**ACEM PRIMARY 2013/1 Pharmacology VIVA** **Morning Session 1** ***Candidate Number:*** **AGREED MARK:**

| TOPIC | QUESTIONS | KNOWLEDGE **(essential in bold)** | NOTES |
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| Question 1:<br>**PHARMACOKINETICS**<br>LOA: 2 | Describe the pharmacokinetic changes that occur in the elderly | **Absorption**: nutritional deficits; delayed gastric emptying (diabetics); co ingested agents (laxatives, antacids)<br>**Distribution:** ↑ body fat, alpha-acid glycoprotein (bases); ↓ lean body mass, body water, albumin (weak acids);<br>**Metabolism**: ↓ phase 1 reactions P450; ↓ liver blood flow, liver disease, CCF, nutritional defic<br>**Elimination:** ↓ renal CL; renal disease; ↓ resp capacity; resp disease | **Hepatic metabolism↓**<br>**Renal clearance↓**<br>**+ 1 other** |
| Question 2<br>**VERAPAMIL**<br>LOA: 1 | Describe the effects of verapamil on the heart. | Binds to α1 receptor L-type Ca channel<br>**Blocks Ca influx**<br>**Reduced contractility** CO, $O_2$ demand<br>**Reduced** impulse generation/**conduction AV node**<br>Reduced coronary artery spasm | **Bolded** |
| | What are the indications for verapamil? | **Angina; hypertension; atrial arrhythmias**<br>migraine | **2 bolded** |
| | Name some clinical adverse effects | Extensions of therapeutic action (exacerbated by β blockers)<br>**Bradycardia; AV block; CCF; hypotension**<br>Other<br>Constipation; peripheral oedema; dizziness; flushing; nausea | **2 bolded** |

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| Question 3<br>**CEPHALOSPORINS**<br>LOA:1 | What is the mechanism of action of cephalosporins?<br><br>How does the spectrum of microbiological activity differ between the cephalosporin generations? | **Inhibit bacterial cell wall synthesis** , cell division and growth ( similar to penicillins)<br>Bacteriocidal<br>Work best in rapidly dividing cells<br><br>**1st generation: very active against GPC**, Ecoli, K.pneumoniae, proteus ok but Pseudomonas not. Anaerobic cocci sensitive<br>**2nd generation:** active against those by 1st generation but **added GN coverage** -klebsiella<br>Some anaerobe cover<br>NO Pseudomonas<br>**3rd generation expanded GN coverage and cross BBB**. Less active re staph . Work against B-lactamase Haemophilis and Neissria.<br>Ceftazadime works re Pseudomonas<br>4th generation more resistant to B- lactamases, extended coverage against enteric GNR-pseudomonas, enterobacteriaceae, S pneumonia, S aureus, Haemophilis and Neisseria. Cross BBB | **Bolded to pass**<br><br>**Understand the principles of the 1st, 2nd and 3rd generations** |
| Question 4<br>**KETAMINE**<br>LOA: 1 | What are the indications for ketamine<br><br>What are the routes of administration?<br><br>What is the IV dose used for induction of general anaesthesia?<br><br>Name some of the adverse effects. | **Induction agent, procedural sedation, analgesia**<br><br>**IV, IM,** IN, epidural, PO, PR, SC<br><br>**1-2 mg/kg**<br><br>**Hypersalivation, larygospasm(peds), vomiting(recovery phase), emergence reactions, Hypertension, tachycardia, raised ICP** | **2 of bolded**<br><br>**IV, IM + 1 other**<br><br>**Bolded**<br><br>**Emergence reactions + 2 other** |

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| Question 5<br>**N-ACETYLCYSTEINE**<br>LOA: 2 | What is the mechanism of action of N-acetylcysteine in paracetamol overdose? | Paracetamol metabolism by hepatic glucuronidation/sulphation is saturated resulting in increased metabolism via cytochrome p450 system to form N –acetylbenzoquinoneimine (NAPQI), a **toxic intermediate**. Elevated NAPQI production leads to depletion of hepatic glutathione stores, resulting in hepatotoxicity. NAC prevents paracetamol induced hepatotoxicy by 4 possible mechanisms:<br>**1) Increased glutathione availability**/Sulfhydryl donor<br>2) Direct binding to NAPQI<br>3) Provision of inorganic sulphate<br>4) Reduction of NAPQI back to paracetamol | **Bold to pass** |
| | Name an adverse effects of N-acetylcysteine. | Mild **anaphylactoid reactions**(15-20%)- mild flushing, rash and angio-oedema. | **Bold or description** |

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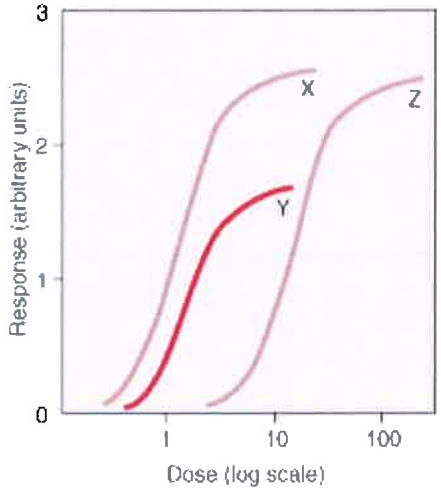
| Question 1:<br>**POTENCY & EFFICACY**<br>LOA: 1 | Define "potency". | Potency refers to the affinity or attraction between an agonist and its receptor. It reflects the dose axis of dose response curves. A measure of drug potency is the $EC_{50}$ – the conc'n/dose req'd to produce 50% of maximal response. | **Be able to explain potency and efficacy** |
| | How is this different to Efficacy? | Efficacy is the maximal response that a drug (agonist) can produce ($E_{max}$) when all receptors are occupied, irrespective of the concentration required to produce that response. Efficacy determines a drugs clinical effectiveness and reflects the response axis |
| | Draw a concentration-response curve showing 2 drugs with the same potency but different efficacy. |  |
| | | X and Z have similar efficacies, X and Y have similar potencies; X and Y are more potent than Z | |

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| Question 2<br>**PROPRANOLOL**<br>LOA: 1 | Describe the pharmacodynamics of propranolol.<br><br><br><br><br><br><br>What are the potential adverse effects? | B antagonist; competitive; non-selective<br>CV ↓BP if high -ve inotrope –ve chronotrope<br>↑PR interval ↓renin release<br>Resp bronchospasm<br>Eye ↓pressure (↓humour production)<br>Metabolic ↓glycogenolysis ↑VLDL ↓HDL<br><br>Bradycardia; ↑CCF; ↑PVD<br>↓hypoglycaemia response<br>Bronchospasm<br>Sedation/depression<br>Abrupt withdrawal effects<br>Exacerbate Ca channel blocker effects | 2 CV + 1 other<br><br><br><br><br><br><br>Bradycardia, bronchospasm and 1 other |
| Question 3<br>**TRIMETHOPRIM**<br>LOA: 2 | Describe the mechanism of action of trimethoprim.<br><br><br><br><br><br>What is the rationale for combining trimethoprim with sulphonamides? | Selectively **inhibits bacterial enzyme (**dihydrofolic acid reductase) which is required in the conversion of dihydrofolic acid to tetrafolic acid. **Hence inhibits** purine and **DNA synthesis.** Less efficient in inhibiting mammalian dihydrofolic acid reductase<br><br>**Enhanced effect** - sulphonamides **inhibit sequential steps (** acts step before triprim). Inhibits dihydropteroate synthase involved in conversion PABA to dihydrofolic acid<br>As sequential steps are blocked in folate synthesis usually bacteriocidial c.f bacteriostatic of 1 alone. | **Inhibits bacterial enzyme Resulting in Inhibition DNA synthesis**<br><br><br><br><br><br>**Bold** |

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| Question 4<br>**MIDAZOLAM**<br>LOA: 1 | What are the clinical indications for the use of midazolam? | Anxiolysis, **sedation, anticonvulsant,** antiemetic | **Bold to pass** |
| | What are the advantages and disadvantages of the various routes of administration? | PO, IV, IM, PR, IN, Buccal | **Reasonable discussion of IV + 1 other** |
| | What are the adverse effects? | **Excess sedation, respiratory depression,** decreased motor skills, impaired judgment, hypotension + occasionally rashes | **Bold to pass** |
| Question 5<br>**OCTREOTIDE**<br>LOA: 2 | What are the therapeutic uses for octreotide? | Control of **bleeding gastro-oesophageal varices,** sulphonylurea induced hypoglycaemia, pituitary and carcinoid tumors. | **Bold to pass** |
| | What is the mechanism of action of octreotide in acute variceal bleeding? | **Reduces splanchnic blood flow/portal venous pressure.** Exact mechanism of how this occurs is not known. | **Bold to pass** |
| | How is it administered in acute variceal bleeding? | **IV bolus and infusion** (50mcg bolus then 25-50mcg/hr) or SC | **Bold to pass** |
| | Why is an infusion required? | **Short half-life** | **Bold to pass** |

**ACEM PRIMARY 2013/1 Pharmacology VIVA** **Morning Session 3** ***Candidate Number:*** **AGREED MARK:**

| TOPIC | QUESTIONS | KNOWLEDGE **(essential in bold)** | NOTES |
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| Question 1:<br>Bioavailability<br>LOA: 2 | What is bioavailability? | Fraction of **unchanged drug** reaching the **systemic circulation** following administration by any route. | **Bold to pass** |
| | What factors limit drug bioavailability following oral administration? | **Extent of absorption:**<br>**a) Property of the drug** eg hydrophyllic vs lipophyllic<br>b) Gut factors - reverse transporter pumps p-glycoprotein &gut wall metabolism<br><br>**First pass elimination-** metabolism by liver before reaching systemic circulation or small effect biliary excretion | **Bold to pass** |
| | How can you overcome the effects of high first pass metabolism? | **Change route of administration** to sublingual, transdermal eg GTN, rectal, inhalation, IV, IM<br>**Increase dose**<br>Use pro-drugs | **Bold** |
| Question 2<br>**GLYCERYL TRINITRATE (GTN)**<br><br>LOA: 1 | How does Glyceryl Trinitrate (GTN) exert its effect on smooth muscle? | Nitrate→**Nitric Oxide→↑cGMP→** relaxation→**vasodilation**<br>Also involves Prostaglandin E or prostacyclin | **Nitric Oxide , cGMP/second messenger, vasodilation** |
| | Describe the Pharmacokinetics of GTN<br><br>**Prompt**: How is GTN given? | **Low Bioavail** (<10-20%)<br>Sublingual, transdermal or IV<br>S/L: onset 1-3min, lasting 10-30min<br>Liver metabolism and excreted by kidney<br>Tachyphylaxis with continuous use | **Low Bioavailabilty**<br>**Short halflife** |

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| Question 3<br>**NORFLOXACIN**<br>LOA: 1 | Describe the mechanism of action of norfloxacin. | Fluoroquinolone. Bacteriocidal.<br><br>a. **Inhibition topoisomerase II /DNA Gyrase** → interferes with relaxation of supercoiled DNA, required for normal transcription and replication<br>b. Inhibition topoisomerase IV → interferes with separation of replicated chromosomal DNA | **Bold to pass** |
| | Describe the anti-bacterial activity of norfloxacin | **Gram negative bacteria**<br>Organisms of atypical pneumonia: mycoplasma, chlamydia<br>Limited gram positive activity | **Bold to pass** |
| | How does the anti-bacterial activity of norfloxacin compare to that of ciprofloxacin? | **Ciprofloxacin has greater activity** (4-8 times lower MICs) against gram negatives and much greater activity against gram positives | **Bold to pass** |
| Question 4<br>PROPOFOL<br>LOA: 1 | What are the indications for the use of Propofol? | **Induction agent, maintenance of anaesthesia procedural sedation** | **2 bold to pass** |
| | What properties of Propofol make it suitable for procedural sedation? | **Rapid onset and offset** | |
| | What are adverse effects of Propofol? | Localised pain with bolus administration.<br>Dose related **depression of respiratory drive** (central effect) and apnoea. Muscle movements, hypotonus and rarely tremor.<br>**Hypotension** (reduced arterial resistance venodilation and negative inotropism). | **Bold to pass** |

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| Question 5<br>**NALOXONE**<br>LOA: 2 | What is the mechanism of action of Naloxone? | Pure **opioid antagonist** binds to μ-opioid binding sites. | **Bold to pass** |
| | What is the time to onset and duration of action when administered intravenously? | **Rapid onset 1-3 minutes**<br>**Duration 1-2 hours** | **Bold to pass** |
| | What problems may be associated with naloxone administration? | **Opioid withdrawal**<br>**Resedation** | **Bold to pass** |
| | How can these problems be minimised or avoided? | **Smaller/titrated doses**<br>Infusion<br>Route of administration | **Bold to pass** |