Storage release and metabolism of acetylcholine at the synapse

This will all be the same in any cholinergic synapse, be it neuromuscular or parasympathetic.

Choline is present in the synapse, and is absorbed by a presynaptic sodium-dependent transporter (CHT1). This is the rate-limiting step of Ach synthesis.

Once inside, choline is combined with acetate by choline acetyltransferase (ChAcT).

The finished acetylcholine is stored in vesicles by Vesicular Acetylcholine Transporter (VAcT). There is up to 50,000 molecules per vesicle, and about 300,000 vesicles per nerve terminal.

Hemicholinium blocks the choline transporter, and thus disables the rate limiting step of acetylcholine synthesis. It can be described as an indirect anticholinergic drug.

Arrival of the action potential opens voltage-gated calcium channels, which activates Synaptosome-associated proteins (SNAPs) and vesicle-associated membrane proteins (VAMPs). This causes fusion of the vesicle with the membrane. Acetylcholine is thus released.

Botulinum and tetanus toxins proteolyse the fusion proteins, synaptobrevin specifically, and thus prevent release of catecholamines and acetylcholine. I suppose that also makes botulinum toxin an indirect anticholinergic drug. The tetanus toxin only acts on these proteins at the GABA and glycine vesicles in the CNS.

Acetylcholinesterase is the postsynaptic membrane enzyme responsible for the metabolism of acetylcholine, and it performs this task with incredible speed. Less than a millisecond is required to destroy all the acetylcholine molecules. The result is acetate (which diffuses god knows where, who cares) and choline, which is sucked back into the transporter.

Acetylcholinesterase inhibitors prevent the degradation of acetylcholine; This results in a bouquet of symptoms which is far outside the descriptive scope of a mere round-cornered text box. However, I will list some drugs which act this way:

- Neostigmine
- Physostigmine
- Galantamine
- Donepezil
- Sarin nerve gas
- Organophosphates

From Peck and Hill "Pharmacology for Anaesthesia and Intensive care" as well as the mighty "Handbook of Pharmacology and Physiology in Anaesthetic Practice" by Stoelting and Hillier.