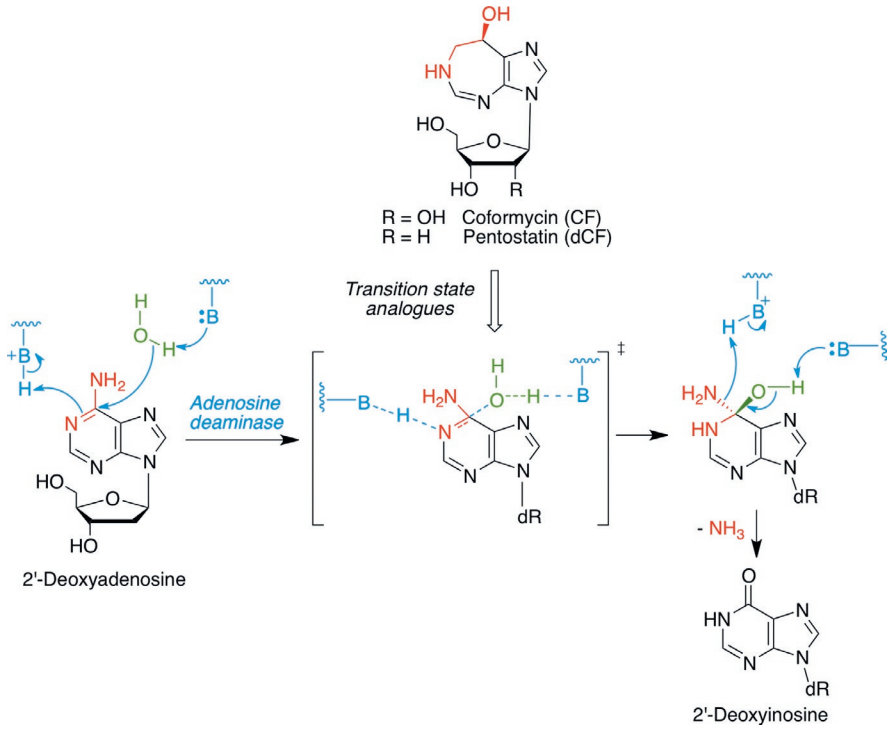

FIGURE 2.51

Inhibitors of adenosine deaminase.

2. Accumulation of deoxyadenosine also leads to high levels of deoxyadenosine triphosphate, which is an inhibitor of ribonucleotide reductase, the enzyme that removes the 2′-hydroxy group of the ribose ring during the biosynthesis of DNA.
3. Pentostatin is triphosphorylated and misincorporated into DNA.

8 INHIBITORS OF LATE STAGES IN DNA SYNTHESIS

As previously mentioned, several ribonucleoside and deoxyribonucleoside analogs are anticancer prodrugs that are activated to their triphosphates by phosphorylation catalyzed by kinases.[79] After bioactivation, the triphosphates act by misincorporation into DNA, resulting in slower chain elongation and alterations in DNA repair. The antitumor action of these compounds is due to the inhibition of DNA polymerase and other mechanisms (e.g., inhibition of ribonucleotide reductase or PNP) are known for particular compounds (Figure 2.53). A general problem associated with these drugs is that due to their cytotoxicity to lymphoid cells, significant and long-lasting immunosuppression results.