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Edited by Anthony B. Ward , Michael P. Barnes
[Plate Section]

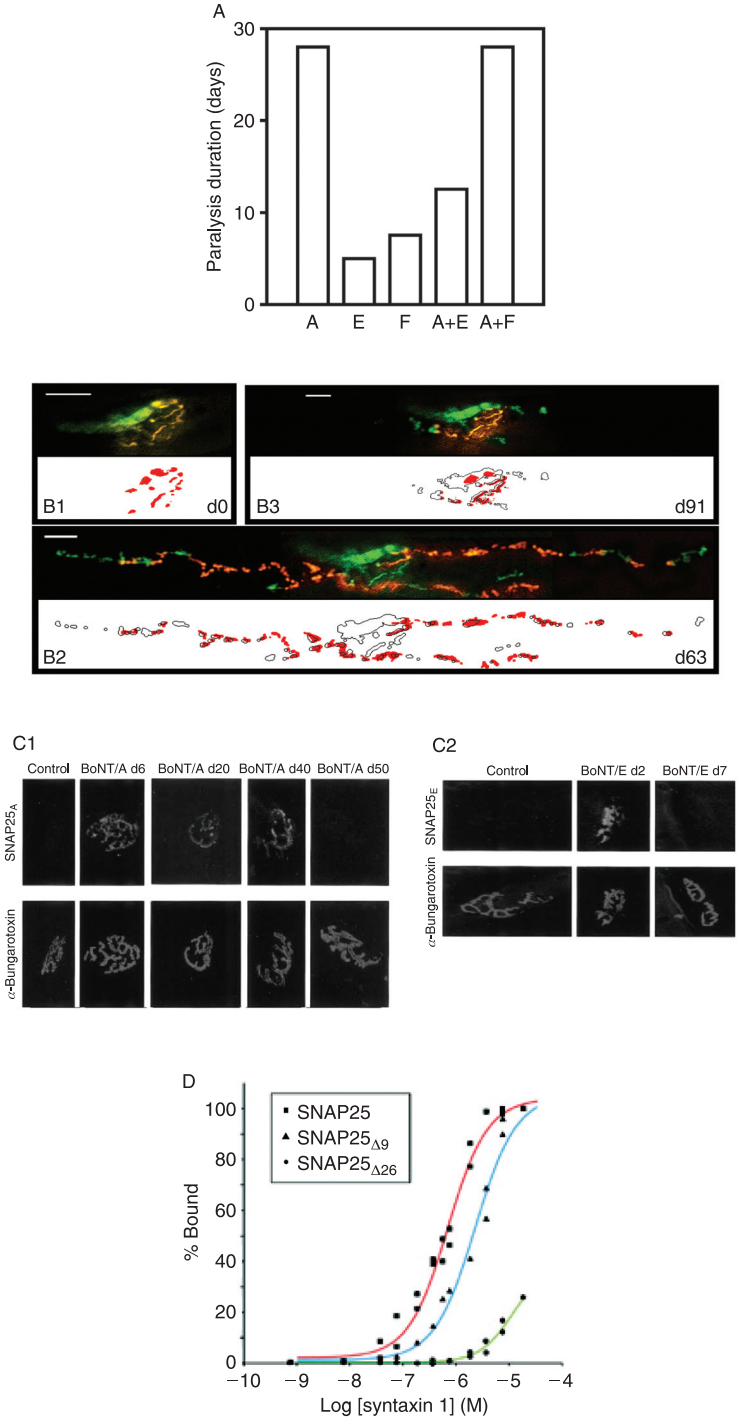

Figure 2.6 Neuromuscular paralysis induced by BoNT/A is very prolonged compared to that produced by other serotypes, accords with the persistence of cleaved SNAP-25 and is accompanied by extensive and reversible remodelling of the end-plates. (A) Extent of paralysis was determined using the toe spread reflex (TSR) assay for mice injected (at day 0) in the hind leg with A, 5 pg BoNT/A; E, 50 pg BoNT/E; F, 4 ng BoNT/F; A+E, 2.5 pg BoNT/A + 25 pg BoNT/E and A+F,

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Caption for Figure 2.6 (*cont.*) 2.5 pg BoNT/A + 2 ng BoNT/F, doses that had been predetermined to produce a maximum TSR score in the absence of any other symptoms of botulism. The plotted data indicate the time taken for the TSR score to return to baseline. (B) The lower panels represent localization of a nerve-terminal and its sprouts with the mitochondrial activity dye 4-di-2-ASP (outlined areas) and detection of vesicle-recycling with FM1-43 labelling (solid areas) in mouse sternamastoid muscle before the injection of 0.5 pg BoNT/A haemagglutinin complex (B1), the original terminal and extensive terminal sprouts at day 63 after injection (B2) and, at day 91, the original terminal with sprouts almost fully retracted (B3). The upper panels show composites of the images captured with each dye. (C) The products of SNAP-25 cleavage by BoNT/A ($SNAP\text{-}25_A$; C1) or BoNT/E ($SNAP\text{-}25_E$; C2) detected in mouse extensor digitorum longus muscles after injection of the requisite neurotoxin. Note that cleavage product can be detected up to 40 days after the injection of BoNT/A, but E-truncated SNAP-25 was removed within a week after administration of BoNT/E. (D) Increasing amounts of syntaxin 1 were incubated with resin-immobilized full-length SNAP-25 or truncated forms equivalent to the products of SNAP-25 cleavage by BoNT/A ($SNAP\text{-}25_{\triangle 9}$) or /E ($SNAP\text{-}25_{\triangle 25}$). Bound syntaxin was quantified by Western blotting. From Bajohrs *et al.* (2004).

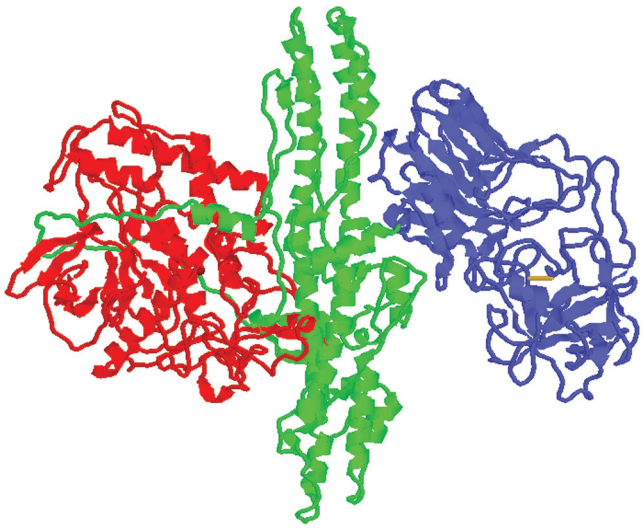

Figure 3.2 Structure and action of the botulinum neurotoxins. The figure shows a representation of the three-dimensional structure of a botulinum neurotoxin. The toxin exerts its neuroparalytic action via a four-step mechanism. Once in the blood stream, domains within the C-terminal portion of the toxin heavy chain (H_C domain, shown in blue) bind to acceptors on the pre-synaptic nerve surface. After binding, the toxin is internalized into endosomes from where it is translocated across the membrane into the cytosol by the translocation domain (H_N domain, shown in green). Once in the cytosol, the light chain (shown in red), which is a highly specific zinc-dependent protease, cleaves and inactivates an essential component of the neuroexocytosis apparatus.

