The ever-increasing capacity to establish the specific loci and manner of gene expression will make it possible to determine the mechanisms by which individual bones are formed. However, we still seem far from being able to understand how the development of a complex structure such as the vertebrate hand or foot, fin or wing, is controlled – or why, once they have evolved, these structures may remain nearly constant for hundreds of millions of years. We still lack understanding of the molecular blueprint or template that maintains exactly five digits and a phalangeal count of 2,3,4,5,3 in the hands of lizards and their ancestors for a period of 340 million years. Neither can we explain how similar expression of identical *Hox* genes can control development of structures as distinct as the forelimbs and hind limbs of birds (Fig. 10.16).

Although the processes controlling development are still incompletely known, we can look further at the specific patterns of development and evolution in both modern and fossil groups to evaluate just how strictly the rules of developmental constraints have been followed during the history of vertebrates.

Morphogenesis and evolution of tetrapod limbs

Patterns of chondrification

Developmental biology textbooks deal with the differentiation of cells and the elaboration of particular tissues, down to the level of the establishment of the general configuration of the limbs; yet they are not concerned with details of the formation of the individual bones whose evolutionary changes enabled vertebrates to adapt to such diverse activities as swimming, running, digging, and flying. Instead, these subjects have the interest of comparative anatomists and vertebrate paleontologists. The gap between the studies of limb development typically pursued by developmental biologists and those conducted by vertebrate paleontologists has been bridged by a series of very important papers by Alberch and his colleagues (Alberch 1985; Alberch and Gale 1985; Shubin and Alberch 1986) documenting the patterns of mesenchymal tissue condensation and the formation of centers of chondrification that can be seen in the limbs of a wide range of living vertebrates. These studies illustrate a basic pattern common to all major groups of tetrapods, one that serves as a starting point for determining what changes have occurred in more specialized lineages, as well as the degree to which these changes may be constrained by underlying rules of development.

At the cellular level, the formation of the limb skeleton in tetrapods involves three basic processes: de novo condensation of undifferentiated mesenchymal cells, and either branching or segmentation of the condensations as they form. Morphogenesis begins with a single proximal condensation that will eventually become the humerus in the forelimb and the femur in the hind limb (Fig. 10.17). The presence of only a single ossification proximally has been postulated as resulting from the small size of the limb bud when it begins to develop. However, the fact that the base of the paired fin in many groups of primitive fish is very wide and is supported by many parallel radials suggests that some additional factor must be active in sarcopterygians and tetrapods to restrict the base of the limb to a single element. More distally, tissue condensations at the distal ends of the presumptive