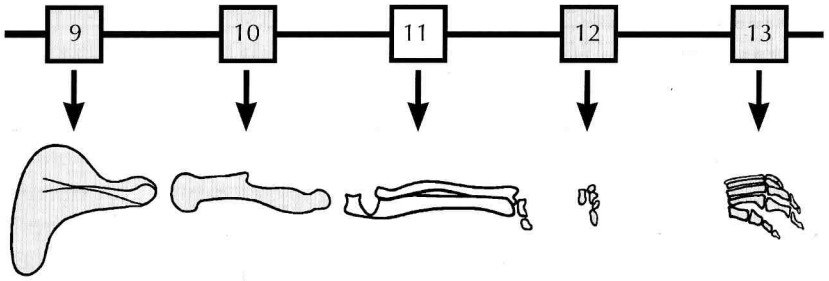

Figure 10.14. Specificity of the *Hox* groups responsible for formation of forelimb elements in the mouse. Homozygous null mutations of *Hoxa-11* and *Hoxd-11* result in the loss of the radius, ulna, and proximal carpals. Reprinted from *Nature* (Davis et al., vol. 375). Copyright © 1995, Macmillan Magazines Limited.

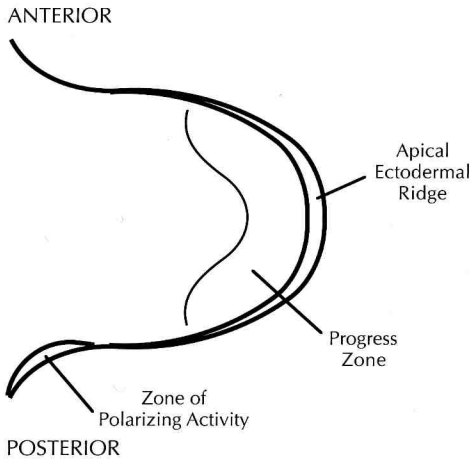

Figure 10.15. Embryological structures associated with development of the limbs.

Even more difficult to explain is the fact that although the areas of expression of *Hoxd* genes in the front and hind limbs are nearly identical, the number and shape of the digits in some groups, particularly birds, are strikingly different (Fig. 10.15). Study of additional paralogous genes may answer this problem (Nelson et al. 1996).

Other factors controlling the development of limbs

While study of the distribution of the *Hox* genes presents a simple, diagrammatic way of looking at the establishment of the pattern of limb development, earlier studies showed that the formation of limb structures is also under the control of several other factors residing within the limbs themselves, including specific areas of differentiation that are present during limb development, molecules termed **morphogens** that diffuse through the developing limb, and other genes that are not part of the *Hox* clusters. The areas of differentiation include the limb fields, the apical ectodermal ridge, the progress zone, and the zone of polarizing activity (Gilbert 1994).

It has long been recognized that the position where the limb buds would develop was established well before they became apparent as extensions from the trunk. These areas were termed the **limb fields** and have since been established