present cont'd.

- Gene therapy
  - Insertion of genetic material into human cells for treatment of a disorder
  - Ex vivo gene therapy
    - Cells are removed from the patient
      - Treated outside the body and then returned to the patient
  - In vivo gene therapy
    - Patient is given a foreign gene directly
    - Gene is incorporated into the genome within the body

# Ex vivo gene therapy in humans

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• Fig. 26.21