A young couple is planning to have children. The husband knows that his grandmother had a child with Down syndrome by a second marriage. Down syndrome is a set of physical and mental disorders caused by the presence of an extra chromosome 21 (Figure 17-1). No records of the birth, which occurred early in the twentieth century, are available, but the couple knows of no other cases of Down syndrome in their families.

The couple has heard that Down syndrome results from a rare chance mistake in egg production and therefore decide that they stand only a low chance of having such a child. They decide to have children. Their first child is unaffected, but the next conception aborts spontaneously (a miscarriage), and their second child is born with Down syndrome. Was their having a Down syndrome child a coincidence, or did a connection between the genetic makeup of the child’s father and that of his grandmother lead to their both having Down syndrome children? Was the spontaneous abortion significant? What tests might be necessary to investigate this situation? The analysis of such questions is the topic of this chapter.

We have seen throughout the book that gene mutations are an important source of change in the genomic sequence. However, the genome can also be remodeled on a larger scale by alterations to chromosome structure or by changes in the number of copies of chromosomes in a cell. These large-scale variations are termed **chromosome mutations** to distinguish them from gene mutations. Broadly speaking, gene mutations are defined as changes that take place within a gene, whereas chromosome mutations are changes in a chromosome region encompassing multiple genes. Gene mutations are never detectable microscopically; a chromosome bearing a gene mutation looks the same under the microscope as one carrying the wild-type allele. In contrast, many chromosome mutations can be detected by microscopy, by genetic or molecular analysis, or by a combination of all techniques. Chromosome mutations have been best characterized in eukaryotes, and all the examples in this chapter are from that group.

Chromosome mutations are important from several biological perspectives. First, they can be sources of insight into how genes act in concert on a genomic scale. Second, they reveal several important features of meiosis and chromosome architecture. Third, they constitute useful tools for experimental genomic manipulation. Fourth, they are sources of insight into evolutionary processes. Fifth, chromosomal mutations are regularly found in humans, and some of these mutations cause genetic disease.

Many chromosome mutations cause abnormalities in cell and organismal func-tion. Most of these abnormalities stem from changes in *gene number* or *gene posi*-*tion.* In some cases, a chromosome mutation results from chromosome breakage. If the break occurs within a gene, the result is functional disruption of that gene.

For our purposes, we will divide chromosome mutations into two groups: changes in chromosome number and changes in chromosome structure. These two groups represent two fundamentally different kinds of events. Changes in chromo-some number are not associated with structural alterations of any of the DNA molecules of the cell. Rather, it is the number of these DNA molecules that is changed, and this change in number is the basis of their genetic effects. Changes in chromo-some structure, on the other hand, result in novel sequence arrangements within one or more DNA double helices. These two types of chromosome mutations are illustrated in Figure 17-2, which is a summary of the topics of this chapter. We begin by exploring the nature and consequences of changes in chromosome number.