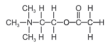
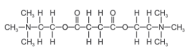
SUCCINYLCHOLINE

General	**-Only depolarizing in clinical use** **-Copycat Ach structure**	Acetylcholine  Succinylcholine 
Onset	Rapid onset (30-60s)	Low lipid solubility as well as relative overdose given
DOA	Short duration of action (< 10 min)	Prolonged by high dose or abnormal metabolism as in: 1.Hypothermia in which there is a decreased rate of hydrolysis 2.Low pseudo-cholinesterase levels due to pregnancy, liver disease, renal failure and drugs e.g Esmolol, metoclopramide, OCP among others table (11-3) 3.Genetically variable enzyme →1 in 50 = one normal and one abnormal gene → Slightly prolonged block (20-30 min) →1 in 3000: -2 abnormal genes, up to 4-8 hour blockade -Dibucaine resistant –most common abnormal pseudocholinesterase
Metabolism	pseudocholinesterase	- Only small fraction of injected dose reach NMJ - **S**uccinylcholine is not metabolized by acetylcholinesterase, it unbinds the receptor and diffuses away from the neuromuscular junction to be hydrolyzed in the plasma and liver by another enzyme, pseudocholinesterase (nonspecific cholinesterase, plasma cholinesterase, or butyrylcholinesterase)
Drug interactions	Cholinesterase inhibitors	→Prolong phase 1 block -Inhibit acetylcholinesterase=higher ach concentration which increase depolarization -Reduce hydrolysis of succinylcholine by Inhibiting pseudocholinestrase
Dosage	Adult	-Intubation ⊡ 1-1.5 mg/kg IV *(possibly excessive) ⊡ .5 mg/kg acceptable if defasciculating dose of non-depolarizer is not used -Maintenance Repeated small bolus (10mg) or drip (1g in 500-1000ml titrated to effect)
	Children	Intubation ⊡ Infants/Small kids: 2mg/kg ⊡ Older children and Adolescents 1mg/kg
Side effects	CVS	▪ Variable Secondary to possible stimulation of nicotinic receptors in parasympathetic and sympathetic ganglia, as well as muscarinic receptors in SA node ▪ Low doses Can produce negative chronotropic/inotropic effects ▪ Higher doses Tend to increase heart rate and contractility as well as elevate circulating catecholamine ▪ Children Particularly susceptible to bradycardia Often treated prophylactically with atropine
	NM	⊡ Fasciculation ▪ Signals onset of paralysis ▪ Prevented by non-depolarizing relaxant ⊡ Muscle Pains ▪ Increased post-op myalgia ▪ Possibly from unsynchronized contraction of muscle groups ▪ ncreased CK and myoglobinemia can be found after succinylcholine given ▪ Reduced by NSAID preoperatively ⊡ Malignant Hyperthermia Potent triggering agent in patients susceptible to MH

	K+	Hyperkalemia At Intubating dose, Normal muscle releases potassium to raise serum potassium level by .5 meq/l Excessive hyperkalemia (k level approaching 7meq/l) in cases of *Preexisting hyperkalemia (renal failure), Burn Injury, Massive Trauma, Neurological disorders (table 11-5)* If cardiac arrest occurs, it is proven to be quite refractory to routine cardiopulmonary resuscitation
	CNS	⊡ Intracranial pressure May lead to increase in cerebral blood flow and ICP ▪ Attenuated with hyperventilation/good airway control ▪ Pre-treat with non-depolarizing muscle relaxant and IV lidocaine 2-3 minutes prior to intubation
	GI	⊡ Intragastric pressure elevation Abdominal wall fasciculations increase pressure ▪ Offset by increased LES tone ▪ No increase reflux/aspiration ▪ Abolished by pretreatment
	Eye	⊡ Intraocular pressure elevation ▪ Extra-ocular muscle ▫ multiple motor-end plates each cell ▪ Prolonged depolarization and contraction of muscle transiently raise IOP ▫ Worrisome in patient's with injured eye

TABLE 11–5 Conditions causing susceptibility to succinylcholine-induced hyperkalemia.

Burn injury
Massive trauma
Severe intraabdominal infection
Spinal cord injury
Encephalitis
Stroke
Guillain-Barré syndrome
Severe Parkinson's disease
Tetanus
Prolonged total body immobilization
Ruptured cerebral aneurysm
Polyneuropathy
Closed head injury
Hemorrhagic shock with metabolic acidosis
Myopathies (eg, Duchenne's dystrophy)

TABLE 11–3 Drugs known to decrease pseudocholinesterase activity.

Drug	Description
Echothiophate	Organophosphate use for glaucoma
Neostigmine Pyridostigmine	Cholinesterase inhibitors
Phenelzine	Monoamine oxidase inhibitor
Cyclophosphamide	Antineoplastic agent
Metoclopramide	Antiemetic/prokinetic agent
Esmolol	β-Blocker
Pancuronium	Nondepolarizing muscle relaxant
Oral contraceptives	Various agents

	Atracurium	Cisatracurium	Mivacurium	Doxacuronium	Pancuronium	Pipecuronium	Vecuronium	Rocuronium	Gantacurium
General	Benzylisoquinoline	-Stereoisomer of atracurium -4 times more potent Benzyl	Benzyl	Benzylisoquinoline	Steroid base	Steroid base (similar to Pancuronium)		Analogue of vecuronium designed for rapid onset	-chlorofumarates -provided as a lyophilized powder bc its not stable as an aqueous solution.
Metabolism / excretion	-Metabolized independent of renal and biliary routes (Hoffman elimination) -Precipitate as free acid if placed in IV line with alkaline solution (thiopental)	Hoffman elimination	-Metabolized by pseudocholinesterase So it is prolonged by low pseudocholinesterase levels	Renal excretion Similar to other long acting non-depolarizers	-metabolized mostly by liver, Liver failure Prolongs pancuronium -Primarily renal excretion → Slowed by renal failure -Some excretion by bile Cirrhotic patients require higher initial dose	Renal excretion	-metabolized by liver mostly but liver failure has less effect on its duration of action than pancuronium. - renal excretion (Satisfactory in renal failure however some prolongation occurs)	-Primary hepatic and renal elimination →Duration of action prolonged by hepatic disease and pregnancy →Not Significantly affected by renal failure	Nonenzymatic degradation by 2 chemical mechanisms: 1)rapid formation of inactive cysteine adduction product 2)ester hydrolysis
Side effects/cons	-Laudanosine toxicity Product of breakdown of atracurium causes CNS excitation: possibly seizures but it is Only relevant at extremely high doses or hepatic failure -Triggers dose –dependent histamine release above .5mg/kg (intubating dose) {Hypotension/reflex tachycardia/cutaneous flush} anchorperm	-PH/Temperature sensitive occurs Secondary to unique metabolism So Prolonged action by hypothermia/acidosis	causes histamine release		-HTN and tachycardia →Combination of vagal blockade and sympathetic stimulation (autonomic effects) →Caution with CAD, aortic stenosis -Arrhythmias →Increases AV conduction and catecholamine release →Worsened in patients using TCA and halothane -Allergic reaction possible in patients hypersensitive to bromide		-Can cause potentiation of opioid-induced bradycardia -Long term administration causes buildup of active 3-hydroxy metabolite: elongates drug clearance and can cause polyneuropathy	-Can cause prolonged duration of action in elderly -Slight vagolytic tendencies	Cardiovascular effects suggestive of histamine release were observed following the use of three times the ED95 dosage.
	Autonomic side effects: Older agents (tubocurarine/metocurine) ⊡ Blocked autonomic ganglia → Decreased contractility/response to hypotension Newer agents ⊡ Devoid of significant autonomic effects								
pros		-Does not produce a dose-dependent increase in histamine -Also lower laudaonsine toxicity		No cardiac or histamine-release side effects		No cardiovascular side effects (Advantage over pancuronium)	No significant CV effects	-No active metabolite (Better choice for long term infusion) -.1 mg/kg shown to be rapid and effective agent (decreased fasciculations and post-op myalgias) for precurarization administration of succinylcholine	The newer neuromuscular blocking agents, such as gantacurium, which are still under investigation, show promise as ultrashort-acting nondepolarizing agents; they undergo chemical degradation by rapid adduction with L-cysteine.

DOA (blockade)	(INTERMEDIATE ACTING)	(INTERMEDIATE ACTING)	-Brief duration of action About half of atracurium/vec/ rocuronium -Markedly prolonged by prior administration of pancuronium (SHORT ACTING)	Duration:60-90 minutes (LONG ACTING) (like succinylcholine)	(LONG ACTING)	(LONG ACTING)	(INTERMEDIAT E ACTING)	(INTERMEDIATE ACTING)	Ultrashort DOA, similar to succinylcholine
	Factors affecting the blockade duration 1.Temperature ▪ Hypothermia prolongs blockade by decreasing metabolism and excretion 2.Acid-Base ▪ Respiratory acidosis potentiates blockade 3.Hypokalemia/Hypocalcemia ▪ Prolong blockade 4.Hypermagesemia ▪ Prolongs blockade by competing with Ca++ at motor-end plate, Seen in preeclampsia								
Onset Generally: (Greater Potency= slower onset)				Slow onset (4-6 minutes) .05mg/kg for tracheal intubation within 5 min				-Useful for quick onset of action (Closest non-depolarizer to succinylcholine)	-At a dose of 0.2 mg/kg (ED95), the onset of action has been estimated to be 1-2 min -Its clinical duration of action ranged from 5-10 min; recovery can be accelerated by edropho- nium, as well as by the administration of exogenous cysteine

- Three types
  - Benzylisoquinolines
    - Release histamine
  - Steroids
    - Vagolytic
    - Related allergic history
  - Other compounds (like chlorofumarates)

Drug	Structure	Metabolism	Primary Excretion	Onset	Duration	Hist. release	Vagal Blockade
Atracurium	Benzylisoquinolone	+++	x	++	++	+	0
Cisatracurium	Benzylisoquinolone	+++	x	++	++	0	0
Mivacurium	Benzylisoquinolone	Cholinesterase	x	++	+	+	0
Doxacurium	Benzylisoquinolone	Insignificant	Renal	+++	+++	0	0
Pancuronium	Steroidal	+	Renal	+++	+++	0	++
Pipercuronium	Steroidal	+	Renal	+++	+++	0	0
Vecuronium	Steroidal	+	Biliary	++	++	0	0
Rocuronium	Steroidal	insignificant	Biliary	+	++	0	+

Depolarizing	Non-depolarizing
Short-acting Succinylcholine	Short-acting Mivacurium
	Intermediate-acting
	Atracurium; Cisatracurium
	Rocuronium; Vecuronium
	Long-Acting
	Doxacurium
	Pancuronium; Pipecuronium

non-depolarizers:

- Intubation
  - None as rapid onset as succinylcholine
  - Quickened by larger dose or priming dose → but Prolongs duration of blockade and exacerbates SE
  - Priming dose: 10-15 % of intubating dose 5 minutes before induction will occupy enough receptors so that paralysis quickly follows full dose:
    - Intubation conditions at 60s (Rocuronium), 90s with other intermediate-acting depolarizers
    - Does not usually lead to clinically significant paralysis (75-80% of receptors blocked)
    - Can cause dyspnea, dysphagia and diplopia

- Maintenance relaxation
  - LARGE VARIABLE IN DOSE RESPONSES
  - Requires Close monitoring with Neuro-stimulator
  - Bolus or infusion should be guided by stimulator as well as clinical signs e.g. Movement or Spontaneous ventilation
  - Some return of neuromuscular transmission should be evident prior to bolus dose
  - Infusion should be titrated at or just above rate that allows return of neuromuscular transmission

- Potentiated by inhalational anesthetics
  - Volatile agents decrease dosage requirements by at least 15 %
  - Depends on agent
    - Des> Sevo > Iso and Enflurane > Halothane > N202
  - Muscle relaxant
    - Pancuronium > vecuronium and atracurium
    - Hypothetically due to volatile induced enhanced affinity for non-depolarizing muscle relaxants
- Excretion

1- hepatic
  - Pancuronium\Vecuronium metabolized mostly by liver
  - Liver failure
    - Prolongs pancuronium as well as rocuronium blockade
    - Less effect on vecuronium
    - No effect on Cisatracurium or atracurium

2- Renal
  - Doxacurium/Pancuronium/Vecuronium and pipecuronium excreted by kidneys
    - Prolonged action in patients with renal failure

- Age
  - Neonates have an increased sensitivity to nondepolarizing relaxants because of their immature neuromuscular junctions. This sensitivity does not necessarily decrease dosage requirements, as the neonate's greater extracellular space provides a larger volume of distribution.
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Drug	Intubation dose (mg/kg)	Onset of action for Intubating dose (min)	Duration of action (min)	Maintenance dosing by boluses(mg/kg)	Maintenance dosing by infusion (ug/kg/min)
Succinylcholine	1-1.5	.5-1	5-10	.15	2-15 mg/min
Rocuronium	.6	1.5-2.5	35-75	.15	9-12
Mivacurium	.2	2.5-3.0	15-20	.05	4-15
Atracurium	.5	2.5-3.0	30-45	,1	5-12
Cisatracurium	.2	3-4	40-75	.02	1-2
Vecuronium	.12	2-3	45-90	.01	1-2
Pancuronium	.12	2-3	60-120	.01	x
Pipercuronium	.1	2-3	80-120	.01	x
Doxacurium	.07	4-5	90-150	.05	x

TABLE 11–8 Additional considerations in special populations.

Pediatric	Succinylcholine – should not be used routinely Nondepolarizing agents – faster onset Vecuronium – long-acting in neonates
Elderly	Decreased clearance – prolonged duration, except with cisatracurium
Obese	Dosage 20% more than lean body weight; onset unchanged Prolonged duration, except with cisatracurium
Hepatic disease	Increased volume of distribution Pancuronium and vecuronium – prolonged elimination due to hepatic metabolism and biliary excretion Cisatracurium – unchanged Pseudocholinesterase decreased; prolonged action may be seen with succinylcholine in severe disease
Renal failure	Vecuronium – prolonged Rocuronium – relatively unchanged Cisatracurium – safest alternative
Critically ill	Myopathy, polyneuropathy, nicotinic acetylcholine receptor up-regulation