Mutations that affect the presence or extent of the apical ectodermal ridge result in malformation of the limb. In the chick, the mutation *polydactylous,* in which the ridge is longer than normal, results in extra digits. The mutation *eudiplopodia* results in two complete rows of digits on each hind limb. *Limbless,* in which the ridge fails to form, results in complete limb loss. Although these are naturally occurring mutations, the alterations they produce are unlikely to be comparable with those seen in vertebrate evolution. The multiplications of digits that are seen in vertebrate groups can usually be attributed either to the reappearance of previously lost digits, as in polydactyly in dogs and horses (Hall 1984) or can be seen as the splitting of digits distal to the level of the carpals or tarsals, as in ichthyosaurs, rather than the formation of entirely new structures. In snakes and whales, fossil evidence demonstrates that limb loss is progressive, from distal to proximal, rather than occurring in a single step (Haas 1980; Gingerich, Smith, and Simons 1990). Double rows of digits have never been reported from the fossil record.

The configuration of particular elements of the hands and feet may be controlled by specific genes that influence the structure of small groups of bones. Each of several bone- and cartilage-inducing molecules, the **bone morphogenetic proteins (BMPs)**, has different genetic control. For example, the mutations *brachypodism (bp)* and *short ear* in the mouse both disrupt the condensation of mesenchyme cells into outlines of particular skeletal elements, but at different sites (Storm et al. 1994). *Short ear* mutations alter the size and shape of the ears, sternum, ribs, and vertebral processes but do not affect other skeletal elements. *Brachypodism* mutations alter the length of the long bones, change the length of the metapodials, slightly disrupt the organization of the carpals and tarsals, and reduce the number of phalanges in the digits of all four limbs by the fusion of proximal and medial segments. In mice not affected by the mutation for brachypodism, the specific **growth/differentiation factors (GDF)** produced by the wild-type gene is expressed in both distal precartilaginous mesenchymal condensations and in the perichondrium of more proximal skeletal structures. Other mutations differentially affect the forelimbs and hind limbs of mice, but most result in such severe abnormalities that it is unlikely that they provide plausible analogies for changes that might have occurred during their evolutionary history (Lyon and Searle 1989).

Presumably there are other genes that regulate the formation of individual bones, particular aspects of bones, or a simple bone complex such as the assemblage of phalanges that make up a single digit, but these are unlikely to be recognized in screens of populations. It would also be difficult to establish whether such minor differences were under genetic control, appeared randomly, or as the result of environmental factors, but this might be determined in specific cases such as that of the extensive variability that occurs in the hands and feet of very small salamanders (Hanken 1982; Alberch and Blanco 1994; Shubin 1995).

If such genes, which bridge the gap between *Hox* activation and the structure of individual bones, are common, they would answer the question as to how selection on minor anatomical variants could produce significant changes in developmental patterns within the major vertebrate groups. Quantitative genes with such limited effects would provide an explanation for continuous, incremental change over long periods of time, as argued by Darwin and as seen in the fossil record.