



**FIGURE 2-4.** The sequence of events in penetration of the coverings and plasma membrane of the egg. **A and B,** Penetration of the corona radiata. **C and D,** Attachment to the zona pellucida and acrosomal reaction. **E and F,** Binding to plasma membrane and entry into the egg.

(Fig. 2-5). The zona pellucida of an unfertilized mouse egg is estimated to contain more than 1 billion copies of the  $ZP_3$  protein.

After they have penetrated the corona radiata, spermatozoa bind tightly to the zona pellucida by means of the plasma membrane of the sperm head (see Fig. 2-4). The  $ZP_3$  molecule, specifically the O-linked oligosaccharides attached to the polypeptide core, acts as the sperm receptor in the zona in the mouse. Molecules on the surface of the sperm head are specific binding sites for the  $ZP_3$  sperm receptors on the zona pellucida. More than 24 molecules have been proposed, but the identity of the zona-binding molecule remains unknown. Interspecies molecular differences in the sperm-binding regions of the  $ZP_3$  molecule may serve as the basis for the inability of spermatozoa of one species to fertilize an egg of another species. In mammals, there is less species variation in the composition of  $ZP_3$ ; this may explain why penetration of the zona pellucida by spermatozoa of closely related

mammalian species is sometimes possible, whereas it is rare among lower animals.

On binding to the zona pellucida, mammalian spermatozoa undergo the **acrosomal reaction**. The essence of the acrosomal reaction is the fusion of parts of the outer acrosomal membrane with the overlying plasma membrane and the pinching off of fused parts as small vesicles. This results in the liberation of the multitude of enzymes that are stored in the acrosome (Box 2-1).

The acrosomal reaction in mammals seems to be stimulated by the  $ZP_3$  molecule acting through G proteins in the plasma membrane on the sperm head. In contrast to the sperm receptor function of  $ZP_3$ , a large segment of the polypeptide chain of the  $ZP_3$  molecule must be present to induce the acrosomal reaction. An initiating event of the acrosomal reaction is a massive influx of  $Ca^{++}$  through the plasma membrane of the sperm head. This process, accompanied by an influx of  $Na^+$  and an efflux of  $H^+$ , increases the intracellular pH. Fusion of the outer