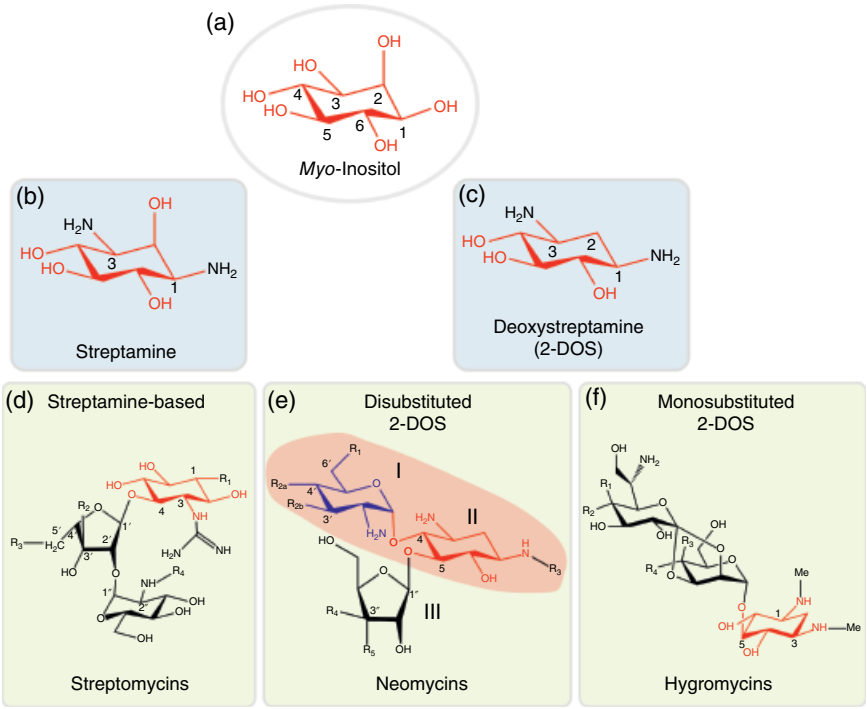

Figure 1.1 Core structural elements of the aminoglycosides and examples of clinically relevant AGA families. Each family has a primary structure with different substitutions (Rn) at hydroxyl and amino groups. The rings (I–III) of the neomycins' representative structure are numbered as usually observed in the literature for disubstituted 2-DOS AGAs. In panel (e), the pseudodisaccharide core structure paromamine, also termed as neamine, is demarked.

with target sequences on the rRNA and for impairing normal ribosomal function. Although natural AGAs share the same *myo*-inositol-based core (Figure 1.1), these molecules exhibit significant structural differences depending on the bacterial origin, which result in different biological activities. Importantly, the bacterial origin is also the driving force behind bacterial resistance, as it enables bacteria to alter the structure of AGAs by modifying their amino and hydroxyl groups.

Streptomycin was the first identified and characterized AGA and the first useful antibiotic obtained from a bacterial source (1944). This AGA was isolated from the soil-dwelling bacterial species *Streptomyces* and *Micromonospora* and successfully introduced into clinical practice in 1940 to treat tuberculosis. After the initial discovery of streptomycin and its streptamine-based relatives (Figure 1.1a), several others followed, and the development of bacterial