Physical Properties

There are 7 distinct strains of Clostridium botulinum that have been identified. Each strain is characterized by the type of botulinum neurotoxin that it is capable of producing and has been classified as type A, B, C, D, E, F, or G. While all of these neurotoxins inhibit the release of ACh at the myoneural junction, they all vary in their chemical structure and size as well as their mechanism of action within the nerve terminal itself. Five of these subtypes (A, B, E, F, G) affect the human nervous system, while 2 subtypes (C and D) do not. Types A and B are the 2 most clinically relevant subtypes and, therefore, are commercially produced. Botulinum toxin type-A is felt to exert the most powerful neuromuscular blockade and is also capable of exerting its effect for the longest duration of time. In contrast, botulinum toxin type-E and type-F are also capable of blocking myoneural transmission, but they have a shorter duration of action when compared to types A and B and, therefore, are not commercially produced.

Both botulinum toxin type-A and type-B are composed of a 150 kD polypeptide consisting of a disulfide bond-linked light chain and heavy chain. These disulfide-linked molecules are associated with other non-neurotoxin proteins during their synthesis to form a neurotoxin complex, which is approximately 500 kD in size (Figure 2-1). These non-neurotoxin accessory proteins may serve a beneficial role in stabilizing the fragile botulinum toxin molecule when it is reconstituted.

Mechanism of Action

At the neuromuscular junction, the motor nerve terminal lies in close apposition with the adjacent muscle fiber. When botulinum toxin is administered, the heavy chain binds selectively to cell membrane receptors on the outer surface of the presynaptic nerve terminal (Figure 2-2). The entire neurotoxin complex (both light and heavy chains) is then internalized into the nerve terminal via receptor-mediated endocytosis (Figure 2-3). The vesicles containing the botulinum toxin then fuse with digestive vacuoles that cleave the botulinum toxin molecule into separate light and heavy chains.