Drugs used for maintenance of anaesthesia will provide mild to moderate muscle relaxation at a depth of anaesthesia suitable for surgery. Sometimes more profound muscle relaxation is required. This can be achieved by:

- Increasing the depth of anaesthesia. ‘Deep’ anaesthesia will increase the degree of muscle relaxation, however this is not recommended due to the severe cardiovascular and respiratory depression associated with the high doses of anaesthetic agents needed.

- Local anaesthetic techniques. A retrobulbar nerve block can be used to achieve a central eye position by paralysing the motor nerves supplying the extra ocular muscles, however the associated risks and technical difficulty mean it is rarely used in small animals.

- Centrally acting muscle relaxants such as benzodiazepines provide muscle relaxation by affecting the central nervous system. They do not produce the profound muscle relaxation seen with drugs acting directly on the neuromuscular junction and they have other side effects which may be undesirable.

- Peripherally acting muscle relaxants. Neuromuscular blocking agents (NMBAs) act at the neuromuscular junction (See figure 1), abolishing all muscle tone, providing complete skeletal muscle relaxation throughout the body and are the usual way to achieve the required muscle relaxation for a variety of surgical techniques.
Indications for Neuromuscular Blockade

- Intra-ocular or corneal surgery
A non-moving, central eye is required to perform intra-ocular or corneal surgery. Under anaesthesia the eye rotates ventromedially. NMBAs produce a central eye due to paralysis of the extra ocular muscles. They also prevent coughing or patient movement which can have disastrous consequences during ocular surgery.

- Abdominal surgery
NMBAs facilitate abdominal surgery, especially in deep chested dogs or for deep dissection during cranial abdominal surgeries such as adrenalectomies or nephrectomies. NMBAs may also be useful for cervical spinal surgery in dogs with large cervical muscles.

- Thoracic surgery
Although not always required, NMBAs can be useful to control ventilation during thoracotomies in patients who resist the intermittent positive pressure ventilation (IPPV) required, making surgical conditions difficult.

- To assist reduction of dislocated joints
Although controversial in small animals patients, NMBAs are used to improve surgical conditions for fracture repairs in equine patients.

- To facilitate endotracheal intubation in cats
Cats have very sensitive larynxes which easily spasm when stimulated. Normally this is avoided by the use of topical local anaesthetic spray, however this takes about one minute to reach peak effect. In patients with severe respiratory compromise (eg. diaphragmatic hernia), a faster intubation may be beneficial. The use of suxamethonium, a fast acting NMBA, can be used to allow rapid endotracheal intubation and is the only time when NMBAs are administered before the airway is secured.
NMBAs cause paralysis of all skeletal muscle groups including the respiratory muscles, therefore equipment must be prepared and checked for endotracheal intubation and IPPV prior to their administration. NMBAs have no analgesic or anaesthetic effects so adequate anaesthetic depth must be maintained throughout the procedure and appropriate analgesia administered.
Anatomy of the Neuromuscular Junction (NMJ)

The nerve ending contains vesicles containing the neurotransmitter acetylcholine (ACh) which when released crosses the synaptic cleft and binds to the ACh receptors on the motor end plate of the muscle. The binding of ACh to these receptors stimulates muscle contraction.

There are 2 types of NMBA, depolarising and non-depolarising

- Depolarising (non-competitive) NMBAs
  These are similar in structure to acetylcholine (ACh) and they bind to the post-junctional receptors causing initial muscle contraction before relaxation. This is seen as short-lived painful muscle fasciculations throughout the body, before relaxation occurs. The only depolarising muscle relaxation used clinically is suxamethonium. In the cat, suxamethonium has a rapid onset and short duration of action (2-5 minutes).

- Non-depolarising (competitive) NMBAs
  Non-depolarising NMBAs compete with ACh for post-junctional binding sites causing complete muscle relaxation without the initial muscle contractions seen with depolarising NMBAs. Non-depolarising NMBAs are widely used because their effects can be reversed and they can be ‘topped up’ as required. There are several different non-depolarising NMBA’s available.
Pancuronium is an aminosteroid which causes tachycardia after injection. It used to be commonly used although it has been superceded by newer aminosteroid agents such as vecuronium.

Vecuronium is derived from pancuronium and is commonly used in dogs and cats. It has a dose dependent duration of action of about 20-30 minutes, can be ‘topped up’ and administered as an infusion. It is metabolised by the liver and excreted by the kidneys.

Atracurium is broken down spontaneously in a pH and temperature dependent reaction called Hofmann degradation. This means it is useful in patients with renal or hepatic impairment, however hypothermia or acid-base disturbances may prolong the duration of action. Atracurium can cause histamine release so should be injected slowly and diluted. Duration of action is dose dependent but typically lasts about 30-40 minutes. It can also be administered as an infusion.

Mivacurium is rarely used in small animals. In cats it has a rapid onset and medium duration of action, however in dogs it has a very long duration of action so should be avoided.

Rocuronium is a relatively recently developed aminosteroid with a very rapid onset and medium duration of action. The main advantage over more commonly used NMBAs such as vecuronium is the recent development of a rocuronium specific antagonist (see final paragraph)
Monitoring NMBA

An adequate depth of anaesthesia must be maintained when NMBAs are used, otherwise the patient may become ‘awake’ but paralysed. It is more difficult to assess anaesthetic depth when using NMBAs. If there is inadequate anaesthetic depth the eye position will remain central, there will be no palpebral reflex, the respiratory pattern will not change and the animal will not move. Signs of inadequate anaesthetic depth when using an N MBA include: increased heart rate and blood pressure, increase in end-expired carbon dioxide unrelated to changes in ventilation. Lacrimation, salivation, muscle fasciculations and ‘bucking of the ventilator’ may also be observed.

The onset, duration and depth of neuromuscular blockade should be monitored, this helps determine when the neuromuscular blockade has worn off or can be reversed. Neuromuscular blockade is monitored using a peripheral nerve stimulator (PNS). These stimulate muscle contraction following stimulation of the corresponding motor nerve. The degree of muscle contraction can be assessed (by feel or by sight) and compared before and after N MBA administration. Commonly used nerves are the peroneal nerve, the ulna nerve, or a branch of the facial nerve. There are a number of different patterns of stimulation which can be used. The most commonly used is the ‘train of four’ (TOF) pattern of stimulation. Four electrical stimuli are given over two seconds producing four corresponding muscle twitches. After administration of an N MBA the strength of the twitches will reduce, starting with the fourth twitch, until they disappear. This is called ‘fade’. Once neuromuscular blockade begins to wear off, the reverse will occur, i.e. the first twitch will begin to appear faintly at first before getting stronger until four equal strength twitches have returned. The strength of the forth twitch is compared to the last twitch and is referred to as the T4:T1 ratio, which should be equal (a ratio of one) prior to recovery from anaesthesia. The double burst stimulation (DBS) gives two individual muscle twitches (D1 and D2) which can be useful at the end of anaesthesia as it is easier to detect fade than with the TOF. D2:D1 ratio using the DBS correlates to the T4:T1 ratio but it is easier to palpate. It is important to remember that visual and tactile assessment of DBS and TOF is unable to detect small differences in strength of muscle contractions (i.e. there may be differences between T4 and T1 but they will feel the same strength), therefore there may be residual neuromuscular blockade and inadequate neuromuscular function. This demonstrates that care should be taken to ensure when discontinuing the anaesthetic that the patient is able to adequately ventilate and has adequate laryngeal function. Close
monitoring of chest excursions and the capnograph is necessary when weaning from the ventilator and recovering from anaesthesia. Any paradoxical breathing, inadequate chest excursions, rising end-expired carbon dioxide or a falling SpO₂ may be signs of residual neuromuscular blockade causing inadequate ventilation.

Reversal of Neuromuscular Blocking Agents

Depolarising neuromuscular blocking agents cannot be reversed, however the effects of non-depolarising NMBAs can be reversed by the use of anticholinesterases. These inhibit the enzyme acetylcholinesterase, which is responsible for the break-down of ACh, therefore the administration of an anticholinesterase such as neostigmine or edrophonium increases the amount of ACh at the NMJ displacing the non-depolarising agent that is bound to the post-junctional receptors. These effects occur not just at the NMJ, but the concentration of ACh increases throughout the body causing unwanted side effects such as bradycardia or even asystole, bronchospasm and diarrhoea. These side effects are prevented by the concurrent administration of an anticholinergic such as atropine or glycopyrrolate.

Sugammadex
Sugammadex has been recently developed to antagonise some non-depolarising NMBAs. Human studies have demonstrated it to fully and rapidly antagonise the effects of rocuronium. Subject to clinical trials of Sugammadex in animals this recent development may mean NMBAs (especially rocuronium) are more commonly used in veterinary medicine.