embryo is determined by the Spemann organizer, located in the gray crescent of a zygote. In *Drosophila* the anteroposterior axis is determined even before an egg is fertilized. Christiane Nüsslein-Volhard and her colleagues in Germany found that this determination is due to a gradient of mRNA that is secreted into the egg by nurse cells in the mother. The end of the egg that receives the highest level of this mRNA is fated to become the anterior of the embryo and eventually of the adult. The mRNA is transcribed from a gene called *bicoid* (pronounced BICK-oyd) in the nurse cells. After an egg is fertilized, *bicoid* mRNA is translated into a protein morphogen called bicoid (not italicized) that binds to certain other genes. The products of these genes in turn activate others in a cascade that ultimately causes the production of structures appropriate to the anterior. *Bicoid* is one of about 30 maternal genes that control pattern formation in an embryo. Some of these determine the dorsoventral axis. The gene *short gastrulation* leads to development of ventral structures, such as the nerve cord.

One of the most exciting discoveries in developmental genetics has been that the developmental genes of vertebrates and many other animals are similar to those of *Drosophila;* they are conserved over a wide range of animals. A gene similar to *bicoid* is also important in pattern formation in vertebrates. In vertebrates, however, the gene, called *Pitx2,* determines positioning of certain internal organs to either the left or right side of the body. Mutations in *Pitx2* in frogs, chicks, and mice can result in the heart and stomach being on the right instead of the left side. Such mutations may also be responsible for a reversal of organ position that sometimes occurs in humans. *Pitx2* is in turn activated by a protein produced by the gene *sonic hedgehog (Shh),* which is similar to a *Drosophila* gene called *hedgehog*. (The name *hedgehog* refers to the bristly appearance of fruit flies lacking the gene. The *"sonic"* comes from the video-game character Sonic the Hedgehog.) In vertebrates, *sonic hedgehog* is active in the left side only at the anterior end of the primitive streak (see Figure 8-13). *Short gastrulation* also has a counterpart in vertebrates—the gene *chordin,* which produces one of the proteins from the Spemann organizer.

In *Drosophila,* as well as other arthropods, annelid worms, chordates, and a few other groups, one important aspect of pattern formation along the anteroposterior axis is **segmentation,** also called **metamerism.** Segmentation is a division of the body into discrete segments or metameres (see Figure 9-7, p. 186). The segments are identical early in development, but later activation of different combinations of genes causes each segment to form different structures. For example, the anterior segment of insect embryos will form antennae, eyes, and mouthparts, while segments farther back will form legs. Segments are obvious in insects, but in chordates segmentation is apparent only in somites that produce such structures as vertebrae and repeated muscle bands (myomeres) of fishes (see Figure 24-24, p. 515). In *Drosophila* the number and orientation of segments is controlled by **segmentation genes.** There are three classes of segmentation genes: gap, pair-rule, and segment polarity. **Gap genes** are activated first and divide an embryo into regions such as head, thorax, and abdomen. **Pair-rule genes** divide these regions into segments. Finally, **segment-polarity genes,** such as *hedgehog,* organize the anterior-to-posterior structures within each segment.

Homeotic and *Hox* Genes

Segmentation genes apparently regulate expression of other genes, ensuring that they are active only in appropriate segments. Such segment-specific genes are called homeotic genes. Mutations in homeotic genes, called **homeotic mutations,** result in formation of appendages or other structures in the wrong part of the body. For example, in *Drosophila* the homeotic gene *Antennapedia,* which helps trigger development of legs, is normally active only in the thorax. If the *Antennapedia* gene is activated by a homeotic mutation in the head of a maggot, the adult will have legs in place of antennae (Figure 8-17). *Antennapedia* and some other homeotic genes, as well as many other genes involved in development, include a sequence of 180 DNA base pairs, called the **homeobox.** The homeobox produces the part of a protein that attaches to the DNA of other genes, activating or blocking their expression.

Several other homeotic and nonhomeotic genes that are clustered close to *Antennapedia* on the same chromosome in *Drosophila* also include a homeobox. Genes in this cluster are called *Hom* genes. *Hom* genes do not encode specific limbs and organs. Instead, they function by specifying the location in the body along the anteroposterior axis. Intriguingly, the order of the *Hom* genes within the cluster on the chromosome is the same as the order in which they are expressed along the length of the body (Figure 8-18). One of the most exciting discoveries of the late twentieth century was that genes similar to *Hom* genes of *Drosophila* occur in other insects, as well as in chordates and unsegmented animals such as hydra and nematode worms. They also occur in plants and yeasts, and perhaps in all eukaryotes. These genes in organisms other than *Drosophila* are usually called *Hox* genes. Like *Hom* genes of *Drosophila,* most *Hox* genes occur in a cluster on one chromosome. Mammals have four clusters, each on a different chromosome, with from 9 to 11 *Hox* genes each. As in *Drosophia,* the sequence of *Hox* genes within a cluster is the same as the front-to-rear order in which they are expressed in the body.

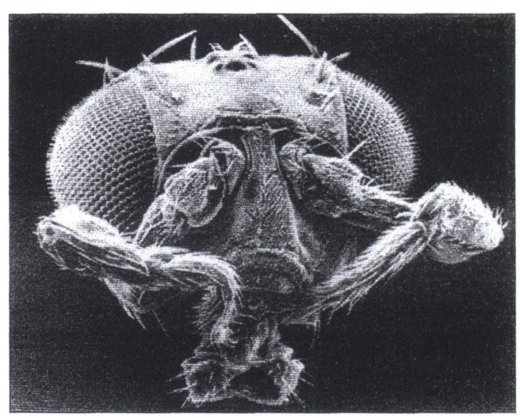

Figure 8-17
Head of a fruit fly with a pair of legs growing out of head sockets where antennae normally grow. The *Antennapedia* homeotic gene normally specifies the second thoracic segment (with legs), but the dominant mutation of this gene leads to this bizarre phenotype.