Muscle relaxants (peripherally acting) and cholinesterase inhibitors
**Muscle relaxants**

Muscle relaxants used in surgery include suxamethonium, alcuronium, and vecuronium; for further details see section 1.4.

**Cholinesterase inhibitors**

**MYASTHENIA GRAVIS**

Cholinesterase inhibitors, such as neostigmine and pyridostigmine, are used in the symptomatic treatment of myasthenia gravis. They act by inhibiting acetylcholinesterase, thereby prolonging the action of acetylcholine, and thus enhancing neuromuscular transmission; this produces at least a partial improvement in most myasthenic patients but complete restoration of muscle strength is rare. Unless the patient has difficulty in swallowing, cholinesterase inhibitors are given by mouth. Pyridostigmine has a slower onset (usually within 30–60 minutes), but a longer duration of effect than neostigmine; it also tends to cause fewer muscarinic effects such as diarrhoea, abdominal cramps, and excess salivation, so is usually preferred. Doses should be carefully adjusted to avoid precipitating a cholinergic crisis due to overdosage; this must be differentiated from a myasthenic crisis due to disease progression, and consequent underdosage; the principal effect in both cases is increased muscle weakness.

In myasthenic crisis, if the patient has difficulty in breathing and in swallowing, the cholinesterase inhibitor must be given by intramuscular or subcutaneous injection; neostigmine is usually preferred. To reduce muscarinic effects, atropine (section 1.3) should also be given.

For the use of neostigmine in surgery, see section 1.4.

A corticosteroid such as prednisolone (section 18.1), is used for the treatment of myasthenia gravis; addition of azathioprine (section 8.1) may allow a dose reduction of both the corticosteroid and of the anticholinesterase.

**Neostigmine**

*Tablets*, neostigmine bromide 15 mg

*Injection* (Solution for injection), neostigmine metilsulfate 500 micrograms/ml, 1-ml ampoule; 2.5 mg/ml, 1-ml ampoule

**Uses:**

myasthenia gravis; reversal of non-depolarizing block, postoperative urinary retention (section 1.4)

**Contraindications:**
recent intestinal or bladder surgery; mechanical intestinal or urinary tract obstruction; after suxamethonium; pneumonia; peritonitis

**Precautions:**

asthma; urinary tract infections; cardiovascular disease including arrhythmias (especially bradycardia, vagotonia, recent myocardial infarction or atrioventricular block); hyperthyroidism; hypotension; peptic ulcer; epilepsy; parkinsonism; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3);

**interactions:** Appendix 1

**Dosage:**

Myasthenia gravis, *by mouth* as neostigmine bromide, **ADULT** initially 15–30 mg at suitable intervals throughout the day, gradually increased until desired response obtained, total daily dose within range 75–300 mg, taken at appropriate intervals when maximum strength required, but doses above 180 mg daily not usually tolerated; **CHILD** up to 6 years, initially 7.5 mg, 6–12 years, initially 15 mg, total daily dose usually 15–90 mg in divided doses at appropriate intervals

Myasthenia gravis, *by subcutaneous or intramuscular injection* as neostigmine metilsulfate, **ADULT** 0.5–2.5 mg as required, total daily dose 5–20 mg; **NEONATE** 50–250 micrograms 30 minutes before feeds (not usually required beyond 8 weeks of age); **CHILD** 200–500 micrograms as required

**Adverse effects:**

increased salivation, nausea and vomiting, abdominal cramps, diarrhoea; signs of overdosage include bronchoconstriction, increased bronchial secretions, lacrimation, excessive sweating, involuntary defecation and micturition, miosis, nystagmus, bradycardia, heart block, arrhythmias, hypotension, agitation, excessive dreaming, weakness eventually leading to fasciculation and paralysis; thrombophlebitis reported; rash associated with bromide salt

**Pyridostigmine bromide**

Pyridostigmine bromide is a complementary cholinesterase inhibitor

*Tablets*, pyridostigmine bromide 60 mg

*Injection* (Solution for injection), pyridostigmine bromide 1 mg/ml, 1-ml ampoule

**Uses:**

myasthenia gravis

**Contraindications:**

recent intestinal or bladder surgery; mechanical intestinal or urinary tract obstruction; after suxamethonium; pneumonia; peritonitis
Precautions:

asthma; urinary tract infection; cardiovascular disease including arrhythmias (especially bradycardia or atrioventricular block); hyperthyroidism; hypotension; peptic ulcer; epilepsy; parkinsonism; avoid intravenous injection; renal impairment (Appendix 4); pregnancy and breastfeeding (Appendices 2 and 3); interactions: Appendix 1

Dosage:

Myasthenia gravis, by mouth, **ADULT** initially 30–120 mg at suitable intervals throughout the day, gradually increased until desired response obtained; total daily dose within range 0.3–1.2 g, taken at appropriate intervals when maximum strength required, but doses above 450 mg daily not usually advisable in order to avoid acetylcholine receptor downregulation; **CHILD** up to 6 years initially 30 mg, 6–12 years initially 60 mg; total daily dose usually 30–360 mg in divided doses at appropriate intervals

Myasthenia gravis, by intramuscular injection, **ADULT** 2 mg every 2–3 hours; **neonate** 50–150 micrograms before feeds (but neostigmine usually preferred); **CHILD**, total daily dose 1–12 mg given in divided doses at appropriate intervals

Adverse effects:

muscarinic effects generally weaker than with neostigmine: increased salivation, nausea and vomiting, abdominal cramps, diarrhoea; signs of overdosage include bronchoconstriction, increased bronchial secretions, lacrimation, excessive sweating, involuntary defecation and micturition, miosis, nystagmus, bradycardia, heart block, arrhythmias, hypotension, agitation, excessive dreaming, weakness eventually leading to fasciculation and paralysis; thrombophlebitis; rash associated with bromide salt