tissues have little or no ability to respond to thyroxin, indicating that there has been a genetic alteration that precludes metamorphosis. The adult morphology and lifestyle of these animals is hence radically altered by what may have been a very simple genetic change.

Other aspects of heterochrony have been attributed to a particular category of genes, termed **regulatory genes**, that control the timing and degree of expression of other genes that code for the formation of structures.

Heterochrony was extensively discussed by Gould (1977), and many informative examples were provided in the recent volume edited by McNamara (1995). This concept provides a very useful way in which to view significant changes involving particular structures and even major modification of the entire body form and way of life. The remainder of this chapter, however, is devoted to other aspects of development that have the potential for providing detailed molecular explanation of both heterochrony and all other changes in the physical form of the body throughout evolution.

Until recently, it has been extremely difficult to investigate how changes in developmental processes might produce new characters and new body plans; however, the capacity to do so is increasing rapidly as a result of new tools of biotechnology. It is now practical to isolate genes defined by mutations and determine their DNA sequences; this, in turn, establishes the sequence of the amino acids in the proteins coded for by the genes, which often gives hints as to their probable function. The function of a gene can also be investigated by establishing the spatial and temporal regulation of its expression throughout development in both normal and mutant individuals. Specific genes can also be disrupted or deleted, and their normal function be inferred by what happens when they are absent.

Among the most important families of genes for studying the development of major structural elements are *homeotic genes,* discussed in the next section. Knowledge of these genes has already provided significant insights into the appearance of major new structures associated with the origin of vertebrates from nonvertebrate chordates and into the processes that control the way in which the vertebrate head, trunk, and limbs originated and evolved.

Homeobox genes

Homeotic mutants were first recognized and named by Bateson (1894) more than a century ago. In the fruit fly *Drosophila,* such mutations result in the appearance of structures in inappropriate segments of the head and thorax. One of the earliest mutants to be identified was *Antennapedia,* in which a pair of legs, similar to those of the second thoracic segment, developed in place of the normal antennae on the head. Goldschmidt (1938, 1940) used these and comparable observations to argue that new developmental patterns and adult structures might have appeared as the result of single, major chromosomal changes termed *systemic mutations*. Since most changes in the expression of major body structures are not advantageous, Goldschmidt coined the term **hopeful monsters**, indicating that out of thousands (or perhaps millions) of maladaptive mutations, a very few might confer a significant advantage and lead suddenly to major new structures or body