**Question 1**

Verapamil acts on this type of plasma membrane channel

A Ligand regulated-transmembrane receptor

B Secondary messenger

C Voltage gated ion channel

D Ligand gated ion channel

Explanation C

Voltage gated ion channels

This question can present as an EMQ

Voltage gated ion channels do not bind neurotransmitters directly but are controlled by membrane potential; such ion channels are also important drug targets. Verapamil inhibits voltage gated calcium channels that are present in the heart and in the vascular smooth muscle, producing antiarrhythmic effects and reducing blood pressure without mimicking or antagonising any known endogenous transmitter

**Question 2**

Which of the following drugs induce the CYP450 enzymes?

A Sulphonylureas

B Erythromycin

C Fluconazole

D Grape fruit juice

Explanation A

Inhibitors of CYP450 enzymes

Clarithromycin, diltiazem, erythromycin, fluconazole, grapefruit juice, ketoconazole, ritonavir, isoniazid, acute alcohol binging, cimetidine, ciprofloxacin, omeprazole, metronidazole

Inducer of the CYP450 enzymes

Barbiturates, carbamazepine, glucocorticoids, phenytoin, rifampin, St John’s Wort, ethanol (chronic) and charcoal broiled foods, griseofulvin, sulphonylureas (websourced- USMLE)

Note: in the current TB, it states that INH is an enzyme inducer

Extra:

Enzyme Inhibitors: SICKFACES.COM + Grapefruit

Sodium valproate; Isoniazid (noting current text states inducer); Cimetidine; Ketoconazole; Fluconazole; Alcohol (binge); Chloramphenicol; Erythromycin; Sulphonamides; Ciproflox; Omeprazole; Metronidazole.

Enzyme inducers: CRAP GPs

Carbamazepine; Rifampicin; Alcohol (chronic); Phenytoin; Griseofulvin; Phenobarbitone; Sulphonylureas

**Question 3**

Which of the following opiod analgesia is not metabolised by isoenzyme CYP2D6?

A Hydrocodone

B Oxycodone

C Codiene

D Fentanyl

Explanation D

Codeine, oxycodone and hydrocodone undergo metabolism in the liver by P450 isoenzyme CYP2D6, resulting in the production of metabolites of greater potency. Fentanyl is metabolised by CYP3A4 isoenzyme

**Question 4**

Regarding potency, which statement is correct?

A Potency of a drug depends only on the affinity (Kd) of receptors for binding the drug

B The clinical effect of a drug depends on its potency

C Potency refers to the concentration of a drug to produce 100% of its maximal effect

D The smaller the EC50, the greater the potency of the drug

Explanation D

Potency of a drug depends in part on the affinity (Kd) of receptors for binding the drug and in part on the efficiency with which drug-receptor interaction is coupled to response. A drug is more potent if its EC50 is less than that of another drug's EC50. Potency refers to the concentration (EC50) or dose (ED50) of a drug required to produce 50% of that drug's MAXIMAL effect. The clinical effect of a drug depends not on its potency (EC50) but on its maximal efficacy and its ability to reach the relevant receptors

**Question 5**

Which of the following drugs has a half-life of 6 hours?

A Aspirin

B Digoxin

C Atenolol

D Diazepam

Explanation C

Aspirin's half life is 15min. Aspirin's elimination half life is 3-5hrs (first order kinetics) and 15hrs (zero order kinetics).

Digoxin’s half life is 50 hrs

Diazepam’s is 20-40hrs

**Question 6**

Regarding irreversible antagonists, which of the following statements is correct?

A Require regeneration of receptors for further agonist action

B Can be displaced by increasing concentration of agonist

C Can be displaced by increasing potency of agonist

D Can be displaced by increasing efficacy of agonist

Explanation A

Competitive antagonists can be overcome by sufficiently high concentration of agonists.

Irreversible antagonists cannot. Consequently, the duration of action of such an irreversible antagonists relatively independent of its own rate of elimination and more dependent upon the rate of turnover of receptor molecules

Note: this question can present as an EMQ: stem: results in a receptor being unavailable for binding of an agonist

**Question 7**

Calculate an IVI Phenytoin loading dose for a 70 kg male; Target concentration 10 mg/L, Vd 0.5 L/kg

A 350 mg

B 300 mg

C 400 mg

D 3500 mg

Explanation A

Loading dose

e: (Vd X target concentration)/bioavailability

Bioavailability in this case is 1 as it is given IVI

0.5L/kg in a 70kg man -35L.

The LD = (35 X 10)/1

35 x 10=350

Note that in the textbook Phenytoin is given a Vd of 45L (in a 70kg man)

**Question 8**

Which of the following is an example of a phase I reaction?

A Sulphation

B Glucuronidation

C Hydrolysis

D Acetylation

Explanation C

Phase one reactions are hydrolysis, oxidation and reduction.

Phase two reactions are glucuronidation, acetylation, glutathione conjugation, glycine conjugation, sulfate conjugation, methylation, and water conjugation

**Question 9**

How many mg in 2ml of a 0.5% weight per volume solution?

A 5mg

B 100mg

C 1 mg

D 10mg

Explanation D

1%=1000mg in a 100ml solution is the starting point.

0.5%=500mg in 100ml solution.

Therefore 1ml=5mg. Therefore 2ml=10mg

Extra: 15ml of a 0.5% Prilocaine solution would equal 75mg

**Question 10**

Which of the following statements is correct?

The volume of distribution...

A Is calculated by dividing the amount of drug by it's clearance

B If high suggests homogeneous distribution throughout tissues

C Abnormal accumulation of body fluids does not effect VD

D Is proportional to half life.

Explanation D

 Vd is an apparent volume.

The volume of distribution= amount of drug in the body/ concentration of the drug in blood or plasma.

Drugs with a high VD have higher extravascular concentrations than intravascular and are not homogenously distributed.

T1/2 = (0.7 x Vd) / CL

Abnormal collection of body fluids: oedema, ascites, pleural effusion, can markedly increase the VD of drugs that are hydrophilic and have low volumes of distribution-e.g. Gentamycin

**Question 11**

Calculate the half life of Digoxin in a 70 kg patient with a renal clearance of 9L/h and volume distribution of 500 L/70kg

A 28 hours

B 39 hours

C 44 hours

D 32 hours

Explanation B

 T1/2 = (0.693 x VD)/CL

T1/2= (.693 x 500)/9

T1/2=39 hours

Note: If you used 0.7 instead of 0.693 to work out the calculation in your head, T1/2=38.88 which is close to the half life given in the textbook (39)

Other facts of digoxin: oral bioavailability-70%, 25 bound in plasma, VD=500L/70kg. Digoxin's bioavailability is increased by antibiotics like erythromycin- gut flora changes reduce gut bacterial metabolism of the digoxin.

**Question 12**

What is the half life of Lignocaine?

A 10 minutes

B 30 minutes

C 60 minutes

D 120 minutes

Explanation D

Lignocaine has a t1/2 of 1-2 hours.

Note: in older editions, it writes that lignocaine has a half life of 1-2 hours. The latest edition reports that it has an elimination half life of 1-2 hrs (1.6hrs) and may be increased to 6hrs in patients with liver failure.

**Question 13**

Which of the following statements regarding the bioavailability of a drug is correct?

A Must be 100% if given by inhalation.

B Is high if the drug is hydrophilic.

C Is equal to 1 minus the extraction ratio (ER)

D Is 70% for orally administered Digoxin.

Explanation D

Inhalation gives a bioavailability of 5 to <100%. Hydrophilic and lipophilic drugs can have low rates of bioavailability. Too lipophilic, the drug will not be soluble enough to cross the water layer adjacent to the cell. The bioavailability of the drug (F) can be predicted from the extent of absorption (f) and the extraction ration (ER).

F=f x (1-ER).

e.g.morphine is almost completely absorbed (f=1) so that the loss in the gut is negligible. However the heaptic extraction ration for morphine is 0.67 (morphine clearance diided by hepatic blood flow). Therefore 1-0.67=0.33

F= 1 X 0.33=0.33-the bioavailability of morphine is expected to be 33%

100% bioavailability is only via intravenous administration

**Question 14**

Which of the following is an example of Type 1 biotransformation reactions?

A Methylation

B Acetylation

C Hydrolysis

D Glucuronidation

Explanation C

Phase one reactions are hydration, oxidation and reduction. Phase two reactions are glucuronidation, acetylation, glutathione conjugation, glycine conjugation, sulfate conjugation, methylation, and water conjugation

**Question 15**

Which of the following statements regarding Naloxone is false?

A Naloxone has equal affinity for mu, kappa and delta receptors

B Tolerance to naloxone does not develop

C Intravenous administration reverses opioid effects in 1-2min

D Naloxone is a pure antagonist

Explanation A

Naloxone is a pure antagonist. It has a very high affinity for mu receptors and a lower affinity for the other receptor binding sites. Naloxone has a half life of 1-2 hours when given by injection and 10 hours when taking via the oral route. Although naloxone is well absorbed via the oral route it undergoes rapid first pass metabolism. IVI administration reverses opioid toxicity in 1-3 minutes. There is no tolerance to the antagonistic action of these agnets, nor does withdrawal of naloxone after chronic administration precipitate an abstinence syndrome

**Question 16**

With regard to properties of a drug, which of the following statements is correct?

A Efficacy is the maximum response produced by a drug

B Spare receptors are present if Kd 50 is the same as EC 50.

C Potency is the same as affinity.

D TD50 is the concentration of a drug necessary to produce toxic effects 50 % of the time

Explanation A

Spare receptors are present if the EC50<Kd.

Potency: how much of a drug that is required to produce an effect.

Affinity: how tight the drug binds to its receptors.

TD50 is the dose required to produce toxic effects in 50% of patients.

**Question 17**

Which of the following is an example of a phase II biotransformation?

A Oxidation

B Reduction

C Methylation

D Hydrolysis

Explanation C

Phase one reactions are hydration, oxidation and reduction. Phase two reactions are glucuronidation, acetylation, glutathione conjugation, glycine conjugation, sulfate conjugation, methylation, and water conjugation

**Question 18**

Regarding t1/2, which of the following statements is true?

Your answer was correct

A Has no relation to protein binding

B It can be poor predictor of clearance

C Is not affected by age

D Is not related to Vd

Explanation B

T1/2 = 0.7 x VD/CL. There is a relation to the Vd. Disease states can affect T1/2. Renal impairment, which occurs in 2/3 of the elderly, will lengthen the half-life of most drugs.

Half-life is related to volume of distribution (t1/2 = 0.69 x Vd/clearance), which in turn is related to protein binding.

Web sources say the protein binding can affect the half-life of a drug. The bound portion may act as a reservoir or depot from which the drug is slowly released as the unbound form. Since the unbound form is being metabolized and/or excreted from the body, the bound fraction will be released in order to maintain equilibrium.

Note: From current textbook- Plasma protein binding is often mentioned as a factor playing a role in pharmacokinetics, pharmacodynamics, and drug interactions. However, there are no clinically relevant examples of changes in a drug disposition or effects that can be clearly ascribed to changes in plasma protein binding. The clinical importance of plasma protein binding is only to help interpretation of measured drug concentrations.

**Question 19**

Regarding efficacy, which of the follwing statements is correct?

Your answer was correct

A It can be measured with a quantal dose response curve

B Partial agonists have higher maximal efficacy than full agonists

C It is the maximum effect a drug can bring about regardless of dose

D It is the drugs ability to produce 50% of its maximal effect

Explanation C

Efficacy: The maximum effect a drug can bring about, regardless of dose.

Efficacy is measured by a graded dose response curve and not a quantal dose response curve. By definition partial agonists have a lower efficacy than full agonists

Potency: the dose or concentration required to bring about 50% of a drug's maximal effect

Question 20

10 ml of 1% weight to volume is equal to:

Your answer was correct

A 1 mg

B 10 mg

C 100 mg

D 1000 mg

Explanation C

1%=1000mg in a 100ml solution is the a starting point.

Therefore 1ml=10mg.

Therefore 2ml=20mg

Therefore 10ml=100mg

Note: These questions seems to follow the local anaesthetic solution makeup/concentration. This is how I then calculate the answer.

Local anaesthetics

A solution expressed as 1% contains 1g of substance in each 100mls. The number of mg/ml can easily be calculated by multiplying the percentage strength by 10. Therefore a 1% solution of lignocaine contains 10mg/ml of solution. A 0.25% solution of bupivacaine has 2.5mg/ml.

Another starting point: 1g/mL = 100% in weight for volume measures (based on water's density being 1g/mL)

**Question 21**

Regarding therapeutic index, which of the following statements is correct?

A Potent drugs are more likely to have a high therapeutic index.

B It is the ratio of ED50/LD50

C It is the ratio of TD50/ED50

D High therapeutic index means a drug is dangerous

Explanation C

Therapeutic index (TI) is relationship of the dose of a drug required to produce a desired effect to that which produces an undesirable effect. TI= Median toxic dose (TD50)/median effective dose (ED50). Drugs with a high TI are safer. Potency of drugs has no relationship to the TI

The therapeutic index and therapeutic window are related, but not the same. Ti= TD50/ED50 => Ratio, high ratio means effective dose much lower than toxic dose (corollary is that there is significant margin of safety) Therapeutic window= Minimum toxic dose-Minimum effective dose. => Range over which we assume drug can be safely used

**Question 22**

Regarding pharmacokinetics, which of the following statements is true?

A Potency is maximal drug effect.

B Potency is dose of maximal effect.

C Efficacy is the maximal effect of a drug

D Efficacy is measured by gram-for-gram effect

Explanation C

Potency is the dose required to bring about 50% of the drug’s maximal effect. Efficacy is only measured by a graded dose response curve and not by a quantal dose response curve

**Question 23**

Which drug has a half life of 6hrs

A Disopyramide

B Diazepam

C Atropine

D Acetaminophen

Explanation A

This question is taken form a table in section 1-basic principles

Diazepam > 40hrs

Atropine= 4.3hrs

Acetaminophen=2hrs

Others: atenolol-6.1hrs, fluoxetine-53hrs, amoxicillin-1.7hrs, ciprofloxacin-4.1hrs, digoxin-50hrs and clonidine-12hrs cyclosporin - wide range reported, up to 20 hours

**Question 24**

The type of metabolism which leads to the accumulation of toxic metabolites in a paracetamol overdose is?

A Methylation

B Sulphation

C Glucuronidation

D Hydroxylation

Explanation D

Acetaminophen is conjugated to harmless glucuronide and sulfate metabolites when it is taken in normal doses. If large overdose is taken, the metabolic pathway gets overwhelmed and a P450 dependent system converts some of the drug to a reactive intermediate NAPQI. If the gluthathione stores are exhausted (in an overdose), NAPQI binds with proteins in the hepatocytes inducing liver damage.

Example of P450-dependent oxidation reactions: hydroxylation, N-dealkylation, O-dealkylation, N-oxidation, S-oxidation and deamination. Other type I reactions: oxidation P450 independent systems, reductions and hydrolyses.

Example of phase II reactions: glucuronidation, acetylation, glutathione conjugation, glycine conjugation, sulfate conjugation and methylation.

**Question 25**

How many mmol/l of Sodium does 1L of 3% saline contain?

A 600mmol/L

B 550mmol/L

C 500mmol/L

D 450mmol/L

Explanation C

It contains exactly 513mmol/l

Remember 1% NACL of 100ml solution = 1g of NACL in that solution

0.9% NACL of 100ml solution= 0.9g of NACL

0.9% NACL of 1000ml solution= 9g of NACL

3% NACL of 1000ml solution= 30g of NACL

There are 154mmol and 9 grams in 1L of 0.9% NACL.

There are thus 17mmol and 1 gram in 1L of 0.9% NACL

Therefore 30 grams requires 513mmol in 1L of 3% NACL (30 X 17)

Alternative approach:

3% = 30mg/ml = 30 g/L solution of NaCl NaCl molar mass = 23 + 35.5 g/mol = 58.5 g/mol It follows that in 3% NaCl = 30g/L = 30/58.5 mol/L = 0.513mol/L = 513mmol/L. Therefore 0.9% NaCl is known to contain 154mmol/L 3% NaCl would then contain 3/0.9 x 154 = 513mmol/L

**Question 26**

Which of the following is equal to the molar mass of a substance divided by its valence?

A Daltons

B Molecular wieght

C Equivalents

D Osmolality

Explanation C

Equivalents: The concept of electrical equivalents is important as many of the important solutes in the body are in the form of charged particles. One equivalent (eq) is 1 mol of an ionized substance divided by its valence. One mole of NACL dissociates into 1 eq of Na and 1 eq of Cl. One equivalent of Na =23grams but 1equivaent of Ca is 40g/2=20grams. Electrical equivalence is not the same as chemical equivalence.

**Question 27**

Phase 3 drug trials involve the following guidelines

A The drug effect on healthy volunters with small trial numbers

B A retrospective case specific analysis

C Specific patient selection within populations expressing the disease intended for treatment with large trial numbers

D Monitoring the marketed drug safety in actual large numbers

Explanation C

Phase 1= the effects of a drug as a function of dose in a small group of healthy volunteers (25-50). If however, the drug is suspected to have significant side effects/toxicity, volunteers with the disease are used instead.

Phase2= the drug is studied for the first time in patients with the target disease to determine its efficacy. A small number of patients are studies in great detail (100-200). This stage is usually done in a university/hospital setting.

Phase 3= the drug is evaluated in much larger number of patients >1000 to further establish safety and efficacy. Information gathered in 1,2,3 trials are used to minimize errors caused by placebo effect, variable course of disease etc.

Phase 4= the drug has been approved for marketing. The drug is monitored under actual conditions of use in a large number of patients