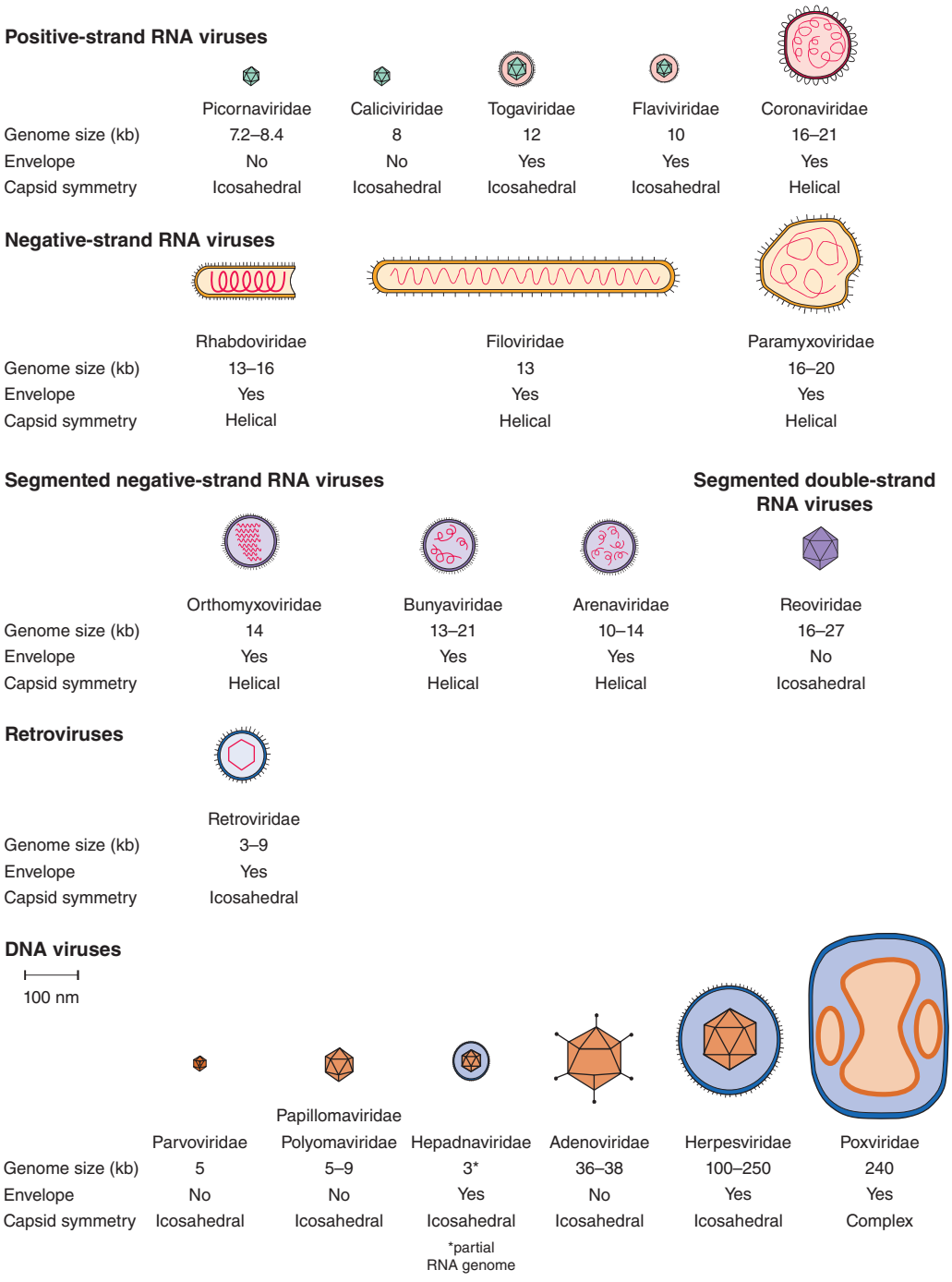

FIGURE 214e-2 Schematic diagrams of the major virus families including species that infect humans. The viruses are grouped by genome type and are drawn approximately to scale. Prototype viruses of each family that cause human disease are listed in Table 214e-1.

Viruses have evolved a wide range of strategies to enter cells. Influenza virus has an outer-membrane hemagglutinin glycoprotein that binds to sialic acid on respiratory tract cell plasma membranes. The hemagglutinin mediates adsorption to cell membranes, receptor aggregation, and endocytosis. As the endosome pH decreases in the cell cytoplasm, the influenza hemagglutinin conformation changes, enabling hydrophobic helices, which are initially at the base of the hemagglutinin, to extend, interacting and fusing with the endosome membrane and thereby releasing the viral genome into the cell cytoplasm. The influenza virus M2 membrane channel protein has a key role in lowering endosome pH and permitting virus and cell membrane fusion.

Nonenveloped viruses (e.g., human papillomaviruses [HPVs]) and some enveloped viruses have evolved to partially fuse with cell plasma membrane receptors and be internalized into endosomes. The low pH in an endosome can then trigger virus membrane or capsid fusion with the endocytic membrane, releasing viral DNA into the cytoplasm to initiate infection.

Hydrophobic interactions required for fusion can be susceptible to chemical inhibition or blockade. The HIV envelope glycoprotein gp120 is associated with gp41 on the viral surface. HIV gp120 binding to CD4 and then to specific chemokine receptors results in conformational changes that allow gp41 to initiate cell membrane fusion. The anti-HIV drug enfuvirtide is a small peptide derived from the gp41 structure. Enfuvirtide binds to gp41 and prevents conformational changes required for fusion. In contrast, maraviroc prevents virus entry by binding to the CCR5 receptor, thereby blocking gp120 binding to CCR5 and preventing gp120 fusion with CCR5.