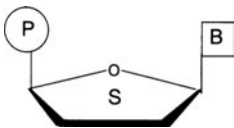


CHAPTER ONE

Overview of Genetic Organization and Scale

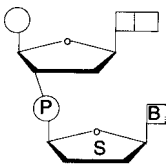
The genetic material is a molecule called **deoxyribonucleic acid (DNA)**. Each **chromosome** contains a single long strand of DNA that encodes the information needed to produce hundreds or even thousands of different proteins. Each species has a characteristic array of chromosomes that carries all the **genes** needed to produce that organism from a single cell. The relationship between the genetic makeup of an organism (the **genotype**) and the developmental effects of these genes (the **phenotype**) can be complex. It is, therefore, useful to begin with a simple overview of these processes. Here we introduce some of the key concepts of genetics using an illustrated guide that begins at the smallest unit of genetic organization within a **nucleus** and ends at the level of the **population**. Some important terms are shown in boldface type, and definitions are given in the Glossary.

- DNA is made up of subunits called **nucleotides** composed of a sugar (S), a phosphate group (P), and a nitrogenous base (B). There are four nucleotides that differ by the nucleotide base they contain: **adenine (A)**, **guanine (G)**, **thymine (T)**, and **cytosine (C)**. Genetic information is encoded in DNA by the sequence of these four bases.



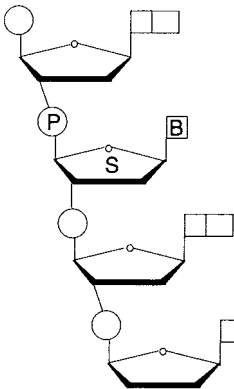
nucleotide

- **Nucleotides** are linked by a bond between the sugar of one nucleotide and the phosphate group of the next.



two nucleotides (schematic representation)

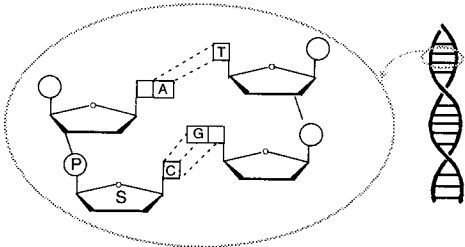
- This produces a long chain that can be literally millions of nucleotides long.



a portion of one strand

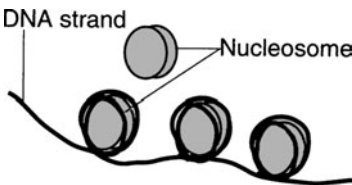
2 OVERVIEW OF GENETIC ORGANIZATION AND SCALE

- A single DNA molecule is composed of two such strands that join together by bonds between the nucleotide bases (A paired with T, and C paired with G). This forms a DNA **double helix**.



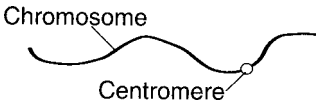
schematic of DNA and double helix

- The DNA is bound to structural proteins (**histones** that make up the **nucleosome**) that help pack the DNA in the nucleus and to regulatory proteins that turn genes on and off during development.

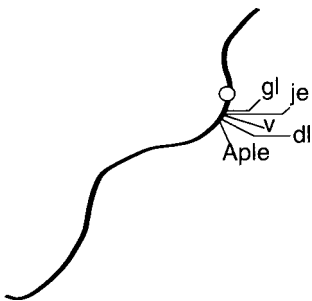


nucleosomes with DNA

- Each **chromosome** is made up of one long DNA molecule (one DNA double helix) and its associated proteins. The **centromere** is the attachment site for the spindle fiber that moves the chromosome during cell division.

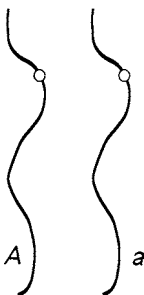


- Along the length of this DNA molecule are the regions that code for the production of proteins. These regions (or genetic **loci**) are the **genes**. Each gene can be up to a thousand or more nucleotides long, and every chromosome carries as many as several thousand different genes. All of the genes on a given type of chromosome are thus linked on a single DNA molecule. This linked group of genes is called a **linkage group**. The linear order of genes on a chromosome can be mapped to produce a linkage map.



chromosome showing a map of five genes in linear order on its linkage group

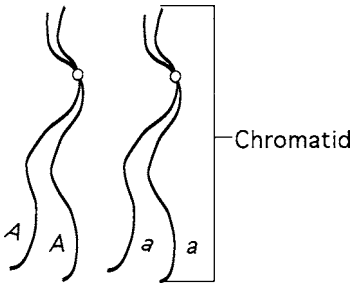
- The body cells (**somatic** cells) of most organisms contain two copies of each type of chromosome (**diploid**). These are the homologous chromosomes. Since **homologous** chromosomes carry the same series of genes, they are members of the same linkage group. They can, however, differ in the form that a given gene takes (that is, normal or mutant). The different forms of a gene are called **alleles**.



two homologous chromosomes carrying alleles A and a

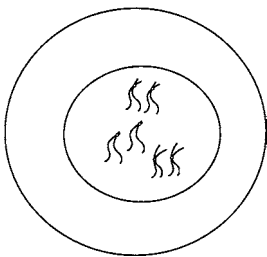
OVERVIEW OF GENETIC ORGANIZATION AND SCALE

- When the nucleus prepares to divide, each DNA molecule **replicates** except for the centromere. This yields two identical copies of the DNA molecule bound at the centromere. At this stage, the two copies are called **sister chromatids**. Since they have not yet divided at the centromere, however, each unit is still considered a single chromosome.



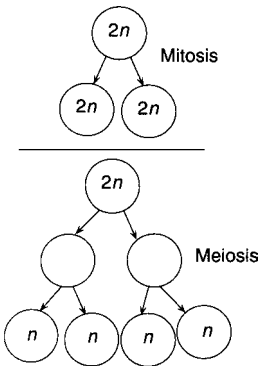
two homologous chromosomes, each with two sister chromatids

- Chromosomes that carry different sets of genes are called **nonhomologous** chromosomes. Every species has its own characteristic number of different chromosomes (n). The total number of chromosomes in a somatic cell is, therefore, $2n$. All the genes needed to produce that organism will be found somewhere on one of these n linkage groups. The total $2n$ genetic makeup is the **genome**. In the figure of the hypothetical cell, there are three pairs of nonhomologous chromosomes in the genome.



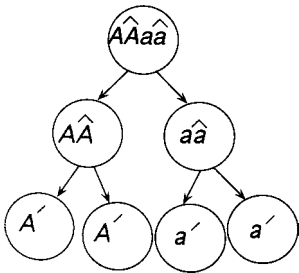
hypothetical cell with $2n = 6$, as seen during nuclear division

- **Mitosis** is a type of nuclear division that yields two identical diploid cells ($2n$). **Meiosis** is a special type of nuclear division found in reproductive (**germinal**) tissue that yields **gametes**. Each gamete carries only one copy of each linkage group and has a haploid (n) number of chromosomes. The diploid chromosome number is re-created at fertilization when the haploid maternal set and the haploid paternal set fuse.



mitosis and meiosis

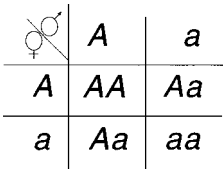
- If we focus our attention on one gene, the alleles on the two homologous chromosomes can either be the same (AA or aa = **homozygous** genotypes) or be different (Aa = **heterozygous** genotype). These separate (**segregate**) during meiosis to produce haploid gametes.



branching diagram to show haploid products

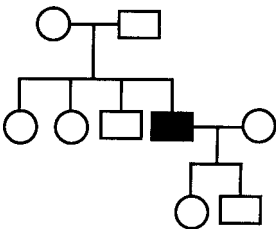
OVERVIEW OF GENETIC ORGANIZATION AND SCALE

- The products of segregation and fertilization are highly predictable, giving rise to the basic rules of **genetic transmission**. Gregor **Mendel** set the foundation for this area of genetics.



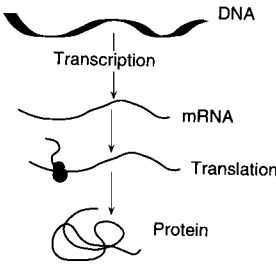
Mendelian cross using Punnett square for two heterozygous parents

- A **pedigree** diagram shows genetic relationships from a series of different Mendelian crosses. Circles indicate females and squares indicate males.



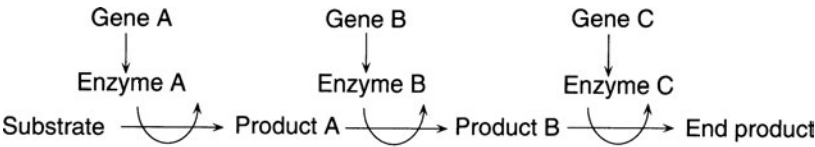
a simple pedigree

- Most genes code for the production of proteins. One of the two strands (the template strand) of a DNA molecule is “read” (through **transcription**) to yield a molecule of messenger **RNA** (mRNA). This then binds with ribosomes, where it defines the sequence of **amino acids** needed to produce the correct **polypeptide** (protein). This is **translation**.



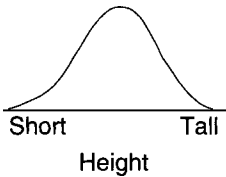
DNA → mRNA → protein

- Many proteins are **enzymes**, which catalyze specific biochemical steps. Thus, genes work by controlling the biochemical activities for growth and function of cells. In this way, the **genome** codes for all of the morphological, physiological, and behavioral characteristics (**phenotypes**) of an animal or plant.



biochemical pathway

- Some characteristics are the result of several genes and environmental factors working together. Their expression is measured on an appropriate scale (such as height in meters). These are **quantitative traits** (**multifactorial** or **polygenic traits**).



OVERVIEW OF GENETIC ORGANIZATION AND SCALE

- The genetic makeup of an individual is the **genome**, whereas the total genetic makeup of all individuals in the **population** is the **gene pool**. The gene pool is described in terms of allele frequencies, where *p* is the frequency of the *A* allele and *q* is the frequency of the *a* allele. By using appropriate assumptions, the genetic makeup of individuals in the population can be predicted.

	<i>a</i>	<i>A</i>
<i>p</i> = .6	<i>A</i>	<i>a</i>
<i>q</i> = .4	<i>A</i>	<i>a</i>

alleles in a hypothetical gene pool

- **Hardy, Weinberg, and Castle** established the foundation for **population genetics** by showing that allele frequencies remain in **equilibrium** unless acted upon by **selection, migration, mutation**, sampling error in **small populations**, or deviations from **random mating**. Population genetics is the study of changes in allele and genotype frequencies that occur when these factors act on animals or plants.

	<i>A</i> (.6)	<i>a</i> (.4)
<i>A</i> (.6)	<i>AA</i> (.36)	<i>Aa</i> (.24)
<i>a</i> (.4)	<i>Aa</i> (.24)	<i>aa</i> (.16)

Punnett square with allele frequencies

Genetics is a dynamic and exciting field (but, of course, you would expect us to say something like that). But it can also be confusing, since there are so many levels at which you can look at inheritance and the use of genetic information. This introduction to genetic organization and scale is intended as a kind of outline to some key levels and processes. Although they overlap, we can readily see three main perspectives. First is the molecular level of DNA structure and coding (nucleotide—DNA—transcription—translation—protein product). Second are the rules of genetic transmission, which are based on probabilities of inheritance (segregation and independent assortment in meiosis—probabilities and genotypes—genes in families—genes in populations). Third is the way the genotype controls biochemical activities during development to produce the organism’s phenotype (proteins—enzyme control of biochemical pathways—gene interactions—development). This primer will investigate these areas of genetics individually. But it is always important to keep in mind that they are really just different ways of looking at the same thing: the coding, transmission, and use of information by cells.

CHAPTER TWO

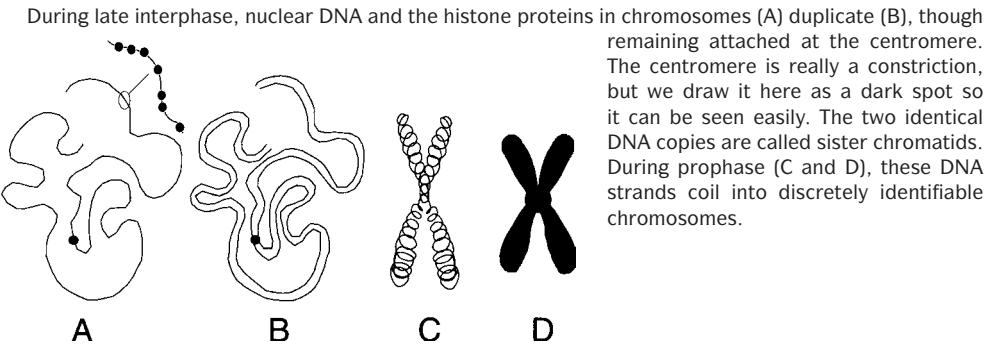
Mitosis and Meiosis

STUDY HINTS

Genes are located on chromosomes, and the stable manner in which chromosomes are first replicated and then distributed to daughter cells during cell division is the basis for genetic inheritance. Since much of genetic theory is based on the behavior of chromosomes and the genes they carry, it is very important to understand clearly how nuclear division occurs. In this way you can predict its consequences and understand the effect of errors that might occur in it. Yet the subject of cell division is complex, with many new terms to memorize and numerous things happening simultaneously. It is a continuous process that has been divided into stages somewhat artificially, so that we can describe it conveniently. All of this makes it rather hard to grasp at the beginning. Do not despair! It is really much simpler than it looks at first. The secret is to learn in stages. First one must understand the “strategies” of mitosis and meiosis, and the differences between them.

Mitosis has evolved as a mechanism to distribute accurately a copy of each chromosome present in the original cell to two new cells. The “goal” of *meiosis* is quite different. Meiosis passes alternate (homologous) copies of each type of chromosome to daughter cells and reduces the total chromosome number by half. These different objectives require slightly different chromosome behaviors. We shall briefly summarize these two processes, keeping in mind the different strategies they represent.

Both processes begin in essentially the same way. The chromosome (and the deoxyribonucleic acid [DNA] molecule it contains) duplicates, forming two identical chromosome strands attached to each other at the centromere. This is accompanied by a physical reorganization (coiling) that greatly reduces the chromosome’s apparent length. The transition between these levels is illustrated in the following figure. One of the earliest signs of coiling is the formation of chromomeres, shown in this “magnified” insert to part A in the figure.

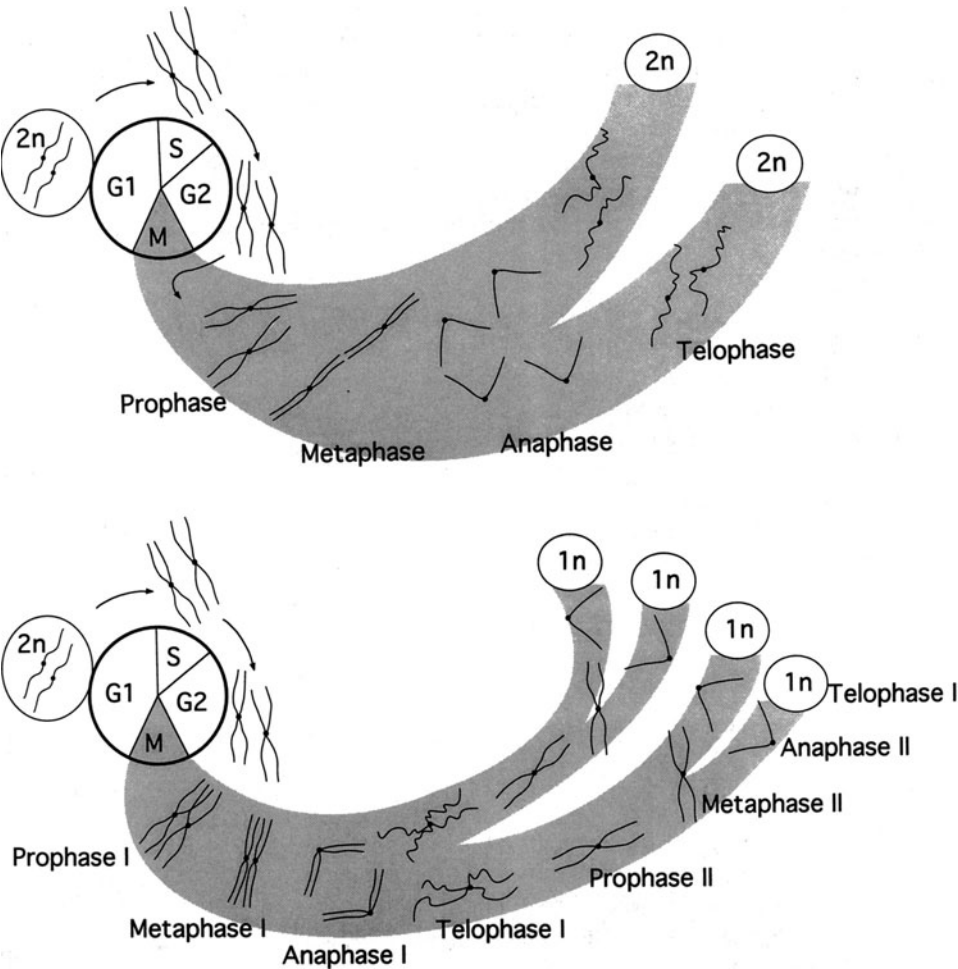


STUDY HINTS

7

Each of the identical chromosome strands coils to form one of the two strands (sister chromatids) in a duplicated chromosome. The shape of the chromosome is determined by the position of the centromere. Without such coiling (or condensation), separating chromosomes would be a little like trying to separate a plate of spaghetti into two piles without breaking anything. People sometimes get confused about chromosome number at this point. Just remember that chromosome means “colored body.” It is a single structural unit, no matter how much DNA it holds. So when counting chromosomes, count the centromeres, since whatever is attached to a centromere is a chromosomal unit.

In meiosis, the objective is to reduce the chromosome number so that there is only one copy of each kind in a gamete. The most direct way to do this is to pair the chromosomes carrying the same type of information or the same linear array of genes (homologous chromosomes). This is one purpose of synapsis. The first meiotic division, therefore, simply separates (segregates) homologous copies of each chromosome. The second meiotic division, like mitosis, distributes the identical copies (sister chromatids) that originated from chromosome replication.



These two strategies are contrasted in the preceding figure, in which the original cell has a chromosome number of $2n = 2$. In the Important Terms section of the chapter we have listed some of the most important terms you need to know to describe these processes. Definitions are given in the Glossary.

The only additional hint we might add concerns prophase I of meiosis. The divisions of this phase of meiosis are described in your text and summarized in Table 2.1. It is sometimes useful to have a mnemonic (memory-assisting) device to help you remember the sequence of events. For the divisions of prophase I, try this phrase, whose first letters are the same as the letters of the terms you need to remember: “Leaping zebras pound down dunes”: that is, *leptotene*, *zygotene*, *pachytene*, *diplotene*, *diakinesis* (see Table 2.1). Also remember these divisions are somewhat artificial, since the process is continuous, and some cell biologists assign events in a slightly different way.

TABLE 2.1 Substages of Prophase I of Meiosis

I. Leptotene
A. Chromatin begins condensing and becomes visible.
1. Chromomeres form as irregular tightly coiled regions of the chromosome.
a. Location, size, and number of chromomeres are chromosome specific.
b. G bands on human chromosomes are represented by several chromomeres coiling together.
c. Homologous chromosomes have the same banding pattern.
B. Homologous search begins.
C. Telomere proteins attach the telomeres to nuclear membrane.
II. Zygotene
A. Pairing of homologous chromosomes occurs.
1. Homologous search and rough pairing take place.
2. Synaptonemal complex is present but homologues are not tightly synapsed.
a. The pairs of chromosomes are called <i>bivalents</i> at this stage.
b. The number of bivalents is equal to the haploid number.
B. Chromosomes continue to coil and shorten.
III. Pachytene
A. Synapsis tightens so homologues are very close together (about 100 Å between the pairs). The term <i>tetrad</i> is often used here to indicate the presence of 4 chromatids (2 for each chromosome).
B. Recombination occurs.
C. The telomeres lose contact with the nuclear membrane.
IV. Diplotene
A. The transition between pachytene and diplotene occurs when the synaptonemal complex breaks down.
B. Homologues begin to move apart.
C. Chiasmata are present.
D. Terminalization begins. ^a
V. Diakinesis
A. The homologous chromosomes continue to terminalize. ^a
B. Nuclear membrane breaks down.
C. Chromosomes move toward the equatorial plate.

^a As terminalization is completed, the chromosomes line up in the center of the cell as the cell enters metaphase I.

PROBLEM SET 2

IMPORTANT TERMS

Acrocentric	Euchromatin	Polar body
Bivalent	Gamete	Primary oocyte
Centriole	Haploid	Primary spermatocyte
Centromere	Heterochromatin	Secondary oocyte
Chiasma (pl., chiasmata)	Homologous chromosomes	Secondary spermatocyte
Chromatid	Linkage group	Spindle
Chromatin	Meiosis	Synapsis
Chromomere	Metacentric	Synaptonemal complex
Cytokinesis	Mitosis	Telocentric
Diploid	Nucleolus	Terminalization
Dyad		Tetrad

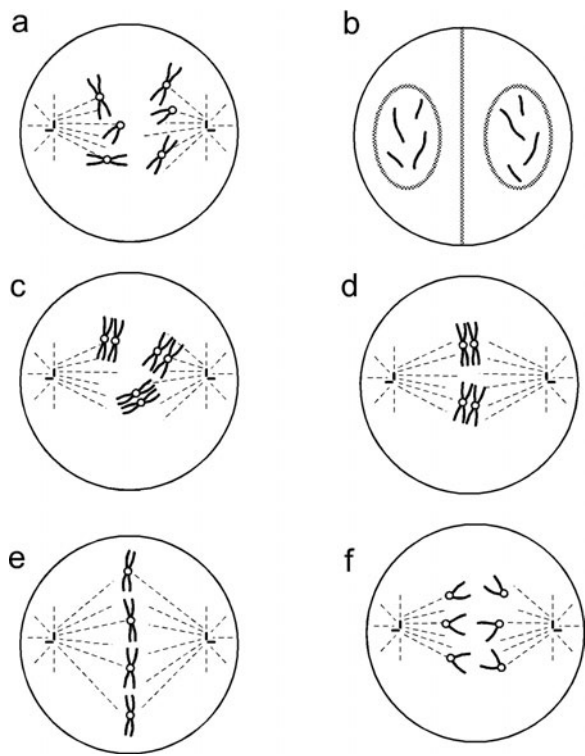
PROBLEM SET 2

General Study Hint: To help reinforce these ideas, you should sketch the cell and its chromosomes before trying to answer these questions.

1. Suppose that you are studying a new species in which the chromosome number is unknown. You are looking at a spread of cells in some unknown stage of cell division, and you discover that there are seven chromosomes (three metacentric, three telocentric, and one acrocentric) visible in each dividing cell. What type of nuclear division have you found, and what conclusions can be drawn about the chromosome makeup of the species?
2. How many chromosomes are there in a human intestinal cell at anaphase?
3. How many different kinds of gametes can be produced by an individual who has three linkage groups with each chromosome identifiable by the forms of the genes (alleles) it carries?
4. In an organism with a haploid chromosome number of 7, how many sister chromatids are present
 - (a) in its mitotic metaphase nucleus?
 - (b) in its meiotic metaphase I nucleus?
 - (c) in its meiotic metaphase II nucleus?
5. A particular beetle species is found to have a chromosome complement of $2n = 16$ chromosomes. How many linkage groups would the beetle have?
6. Recombination can be seen as chiasmata between homologous chromosomes at what stage of cell division? Sketch a bivalent involving metacentric chromosomes having one chiasma.
7. Is it possible for meiosis to occur in a haploid cell? Is mitosis possible? Please explain your answer to each question.

MITOSIS AND MEIOSIS

8. For each of the following figures, identify the specific stage of nuclear division and the diploid, $2n$, chromosome number of the organism.



9. Draw and label a cell at metaphase I of meiosis, where $2n = 8$ metacentric chromosomes.
10. Draw and label a cell at late anaphase of mitosis, where $2n = 6$ chromosomes (two pairs of acrocentric chromosomes and one pair of telocentric chromosomes).
11. Draw and label all cells at telophase II that result from meiosis of a primary spermatocyte ($2n = 8$ acrocentric chromosomes).
12. Draw, label, and compare cells at prophase I and prophase II of meiosis in a species characterized by $2n = 6$ acrocentric chromosomes.
13. Draw, label, and compare cells at anaphase of mitosis and anaphase I of meiosis in a species having $2n = 4$ chromosomes (one homologous pair of metacentric chromosomes and one pair of telocentric chromosomes).
14. In humans, atopic allergic disease (ragweed hay fever) is dependent on a dominant gene A , while a neurological disorder called Huntington disease is determined by a dominant gene H . The normal alleles are a and h , respectively. A man who is $Aa hh$ married a woman who is $aa Hh$. Assume the A and H are on nonhomologous chromosomes and that the relevant chromosomes are all telocentric.