NEUROMUSCULAR BLOCKERS

Drug Name	Adult Dosing	Onset	Duration	Half-Life	Notes
Depolarizing Agents: *Binds directly to nicotinic receptors on the motor end plate and causes excessive depolarization that results in paralysis of skeletal muscle.*					
Succinylcholine (Anectine; Quelicin)	RSI: 1 - 1.5 mg/kg IV push (usually 100-150 mg) Note: NO infusion dosing option IM: Up to 3 - 4 mg/kg (max 150 mg) deep IM (preferably in the deltoid muscle)	IV: 30 - 60s IM: 2 - 3 m	IV: 4 - 6 m IM: 10-30m	< 1 min	• Only one that can be given IM or IV; but IV is preferred • Reduce dose in states of plasma cholinesterase deficiency (genetic deficiencies, infection, decompensated HF, malignant tumors, pregnancy, myxedema) • Caution in CKD, hyperkalemia (can↑ K^+ by 0.5 mEq/L), extensive (>30%) burns (usually after 48-72hrs, malignant hyperthermia, elevated CPK, rhabdomyolysis, skeletal muscle myopathy, high ICP, or IOP. • Bradycardia can occur (esp in pediatrics with 2nd doses) due to cross activation of M2 receptors.
Non-Depolarizing Agents: *Inhibits the binding of acetylcholine to nicotinic receptors on the motor endplate thereby inhibiting depolarization of skeletal muscle.*					
Atracurium (Tracrium)	Surgery: 0.4 - 0.5 mg/kg; then 0.08 - 0.1 mg/kg given 20 - 45 min after initial dose ICU Paralysis: 0.4 - 0.5 mg/kg, then 5 - 10 mcg/kg/min IV infusion	2 - 3 min	20 - 35 min	2 - 20 min	• ED95 = 0.2 mg/kg • Can be cleared independently of renal/hepatic function why no dose adjustments are required. Clearance is by non-enzymatic, spontaneous degradation at normal body temp and pH (aka, Hofmann Elimination) • Forms inactive metabolite (Laudanosine) which has no paralytic activity, but does cause CNS stimulation
Cisatracurium (Nimbex)	Surgery: 0.15 - 0.2 mg/kg; if giving after succinylcholine then 0.1 mg/kg. ICU infusion: 3 mcg/kg/min	2 - 3 min	20 - 35 min	22 - 29 min	• ED95 = 0.05 mg/kg; 3x more potent than atracurium lasts 2 min longer • It is 1 of 10 different stereoisomers of atracurium so undergoes same metabolism • Differs from atracurium in that it does not cause histamine release or have effects on heart
Pancuronium (Pavulon)	Surgery: 0.06 - 0.1 mg/kg; then 0.01 mg/kg given 60-100 min after initial dose ICU Paralysis: 0.06 - 0.1 mg/kg bolus, then 1 - 2 mcg/kg/min	2 - 3 min	60 - 100 m	110 min	• ED95 = 0.07 mg/kg • Longest duration of action of all agents; Half-life doubled when CrCl < 50 mL/min; avoid if CrCl < 10 • Most structurally similar to the structure of acetylcholine giving it a higher degree of neuromuscular blocking activity, but also cross inhibits muscarinic receptors • SE: increase in pulse, CO, MAP especially in AV conduction disorders; does not release histamine
Rocuronium (Zemuron)	RSI: 0.6 - 1.2 mg/kg (some use 1 mg/kg for ease; so 70 -100 mg) Pre-induction: 0.03 - 0.06 mg/kg x1 ICU Paralysis: 0.6 - 1 mg/kg bolus, then 8 - 12 mcg/kg/min IV infusion.	1 - 2 min	30 min	60 - 70 min	• ED95 = 0.3 mg/kg (less potent than vecuronium but has a quicker onset of action because the higher doses of rocuronium needed also means more molecules are available to diffuse into the neuromuscular junction and inhibit more nicotinic receptors thereby causing skeletal muscle paralysis faster) • Cleared hepatically (50%) and renally (30%). Duration prolonged in liver disease; No renal dosing needed • Caution in patients with pulmonary hypertension due to increases in pulmonary vascular resistance
Vecuronium (Norcuron)	Intubation: 0.08 - 0.1 mg/kg (or) 7-10 mg (if priming needed: 10% of dose given 3 - 5 min before intubating dose). ICU Paralysis: 0.08 - 0.1 mg/kg bolus; then 0.8 - 1.7 mcg/kg/min IV infusion.	3 - 5 min	45 - 65 min	65 - 70 min	• ED95 = 0.05 mg/kg (more potent than rocuronium; why dosing is less BUT rocuronium has quicker onset because higher dosing also means more molecules to inhibit nicotinic receptors • Duration of paralysis not really impacted by renal function unless anephric (30% is eliminated in urine) • When able, stop infusions daily until forced to restart to help prevent post-paralytic complications • Children 1-10 years may require initial higher doses and more frequent supplementation

General Notes For All Of The Agents:

- The #1 cause of anaphylactic reactions in the operating room includes: neuromuscular blockers. This is followed by antibiotics and then latex exposure.
- Indications for RSI (rapid placement of ET tube in patients at high risk for aspiration) include: trauma presentation, recent PO intake, diabetics, obesity, pregnancy, GERD, ascites, bowel obstruction, hiatal hernia, high dose opioid use. RSI includes providing: pre-oxygenation (3-5 min of 100% O2 via non-re-breather mask; NOT bag-mask ventilation), cricoid pressure as induction agent being injected, then paralytic), and reasonable belief you can oxygenate and ventilate if needed. Differs from a modified RSI, which also includes providing some positive pressure ventilation (can increase risk of gastric distention). Note: if using methohexital or thiopental (both alkaline agents pH ~10) for induction in RSI, flush IV with NS and or wait 5 secs while line flushes before giving neuromuscular blocker (all acidic formulations) to prevent precipitation in the IV line.
- Most common agents used in RSI: succinylcholine (primarily due to PK profile) and rocuronium (less common because of its duration of action; but reserved for cases with contraindications to succinylcholine)
- In obese patients can give consideration of using ideal body weight versus actual body weight since we neuromuscular blockers are targeting muscle and not fat.
- Factors that increase doses (hyperthermia, chronic alcoholism). Factors that decrease doses (elderly, hypothermia, acute alcohol use, hypotension, pregnancy).
- If used in combination with corticosteroids, recovery from paralysis can be prolonged and there is increased risk of acute quadriplegic myopathy syndrome (AQMS).
- None of these agents provide analgesia and thus patients should be treated adequately for pain and sedation prior to use of paralytics.
- Resistance can occur in burn patients (>30% of body) for up to 70 days post-burn. Also duration of action can be prolonged in states of hypothermia.
- Peripheral nerve stimulator is the most reliable method to monitor effect of neuromuscular blocker paralysis. Depression of tactile response > 90% correlates to skeletal muscle relaxation.
- For continuous infusions or prolonged states of paralysis, tape eyelids closed and use ophthalmic ointment to prevent keratitis and corneal abrasions.
- Reversal of non-depolarizing agents has historically been achieved with acetylcholinesterase inhibitors such as neostigmine (Prostigmin) or edrophonium (Enlon), however in 2015 approved sugammadex (Bridion) to reverse rocuronium and vecuronium in adults undergoing surgery with most patients recovering within 5 mins through a direct binding to the neuromuscular blocker thereby removing the drug from the NMJ. Anaphylactic reactions have occurred with sugammadex use. Note: None of these reversal agents work with succinylcholine and may be harmful.

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