Q2 Suxamethonium is a non-competitive partial agonist. Explain what is meant by this statement using definitions of the underlined terms (50% of marks). List the advantages and disadvantages of suxamethonium within Intensive Care practice (50% of marks) (Sept 2012)

Agonist – an agonist is a drug able to generate a maximal response from a receptor. Not only do they have high affinity for the receptor, they also have high intrinsic activity.

Partial agonist – has significant receptor affinity but low intrinsic activity; ie, produces a submaximal effect compared with a full agonist. The distinguishing feature of partial agonists is that they fail to achieve a maximal effect even in a very high dose (ie, with full receptor occupancy)

Competitive drug – a competitive drug acts at the same receptor site as an endogenous ligand. The ratio of receptor occupation (drug vs endogenous ligand) depends on the relative amounts of each.

Suxamethonium is a noncompetitive drug because increasing the concentration of Ach (whose receptor it occupies) does not alter the binding of suxamethonium.

ADV/DISADV OF SUX IN INTENSIVE CARE

	ADVANTAGES	**DISADVANTAGE**
PHARMACEUTICAL	Inexpensive	Preparation needs to be stored at 4 degrees
PHARMACOKINETICS	Can be given peripherally Bioavailability 100% Rapid hydrolysis by plasma esterases Rapid onset (<1min) and half life (2-5min) – useful in intubation scenarios	Rapid onset/offset of action requires continuous infusion. Continuous infusion may lead to non-depolarising type block changing to a depolarising type block, requiring reversal with neostigmine/ glycopyrrolate Excretion of 10% of drug unchanged in urine means active metabolites may accumulate and prolong the effects. 0.03% of population are abnormal metabolisers resulting in prolonged apnoea Side effects: • Vagal activation – hypotension, bronchoconstriction, salivation, involuntary urination (the latter less significant in the catheterized patient) • Metabolic - Rise of serum K by 0.2-0.4mmol/L (more marked in patients with burns, muscle denervation eg SCI, renal failure – significant as many ICU patients have a degree of renal impairment) • CVS effects – bradycardia / ventricular arrhythmias (significant in haemodynamically unstable ICU patients) • Anaphylaxis • Malignant hyperthermia