Pharm-98B13 Draw and explain the characteristics of a log dose-response curve that describes the major clinical effect of vecuronium. List factors encountered in clinical practice that may alter this curve.

**Background**

Vecuronium is an aminosteroid non-depolarising neuromuscular blocker

Log dose-response curve refers to a plot of response on y-axis against log(dose) on x-axis.

For neuromuscular blockers, response may be quantified by biochemical parameters (e.g. %nAChR blocked) or clinical parameters (e.g. %T1 twitch height reduction compared to baseline)

**Log(dose)-response curve for vecuronium**

![Log(dose)-response curve for vecuronium](image)

Figure illustrating the typical sigmoidal shape of a log(dose)-response curve

Characteristics of the dose-response curve for vecuronium:

**1) ED50 (effective dose – 50)**
Definition = dose of vec that produces 50% reduction in baseline twitch height measured using a peripheral nerve stimulator at adductor pollicis

ED50 for vecuronium = 0.027 mg/kg *(Stoelting 5th)*

**2) Minimal response at low dose**
At low doses of vec → many nAChRs are not blocked (act as spare, due to inherent redundancy of the nAChR system) → minimal clinical response

**3) Steep upslope**
When more than 75% nAChRs are antagonised → reaches threshold (minimal spare receptors) → rapid increase in muscle blockade

**4) Plateau**
Nearly all nAChRs are blocked → further increase in dose results in nil significant further increase in muscle blockade
Factors that alter the vec log(dose)-response curve

Factors that increase potency of vec will LEFT shift log(dose)-response curve and vice versa

**Patient factors**
- ↑ age → relatively less muscle mass (for body weight) → LEFT shift
- obesity → relatively less muscle mass (for body weight) → LEFT shift (esp. if dosing based on TBW)
- male gender → relatively more muscle mass → RIGHT shift
- myasthenia gravis → relatively less spare nAChR → LEFT shift
- acidosis, hypermagnesaemia, hypokalaemia, hypocalcaemia → LEFT shift

**Pharmacodynamic factors**
- acetylcholinesterase inhibitors → ↑ACh at NMJ → competes with vec → RIGHT shift
- sugammadex → sequesters and inactivates vecuronium → RIGHT shift
- volatile anaesthetics → inhibit α-motor neurones, directly inhibit pre-synaptic and post-synaptic nAChRs → LEFT shift
- local anaesthetics (high doses) → blocks fast Na channels → ↓membrane excitability → LEFT shift
- aminoglycosides → blocks pre-synaptic Ca^{2+} channels → ↓pre-synaptic ACh release → LEFT shift
- lithium → ↓membrane excitability → LEFT shift
- frusemide (high doses) → ↓pre-synaptic AMP/ATP synthesis → ↓ACh release → LEFT shift

**Pharmacokinetic factors**
- hepatic dysfunction → ↓hepatic metabolism → LEFT shift
- hypothermia → ↓metabolism → LEFT shift