Variations in Chromosome Number

When an organism or a cell has one complete set of chromosomes or an exact multiple of complete sets, that organism or cell is said to be **euploid.** Thus, eukaryotic organisms that are normally diploid (such as humans and fruit flies) and eukaryotic organisms that are normally haploid (such as yeast) are euploids. Chromosome mutations that result in variations in the number of chromosome sets occur in nature, and the resulting organism or cells are also euploid. Chromosome mutations resulting in variations in the number of individual chromosomes are examples of **aneuploidy.** An **aneuploid** organism or cell has a chromosome number that is not an exact multiple of the haploid set of chromosomes. Both euploid and aneuploid variations affecting whole chromosomes are discussed in this section.

Changes in One or a Few Chromosomes

Generation of Aneuploidy. Changes in chromosome number can occur in both diploid and haploid organisms. The nondisjunction of one or more chromosomes during meiosis I or meiosis II typically is responsible for generating gametes with abnormal numbers of chromosomes. Nondisjunction was discussed in Chapter 12 in the context

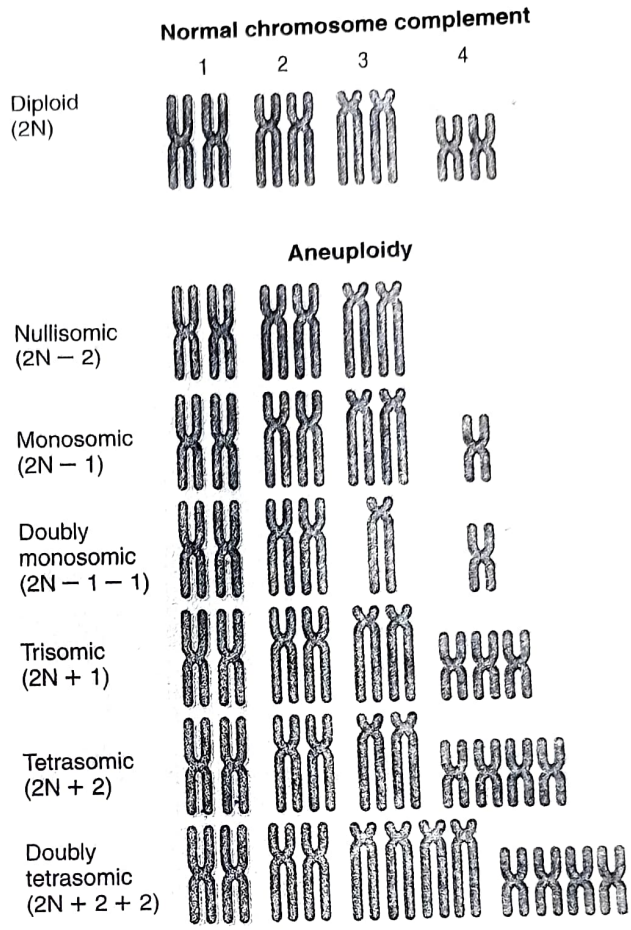
of unusual complements of X chromosomes, with Figure 12.18 (p. 344) illustrating the consequences of nondisjunction at the first and second meiotic divisions. Referring to that figure and considering just one particular chromosome, one can see that nondisjunction at meiosis I produces four abnormal gametes: two with a chromosome duplicated and two with the corresponding chromosome missing. In a male, nondisjunction at meiosis I can produce a gamete with both the X and the Y chromosome; in a female, it produces a gamete with both sets of homologs (and thus possible heterozygotes). Fusion of the former gamete type with a normal gamete produces a zygote with three copies of the particular chromosome instead of the normal two and, unless nondisjunction also involves other chromosomes, there will be two copies of all other chromosomes. The latter gamete type may well be inviable. If it is viable, fusion with a normal gamete produces a zygote with only one copy of the particular chromosome instead of the normal two, and two copies of all other chromosomes. Nondisjunction in meiosis II (see Figure 12.18) is different from nondisjunction in meiosis I in that some normal gametes are produced. As Figure 12.19 shows, nondisjunction in meiosis II results in two normal gametes and two abnormal gametes—that is, a single gamete with two daughter chromosomes and one gamete with that same chromosome missing. Fusion of these with normal gametes gives the zygote types just discussed. Nondisjunction can occur in mitosis, giving rise to somatic cells with unusual chromosome complements.

Types of Aneuploidy. In aneuploidy, one or more chromosomes are lost from or added to the normal set of chromosomes (Figure 16.15). Aneuploidy can occur, for example, from the loss of individual chromosomes in meiosis or (rarely) in mitosis by nondisjunction. In animals, autosomal aneuploidy is almost always lethal, so in mammals it is detected mainly in aborted fetuses. Aneuploidy is tolerated more by plants, especially in species that are considered polyploid (having more sets of chromosomes than the usual two).

In diploid organisms, there are four main types of aneuploidy (see Figure 16.15):

1. **Nullisomy** (a nullisomic cell) involves a loss of one homologous chromosome pair—the cell is 2N − 2. (Nullisomy can arise, for example, if nondisjunction occurs for the same chromosome in meiosis in both parents, producing gametes with no copies of that chromosome and one copy of all other chromosomes in the set.)
2. **Monosomy** (a monosomic cell) involves a loss of a single chromosome—the cell is 2N − 1. (Monosomy can arise, for example, if nondisjunction in meiosis in a parent produces a gamete with no copies of a particular chromosome and one copy of all other chromosomes in the set.)
3. **Trisomy** (a trisomic cell) involves a single extra chromosome—the cell has three copies of a particular chromosome and two copies of all other chromosomes. A trisomic cell is 2N + 1. (Trisomy can arise, for example, if nondisjunction in meiosis in a parent produces a gamete with two copies of a particular chromosome and one copy of all other chromosomes in the set.)
4. **Tetrasomy** (a tetrasomic cell) involves an extra chromosome pair; that is, there are four copies of one particular chromosome and two copies of all other chromosomes—the cell is 2N + 2. (Tetrasomy can arise, for example, if nondisjunction occurs for the same chromosome in meiosis in both parents, producing gametes with two copies of that chromosome and one copy of all other chromosomes in the set.)

Figure 16.15
Normal (theoretical) set of metaphase chromosomes in a diploid (2N) organism *(top)* and examples of aneuploidy *(bottom)*.



Aneuploidy may involve the loss or the addition of more than one specific chromosome or chromosome pair. For example, a *double monosomic* has two separate chromosomes present in only one copy each; that is, it is 2N − 1 − 1. A *double tetrasomic* has two chromosomes present in four copies each; that is, it is 2N + 2 + 2. In both cases, meiotic nondisjunction involved two different chromosomes in one parent's gamete production.

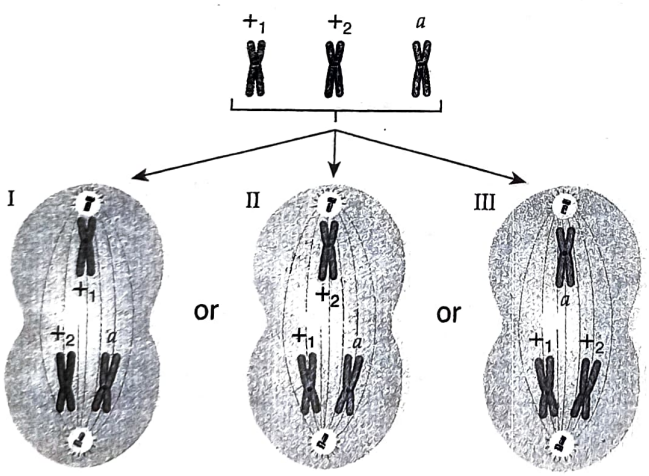
Most forms of aneuploidy have serious consequences in meiosis. Monosomics, for example, produce two kinds

of haploid gametes: N and N − 1. Alternatively, the odd, unpaired chromosome in the 2N − 1 cell may be lost during meiotic anaphase and not be included in either daughter nucleus, thereby producing two N − 1 gametes. For trisomics, there are more segregation possibilities in meiosis. Consider a trisomic of genotype +/+/*a* in an organism that can tolerate trisomy, and assume no crossing-over between the *a* locus and its centromere. Then, as shown in Figure 16.16, random segregation of the three types of chromosomes produces four genotypic classes of gametes: 2 (+ *a*) : 2 (+) : 1 (+ +) : 1 (*a*). In a cross of a +/+/*a* trisomic with an *a*/*a* individual, the predicted phenotypic ratio among the progeny is 5 wild type (+) : 1 mutant (*a*). This ratio is seen in many actual crosses of this kind.

In the sections that follow, we examine some examples of aneuploidy as they are found in the human population. Table 16.1 summarizes various aneuploid abnormalities for autosomes and for sex chromosomes in the human population. Examples of aneuploidy of the X and Y chromosomes are discussed in Chapter 12. Recall that, in mammals, aneuploidy of the sex chromosomes is more often found in adults than is aneuploidy of the autosomes, because of a dosage compensation mechanism (lyonization) by which excess X chromosomes are inactivated.

Figure 16.16

Meiotic segregation possibilities in a trisomic individual. Shown is segregation in an individual of genotype +/+/*a* when two chromosomes migrate to one pole and one goes to the other pole, and assuming no crossing-over between the *a* locus and its centromere. The two + alleles are labeled $+_1$ and $+_2$ to distinguish them.



Gametes produced after 2nd meiotic division

	haploid	disomic
I	$+_1$	$+_2/a$
II	$+_2$	$+_1/a$
III	*a*	$+_1/+_2$

In sum: 2 +/*a* : 2 + : 1 +/+ : 1 *a*

Table 16.1 Aneuploid Abnormalities in the Human Population

Chromosomes	Syndrome	Frequency at Birth
Autosomes		
Trisomic 21	Down	14.3/10,000
Trisomic 13	Patau	2/10,000
Trisomic 18	Edwards	2.5/10,000
Sex chromosomes, females		
XO, monosomic	Turner	4/10,000 females
XXX, trisomic	Viable; most	
XXXX, tetrasomic	are fertile	14.3/10,000 females
XXXXX, pentasomic		
Sex chromosomes, males		
XYY, trisomic	Normal	25/10,000 males
XXY, trisomic		
XXYY tetrasomic	Klinefelter	40/10,000
XXXY, tetrasomic		

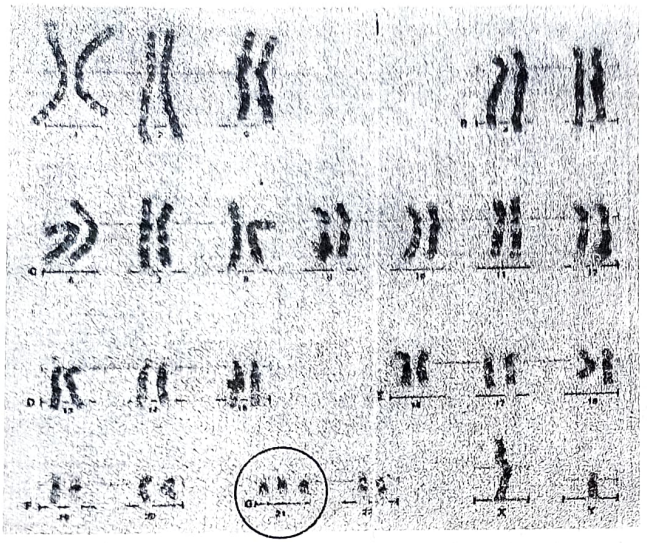
In humans, autosomal monosomy is rare. Presumably, monosomic embryos do not develop significantly and are lost early in pregnancy. In contrast, autosomal trisomy accounts for about one-half of chromosomal abnormalities producing fetal deaths. In fact, only a few autosomal trisomies are seen in live births. Most of these (trisomy-8, -13, and -18) result in early death. Only in trisomy-21 (Down syndrome) does survival to adulthood occur.

Trisomy-21. **Trisomy-21** (OMIM 190685) occurs when there are three copies of chromosome 21 (Figure 16.17a) and with a frequency of about 3,510 per 1 million conceptions and about 1,430 per 1 million live births. Individuals with trisomy-21 have Down syndrome (Figure 16.17b), characterized by such abnormalities as low IQ, epicanthal folds (in which the skin of the upper eyelid forms a layer that covers the inner corner of the eye), short and broad hands, and below-average height. Down syndrome is named for the late-nineteenth-century English physician John Langdon Down, who, in 1866, became the first to publish an accurate description of a person with the condition.

A direct relationship exists between maternal age and probability of giving birth to an individual with trisomy-21. (Table 16.2). (For many years, it was thought that there was no correlation with age of the father. Recent evidence, however, indicates that paternal age has an effect on Down syndrome if the mother is 35 years old or older; in younger women, there is no paternal effect.) During the development of a female fetus before birth, the primary oocytes in the ovary undergo meiosis, but stop at prophase I. In a fertile female, each month at ovulation the nucleus of a secondary oocyte (see Chapter 12) begins the second meiotic division, but progresses only to metaphase, when division

Figure 16.17
Trisomy-21 (Down syndrome).

a) Karyotype (G banding)



b) Individual with trisomy-21 (Down syndrome)

Table 16.2 Relationship Between Age of Mother and Risk of Trisomy-21

Age of Mother	Risk of Trisomy-21 in Child
16–26	7.7/10,000
27–34	4/10,000
35–39	29/10,000
40–44	100/10,000
45–47	333/10,000
All mothers combined	14.3/10,000

again stops. If a sperm penetrates the secondary oocyte, the second meiotic division is completed. The probability of nondisjunction increases with the length of time the primary oocyte is in the ovary. It is important, then, that older mothers-to-be consider testing—for example, by undergoing amniocentesis or chorionic villus sampling (see Chapter 4, p. 74)—to determine whether the fetus has a normal complement of chromosomes.

Are there other risk factors for having a Down syndrome baby? Where a person lives, social class, and race have no influence on the chance of having a baby with Down syndrome. However, mothers under 35 years of age who smoke are at an increased risk of having children with the syndrome. If mothers with these characteristics use cigarettes and oral contraceptives, the risk is increased over using cigarettes alone. Oral contraceptive use alone for this class of mothers has no effect on the incidence of Down syndrome.

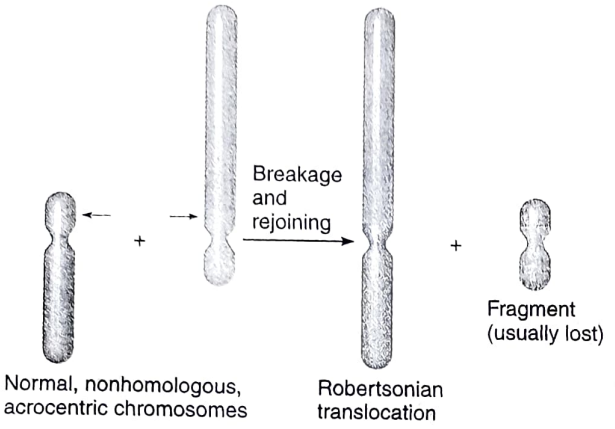
Down syndrome can also result from a different sort of chromosomal mutation called centric fusion or **Robertsonian translocation,** which produces three copies of the long arm of chromosome 21. (The translocation is named for W. R. B. Robertson, an insect geneticist who first described this type of chromosomal mutation.) This form of Down syndrome, called familial Down syndrome, is responsible for 2–3% of Down syndrome cases. A Robertsonian translocation is a type of reciprocal translocation in which two nonhomologous acrocentric chromosomes (chromosomes with centromeres near their ends) break at their centromeres and then the long arms become attached to a single centromere (Figure 16.18). The short arms also join to form the reciprocal product, which typically contains nonessential genes and usually is lost within a few cell divisions. In humans, when a Robertsonian translocation joins the long arm of chromosome 21 with the long arm of chromosome 14 (or 15), the heterozygous carrier is phenotypically normal, because there are two copies of all major chromosome arms and hence two copies of all essential genes.

Animation
Down Syndrome Caused by a Robertsonian Translocation

There is a high risk of Down syndrome among the offspring of pairings between heterozygous carriers and normal individuals (Figure 16.19). The normal parent produces gametes with one copy each of chromosomes 14 and 21. The heterozygous carrier parent produces three reciprocal pairs of gametes, each as a result of different segregation of the three chromosomes involved: (1) 14/21 (translocated 14 and 21) + 21, and 14; (2) 14/21 + 14, and 21; and (3) 14/21, and 14 + 21 (The three gamete pairs do not occur with equal frequency.) The zygotes are produced by pairing these gametes with gametes of normal chromosomal constitution: 14 and 21. Figure 16.19 shows the result of the gamete fusions. In only one case is

Figure 16.18

Robertsonian translocation. Production of a Robertsonian translocation (centric fusion) by breakage of two acrocentric chromosomes at their centromeres (indicated by arrows) and fusion of the two large chromosome arms and of the two small chromosome arms.



a normal zygote produced with chromosomes 14, 14, 21, and 21. One other zygote that leads to a normal phenotype is a carrier zygote with chromosomes 14, 21, and 14/21. A viable trisomy-21 zygote is produced with chromosomes 14, 14/21, 21, and 21. Three inviable zygotes are produced, one with monosomy-21, one with trisomy-14, and one with monosomy-14.

Trisomy-13. **Trisomy-13** produces Patau syndrome (Figure 16.20). About 2 in 10,000 live births produce individuals with trisomy-13. Characteristics of individuals with trisomy-13 include cleft lip and palate, small eyes, polydactyly (extra fingers and toes), mental and developmental retardation, and cardiac anomalies, among many other abnormalities. Most infants die before the age of 3 months.

Trisomy-18. **Trisomy-18** produces Edwards syndrome (Figure 16.21), which occurs in about 2.5 in 10,000 live births. For reasons that are not known, about 80 percent of infants with Edwards syndrome are female. Individuals with trisomy-18 are small at birth and have multiple congenital malformations affecting almost every organ in the body. Clenched fists, an elongated skull, low-set malformed ears, mental and developmental retardation, and many other abnormalities are associated with the syndrome. Ninety percent of infants with trisomy-18 die within 6 months, often from cardiac problems.

Changes in Complete Sets of Chromosomes

Monoploidy and **polyploidy** involve variations from the normal state in the number of complete sets of chromosomes. Because the number of complete sets of chromosomes is involved in each case, monoploids and polyploids are euploids. Monoploidy and polyploidy are lethal in most animal species, but are less consequential in plants.

Figure 16.19

The three segregation patterns of a heterozygous Robertsonian translocation involving human chromosomes 14 and 21. Fusion of the resulting gametes with gametes from a normal parent produces zygotes with various combinations of normal and translocated chromosomes.

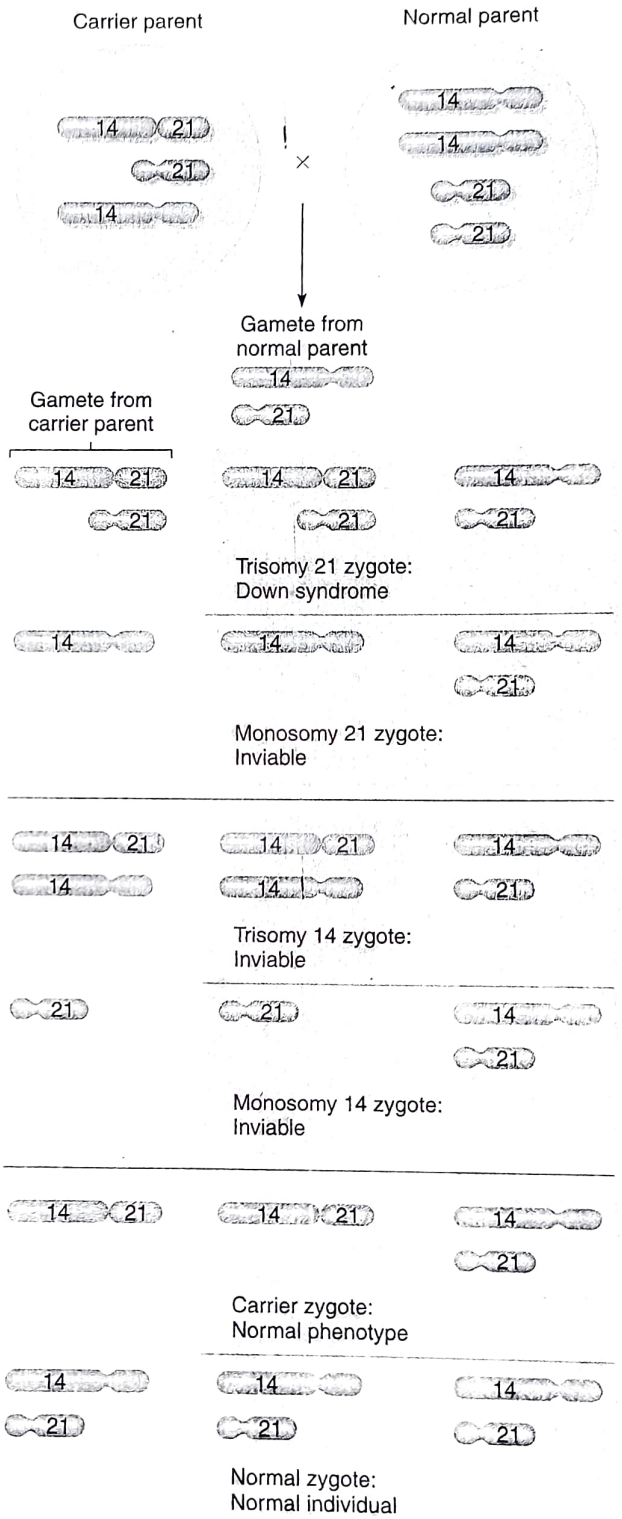
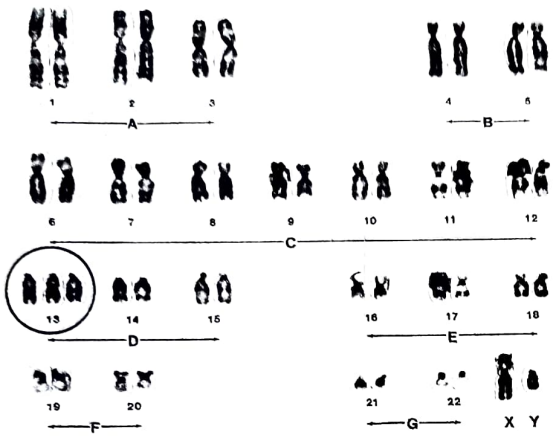
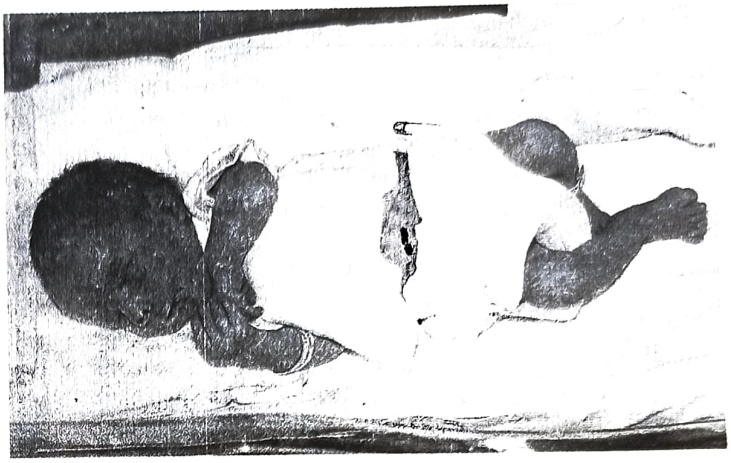


Figure 16.20
Trisomy-13 (Patau syndrome).

a) Karyotype (G banding)



b) Individual with trisomy-13 (Patau syndrome)



Both have played significant roles in plant speciation and diversification.

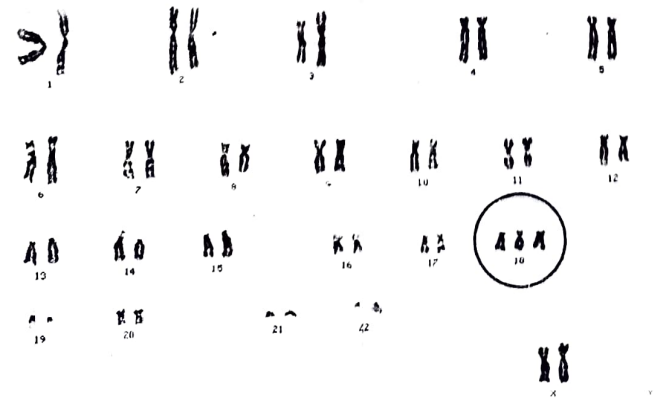
Changes in complete sets of chromosomes result when the first or second meiotic division is abortive (resulting in a lack of cytokinesis) or when meiotic nondisjunction occurs for all chromosomes, for example. If such nondisjunction occurs at meiosis I, half of the gametes have no chromosome sets, and half have two chromosome sets (see Figure 12.18b, p. 344). If such nondisjunction occurs at meiosis II, half of the gametes have the normal one set of chromosomes, one-quarter have two sets of chromosomes, and one-quarter have no chromosome sets (see Figure 12.18c). Fusion of a gamete with two chromosome sets with a normal gamete produces a polyploid zygote—in this case, one with three sets of chromosomes, which is a *triploid* (3N). Similarly, fusion of two gametes, each with two chromosome sets, produces a *tetraploid* (4N) zygote. Polyploidy of somatic cells can also occur following the mitotic nondisjunction of complete chromosome sets. Monoploid (haploid) individuals, by contrast, typically develop from unfertilized eggs.

Monoploidy. A monoploid individual has only one set of chromosomes instead of the usual two sets (Figure 16.22a). Monoploidy is sometimes called haploidy, although the term *haploidy* typically is used to describe the chromosome complement of gametes. Some fungi and males of haploid/diploid species (ants, bees, wasps) are haploid, for example.

Monoploidy is seen only rarely among adults in normally diploid organisms. As a result of the presence of recessive lethal mutations (which are usually counteracted by dominant wild-type alleles in heterozygous individuals) in the chromosomes of many diploid eukaryotic organisms, many monoploids probably do not survive. Certain species produce monoploid organisms as a normal part of their life cycle. Some male wasps, ants, and bees, for example, are monoploid because they develop from unfertilized eggs.

Figure 16.21
Trisomy-18 (Edwards syndrome).

a) Karyotype (G banding)



b) Individual with trisomy-18 (Edwards syndrome)

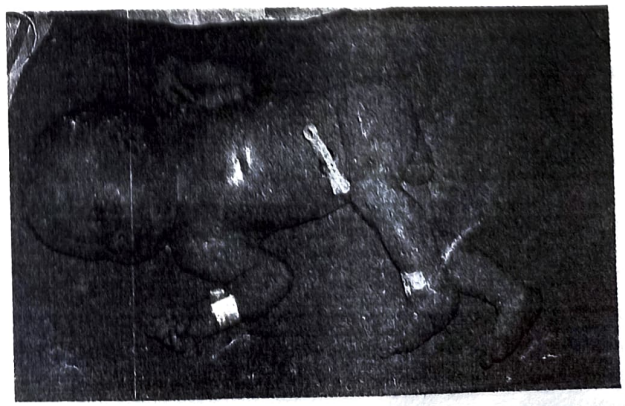
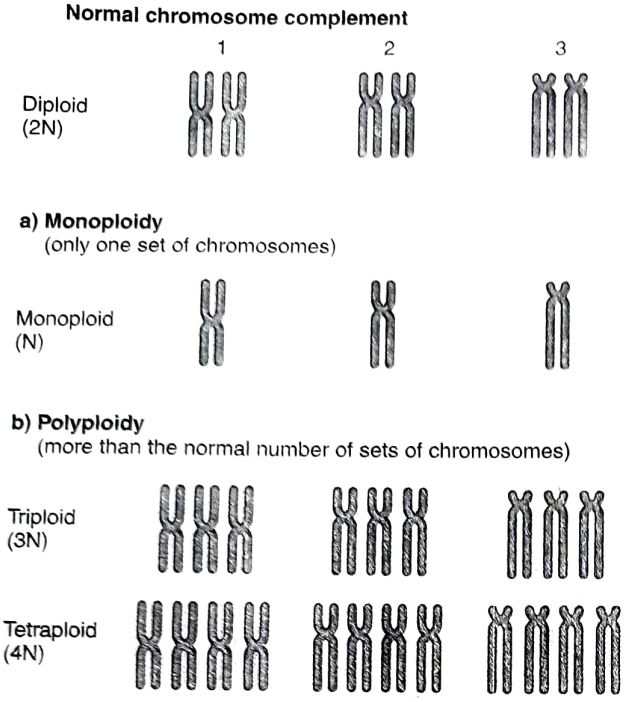


Figure 16.22
Variations in number of complete chromosome sets.



Cells of a monoploid individual are very useful for producing mutants, because there is only one dose of each of the genes. Thus, mutants can be isolated directly without dominance/recessiveness complications.

Polyploidy. Polyploidy is the chromosomal constitution of a cell or an organism that has more than the normal two sets of homologous chromosomes (Figure 16.22b). Polyploids may arise spontaneously or be induced experimentally. They often result from a breakdown of the spindle apparatus in one or more meiotic divisions or in mitotic divisions. Almost all plants and animals probably have some polyploid tissues. For example, the endosperm of plants is triploid, the liver of mammals and perhaps other vertebrates is polyploid, and the giant abdominal neuron of the sea hare *Aplysia* has about 75,000 copies of the genome. Plants that are completely polyploid include wheat, which is hexaploid (6N), and the strawberry, which is octaploid (8N). Some animal species, such as the North American sucker (a freshwater fish), salmon, and some salamanders, are polyploid.

Polyploids fall into two general classes: those with an *even* number of chromosome sets and those with an *odd* number of sets. Polyploids with an even number of chromosome sets have a better chance of being at least partially fertile, because there is the potential for homologs to be segregated equally during meiosis. Polyploids with an odd number of chromosome sets always have an unpaired chromosome for each chromosome type, so the probability of producing a balanced euploid gamete is extremely low; such organisms usually are sterile or have an increased incidence of abortion of zygotes.

In triploids, the nucleus of a cell has three sets of chromosomes. As a result, triploids are highly unstable in meiosis because, as in trisomics, two of the three homologous chromosomes go to one pole and the other goes to the other pole. The segregation of each chromosome from its homologs in the triploid is random, so the probability of producing balanced gametes that contain either a haploid or a diploid set of chromosomes is small; many of the gametes are unbalanced, with one copy of one chromosome, two copies of another, and so on. In general, the probability of a triploid producing a haploid gamete is $(1/2)^n$, where n is the number of chromosomes.

In humans, the most common type of polyploidy is triploidy, and it is always lethal. Triploidy is seen in 15 to 20% of spontaneous abortions and about 1 in 10,000 live births, but most affected infants die within 1 month. Triploid infants have many abnormalities, including a characteristically enlarged head. Tetraploidy in humans is also always lethal, usually before birth. It is seen in about 5% of spontaneous abortions. Very rarely is a tetraploid human born, but such an individual does not survive long.

Polyploidy is less consequential to plants. One reason is that many plants undergo self-fertilization, so if a plant is produced with an even polyploid number of chromosome sets (for example, 4N) it can still produce fertile gametes and reproduce.

Two types of polyploidy are encountered in plants. In **autopolyploidy,** all the sets of chromosomes originate in the same species. The condition probably results from a defect in meiosis that leads to diploid or triploid gametes. If a diploid gamete fuses with a normal haploid gamete, the zygote and the organism that develops from it will have three sets of chromosomes; in other words, it will be triploid. The cultivated banana is an example of a triploid autopolyploid plant. Because it has an odd number of chromosome sets, the gametes have a variable number of chromosomes, and few fertile seeds are set, thereby making most bananas seedless and highly palatable. Because of the triploid state, cultivated bananas are propagated vegetatively (by cuttings). In general, the development of "seedless" fruits such as grapes and watermelons relies on odd-number polyploidy. Triploidy has also been found in grasses, garden flowers, crop plants, and forest trees.

In **allopolyploidy,** the sets of chromosomes involved come from different, though usually related, species. This situation can arise if two different species interbreed to produce an organism with one haploid set of each parent's chromosomes (one set from each species) and then both chromosome sets double. For example, the fusion of haploid gametes of two diploid plants that can cross may produce an $N_1 + N_2$ hybrid plant that has a haploid set of chromosomes from plant species 1 and a haploid set from plant species 2. However, because of the differences between the two chromosome sets, no chromosomes pair

at meiosis, and no viable gametes are produced. As a result, the hybrid plants are sterile. Rarely, through a division error, the two sets of chromosomes double, producing tissues of $2N_1 + 2N_2$ genotype. (That is, the cells in the tissue have a diploid set of chromosomes from plant species 1 and a diploid set from plant species 2.) Each diploid set can function normally in meiosis, so that gametes produced from the $2N_1 + 2N_2$ plant are $N_1 + N_2$. Such fusion of two gametes can produce fully fertile, allotetraploid, $2N_1 + 2N_2$ plants.

A classic example of allopolyploidy resulted from crosses made between cabbages (*Brassica oleracea*) and radishes (*Raphanus sativus*) by Karpechenko in 1928. Both parents have a chromosome number of 18, and the F_1 hybrids also have 18 chromosomes, 9 from each parent. The hybrids produced are morphologically intermediate between cabbages and radishes. The F_1 plants are mostly sterile as a result of the failure of chromosomes to pair at meiosis. However, a few seeds are produced through meiotic errors, and some of those seeds are fertile. The somatic cells of the plants produced from those seeds have 36 chromosomes—that is, full diploid sets of chromosomes from both the cabbage and the radish. These plants are completely fertile and belong to a breeding species named *Raphanobrassica*, a fusion of the two parental genus names. Morphologically, the plants look a lot like the F_1 hybrids.

Finally, many commercial grains, most crops, and many common commercial flowers are polyploid. In fact, polyploidy is the rule rather than the exception in agriculture and horticulture. For example, the cultivated bread wheat, *Triticum aestivum*, is an allohexaploid with 42 chromosomes. This plant species is descended from three distinct species, each with a diploid set of 14 chromosomes. Meiosis is normal because only homologous chromosomes pair, so the plant is fertile.

Keynote

Variations in the chromosome number of a cell or an organism give rise to aneuploidy, monoploidy, and polyploidy. In aneuploidy, a cell or organism has one, two, or a few whole chromosomes more or less than the basic number of the species under study. In monoploidy, an organism that is usually diploid has only one set of chromosomes. In polyploidy, an organism has more than the normal number of complete sets of chromosomes. Any or all of these abnormal conditions may have serious consequences for the organism.

Summary