**Question 1**

Which of the following agents has a pure beta agonist effect in the circulation?

A Dopamine

B adrenaline

C noradrenaline

D isoprenaline

Explanation D

Adrenaline is a very potent vascular bed vasoconstrictor (alpha R) and a cardiac stimulat (B R).

NA is a very potent vacular bed vasoconstrictor (Alpha R) and has B1 effects on the heart.

Isoprenaline activates B receptors almost exclusively and is a potent vasidilator

Dopamine effects several D1 R vacualr bed (Vasidilatation) and at a higher doses B and A receptors

Extra: Agonists

Phenylephrine a1>a2>>>>b

Clonidine a2>a1>>>>b

Dobutamine b1>b2>>>>a Isoproterenol (Isoprenaline) b1=b2>>>>a

Terbutaline, Albuterol, Metaproterenol b2>>b1>>>>a1

Dopamine D1=D2>>b>>a Fenoldopam D1>>D2

Noradrenaline: b1>>b2, a1=a2

Adrenalne: b1=b2, a1=a2

**Question 2**

Which of the following statements regarding carbamazepine is correct?

A Overdose causes seizures

B Sodium valproate increases carbamazepine clearance

C It metabolises to non-active metabolites.

D It is an enzyme inhibitor

Explanation A

Overdose can cause seizures but the most common side effects are diplopia and ataxia. Foetal aplastic anaemia and agranulocytosis can also occur. Carbamazepine in an enzyme inducer and has active metabolites. Sodium valporate inhibits carbamazapine clearance whereas phenytoin and phenobarbitone increase clearance

**Question 3**

Regarding L-dopa, which of the following statements is correct?

A It has a half life of 5 hours

B It causes a negative Coombs test.

C 25% of the oral dose reaches the brain

D It is a precursor to dopamine

Explanation D

L-dpoa is an immediate precursor of dopamine. 1-3% enters the brain unaltered, but this number will be higher if given with dopa decarboxylase inhibitor. Concomitant administration of a peripheral dopa decarboxylase inhibitor (carbidopa) may reduce the daily requirement of levodopa by approximately 75%. L-dopa causes a positive Coombs test. L-dopa has a half life of between 1-3 hours.

**Question 4**

Regarding ergotamine, which of the following statements is incorrect?

A It can be given parenterally

B It works well in the early treatment of acute migraine

C It causes GI haemmorhage.

D It causes vasoconstriction

Explanation C

Ergotamine can be administered orally, via rectum, via aerosol inhaler and intramuscular injection. Ergot derivatives are highly specific for migraine pain. They are not analgesic for any other condition. The vasoconstriction (partial agonist effects at alpha adrenoreceptors and some as a result of effects at 5-HT receptors) produced by ergotamine is long lasting and cumulative. The direct receptor stimulation thus prevents vasodilatation and stretching of the pain endings. The most toxic effects of the ergot derivatives are GIT disturbances, including diarrhoea, nausea and vomiting. GIT haemorrhage does not occur. There have been reports of bowel infarction/ischaemia due to blood vessel vasoconstriction

**Question 5**

Regarding drugs that are used to treat glaucoma, which is the correct pairing of drug-mechanism of action?

A Pilocarpine - ciliary muscle contraction

B Latanoprost - increased aqueous production.

C Acetazolamide - increased aqueous production

D Timolol - ciliary muscle contraction

Explanation A

Pilocarpine: acts on a subtype of muscarinic receptor (M3) found on the iris sphincter muscle, causing the muscle to contract -resulting in pupil constriction (miosis). Pilocarpine also acts on the ciliary muscle and causes it to contract. When the ciliary muscle contracts, it opens the trabecular meshwork through increased tension on the scleral spur. This action facilitates the rate that aqueous humor leaves the eye to decrease intraocular pressure.

Timolol-decreases aqueous secretion.

Acetazolamide-decreases aqueous secretion due to a lack of HCO3.

Latanoprost-increased outflow of aqueous.

PG-increased outflow.

Beta blockers-decreased aqueous secretion

**Question 7**

A young male presents with a high blood pressure, mydriasis and a high temperature. Which drug has he most likely taken?

A Atropine

B Cocaine

C Naloxone

D Adrenaline

Explanation B

Cocaine is a sympathomimetic stimulant which cause cardiovascular, CNS and peripheral sympathetic stimulation

Atropine: the net cardiovascular effects of atropine in patients with normal haemodynamics are not dramatic: tachycardia may occur, but there is little effect on blood pressure.

Anticholinegic syndrome: includes central and peripheral effects e.g. tachycardia, CNS effects and hyperthermia. It does not include hypertension however.

Not a great question

In reality, all these drugs can cause the above symptoms. However, atropine and adrenaline are not frequently ingested, nor abused. Naloxone won’t cause the symptom profile unless it put the patient into opioid withdrawal. In other words the most likely drug taken is cocaine-it is easily ingested and the most abused and causes these symptoms

**Question 8**

Regarding sodium valproate, which of the following statements is correct?

A It is highly protein bound

B T1/2 is 40 hrs

C It has a high first pass metabolism

D It's VD is 0.6L/kg

Explanation A

Sodium valproate (SV) is readily absorbed form the GIT. Its bioavailability is greater than 80% so it has a low first pass metabolism rate. Half-life varies from 9-18hrs. Peak blood levels are observed within 2 hrs. pKa of 4.7. 90% bound to plasma proteins. SV has a VD of 0.15L/kg (it is essentially confined to extracellular water). It is fully ionized at a normal body pH. Clearance of SV is low and dose dependent. Approximately 20% of the drug is excreted as a direct conjugate of valproate

**Question 9**

Which of the following statements regarding L-Dopa is correct?

A L-dopa's half life is unaffected when given with carbidopa

B Ingesting L-dopa with food does not delay its absorption

C Drug holidays are recommended to improve the the responsiveness to levodopa

D Suddenly stopping it will cause tremor

Explanation D

L-dopa is an immediate precursor of dopamine. L-dopa is rapidly absorbed from the small intestine, but its absorption depends on the rate of gastric emptying and the pH of the gastric contents. Food will delay the appearance of L-dopa in the plasma. Ingested food can compete with the drug for absorption from the gut and for transport from the blood to the brain.

Note: When levodopa is given without a peripheral decarboxylase inhibitor, anorexia, nausea & vomiting occur in about 80% of patients. These adverse effects can be minimised by taking the drug in divided doses, with or immediately after meals or by increasing the total daily dose slowly. It is better to add carbidopa, as the prevalence of adverse effect occur in less than 20% of patients.

1-3% enters the brain unaltered, but this number will be higher if given with dopa decarboxylase inhibitor. Concomitant administration of a peripheral dopa decarboxylase inhibitor (carbidopa) may reduce the daily requirement of levodopa by approximately 75%. L-dopa causes a positive Coombs test. L-dopa has a half-life of between 1-3 hours but when administered with carbidopa, the plasma half-life is longer. Suddenly stopping L-dopa will cause tremor. This side effect part of the neuroleptic malignant syndrome that may occur on abrupt stopping of the drug. Because a drug holiday may only temporarily improve responsiveness to levodopa (but is of little benefit in preventing the on off phenomenon) and due to the risks of aspiration, PE, venous thromboembolism and depression (from the increasing immobility) during a drug holiday, they are not recommended.

**Question 10**

What is the most common adverse effect of procainamide?

A Bradycardia

B Anaphylaxis

C Hypotension

D Fever

Explanation C

Hypotension especially when administered IVI as it has ganglion-blocking properties

**Question 19**

Which of the following drugs is a direct serotonin agonist?

A Fluoxeteine

B Sumatriptan

C Moclobemide

D Amitryptiline

Explanation B

Fluoxetein = Selective Serotonine reuptake inhibitor SSRI

Amitryptiline = Tricyclic antidepressant : Blocks reuptake of noradrenaline and serotonin.

Moclobemide = Competitively and reversibly inhibits monoamine oxidase MAO A (selective). Note: from the evidence available, the reversible short acting MAO inhibitor moclobemide, appears to be relatively free of the hypertensive reaction due to tyramine.

Sumatriptan is a selective agonist for 5-HT1D and 5-HT 1B receptors.

**Question 20**

Carbamazepine is closely related to which of the following drugs?

A Quinidine

B Imipramine

C Metoprolol

D Sodium valproate

Explanation B

Carbamazapine resembles (in it's chemical structure only) tricyclic antidepressants, of which Imipramine is one

**Question 21**

Which of the following drugs acts by MAO inhibition?

A Paroxetine

B Clomipramine

C Moclobemide

D Sertraline

Explanation C

Clomipramine is a tricyclic antidepressent that prevents reuptake of noradrenaline (NA), serotonin.

Paroxetine is a selective serotonin reuptake inhibitor, antidepressant, no effect on NA

Sertraline is a selective serotonin reuptake inhibitor, antidepressant, no effect on NA

Note: Paroxetine and sertraline have no antimuscarinic action (unlike chlomipramine)

**Question 22**

Of the following drugs, which is the most dangerous in overdose?

A Imipramine

B Paroxeteine

C Sertraline

D Moclobenide

Explanation A

Imipramine is a tricyclic antidepressant. In OD it causes VF arrest and coma. A dose of 10mg/kg of a TCA is lethal

**Question 23**

A patient on phenytoin is found to have a low blood phenytoin level. Of the following drugs, which is LEAST likely to cause this?

A Carbemazepime

B Hypoalbuminemia

C Disulfiram

D Non-compliance

Explanation C

Disulfiram retards the metabolism of phenytoin. Carbamazapine is an enzyme inducer and will increase phenytoins metabolism. Non compliance obviously lowers blood levels. Because phenytoin is highly protein bound, low levels of albumin will decrease phenytoin blood levels

**Question 24**

Regarding SSRIs, which of the following statements is correct?

A They are safe in overdose due to minimal drug interactions

B They may be associated with seretonin syndrome with muscle weakness, hyperpyrexia and confusion.

C They may cause seizures in overdose

D They are readily removed by dialysis.

Explanation C

SSRis are dangerous in OD because they can cause serotonin syndrome that consists of muscle rigidity, hyperpyrexia, and confusion, which can lead to convulsions, coma and rhabdomiolysis. Dialysis is of no benefit as they have high volumes of distribution

**Question 26**

Regarding neurotransmitters in the brain, which of the following statements is correct?

A Strychnine stimulates glycine receptors

B Ondansetron antagonises serotonin receptors

C Butyrophenones stimulate dopamine receptors

D Atropine antagonises GABA receptors

Explanation B

Strychnine antagonizes glycine receptors. Atropine is an antagonist at the M2 (muscarinic receptor). Butyrophenones (haloperidol) antagonize the dopamine receptor

**Question 27**

Which of the following statements best describes buspirone's mechanism of action?

A Direct GABA stimulation

B None of the above

C Direct noradrenaline receptor stimulation

D Indirect GABA stimulation

Explanation B

Buspirone relieves anxiety without sedation; it is a non-benzodiazapine anxiolytic. It is a partial agonist at 5HT1 and a presynaptic antagonist at D2 (also D3 and D4). It is also a partial alpha one receptor agonist. There is no rebound anxiety on stopping drug. It takes a week to work, unsuitable in acute anxiety.

**Question 28**

Of the following sedatives, which is the most potent?

A Diazepam

B Chloral hydrate

C Phenobarbitone

D Midazolam

Explanation D

Potency is the dose required to produce 50% of THAT drugs effect. Phenobarbitone may have a stronger effect but it is required in much higher doses than midazolam and is therefore not as potent.

**Question 29**

Of the following antipsychotics, which is most likely to cause extrapyramidal side effects?

A Chlorpromazine

B Clozapine

C Haloperidol

D Risperidone

Explanation C

Chlorpromazine (a phenothiazine) causes medium EP side effects. Risperidone (atypical antipsychotic) cause low EP side effects. Haloperidol (a butyrophenone) causes very high side effects. Clozaoine (atypical antipsychotic) cause low EP side effects

**Question 30**

Which of the following is not a pharamcological characteristic of propranolol?

A Lipid soluble

B It has selective B receptor blocking properties

C Half life of 3-6 hours

D Local anaesthetic action

Explanation B

Propranolol is a non-selective beta receptor blocker. It has no sympathomimetic activity. It is highly lipid soluble and readily crosses the BBB. Because of its Na channel blocking activity, it causes widening of the QRS and therefore VF arrest in overdose. It also causes seizures in overdose as it crosses the BBB. Treatment is bicarbonate. Half-life 3.5-6hrs. Bioavailability <25%

**Question 31**

A patient arrives in the ED staggering, agitated, hyperthermic with dilated pupils. Which of the following drugs in overdose is least likely to produce these effects?

A Tricyclic antidepressants

B Atropine

C Amphetamine

D Aspirin

Explanation D

Aspirin overdose does present with hyperthermia and agitation but does not cause mydriasis

There is a spectrum of hypertensive disease it is important to understand. This case is most likely due to ANTICHOLINERGIC toxicity.

Anticholinergic: "Hot as hell (hyperthermia), dry as a chip (xerostomia, anhydrosis), blind as a bat (mydriasis), red as a beet (erythema), mad as a hatter (agitated delirium). Onset <12hrs after drug. Rx supportive, occasionally can give physostigmine (centrally acting ACh-esterase)

Serotonin syndrome: Sweaty, tachycardic, hot, very increased muscle tone, hyper-reflexia and clonus, dilated pupils, diarrhoea. Drugs implicated: SSRI/SNRI/TCA/tramadol/amphetamines/St John's wort. Rx supportive, cooling and benzos.

Neuroleptic Malignant Syndrome: Slower onset. Pale, sweaty, tachycardia, pyrexial, lead-pipe rigidity, bradykinesia, bradyreflexia, normal or dilate pupils. Autonomic instability is key. Dopamine antagonists (antipsychotics) associated. Rx supportive, can consider dantrolene, bromocriptine occasionally.

Malignant Hyperthermia: Sweaty, mottled, tachycardia, pyrexial, pupils normal, tone rigid, bradyreflexic, agitated. Associated with inhalational anaesthetics. Rx dantrolene.

Salicylate toxicity: Not classically considered with the other 4 causes of fever and coma. Classically vomiting, tinnitus, hyperventilation with respiratory alkalosis and metabolic acidosis. Rx early diagnosis (can be hard) urinary alkalinisation and dialysis are effective.

**Question 32**

A young man is injected with an iv drug. He shows a resultant tachycardia, midriasis, normal blood pressure and reduced sweating. Which of the following drugs is most likely to have caused this?

A Nicotinic antagonist

B Adrenergic agonist

C Cholinomimitic

D Muscarinic antagonist

Explanation D

Reduced sweating is a sign of anticholinergic poisoning. Others include mydriasis-blindness, delirium, flushing.

Remember “blind as a bat, mad as a hatter, red as a beet, dry as a chip”

**Question 33**

A woman is taking an antihypertensive medication. Her blood workup reveals an elevated potassium.

Which of the following drugs is LEAST likely to cause this?

A Frusemide

B Spironalactone

C Methyldopa

D ACE inhibitor

Explanation A

Frusemide will decrease serum potassium levels

Spironolactone is a potassium sparing diuretic

ACE inhibitor can cause hyperkalaemia as a side effect

Methyldopa does not affect K levels

**Question 34**

Which of the following is the major side effect of benztropine?

A Miosis

B Bronchorrhea

C Diarrohea

D Delirium

Explanation D

Benztropine is a centrally acting antimuscarinic preparation. It is an antagonist at the M receptors in the basal ganglia. Benztropine reduces tremor and rigidity. It has little effect on bradykinesia. It greatest clinical application is in the treatment of Parkinson’s disease

The side effects are typical antimuscarinic side effects: mydriasis, delirium, flushing, decreased sweating (remember: blind as a bat, mad as a hatter, dry as a chip, red as a beet). The other options here represent cholinergic poisoning.

**Question 35**

Regarding St Johns Wort, which of the following statements is correct?

A Has been trialed for use in viral diseases

B It has a side effect profile comparable to placebo

C It is more effective than placebo in the management of

D Can cause hyperthermic or hypertensive reaction

Explanation C

St John’s wort is an enzyme inducer and has been trialed for depression. It has not trialed, and should therefore not be used for viral disease or cancers. Side effects: mania, photosensitization, autonomic arousal. It can lower the clinical concentration and efficacy of a number of drugs including benzodiazopines by induction of cytocrome p450 enzymes cyp3A4 and cyp2C19

**Question 36**

What is the correct order of catecholamine synthesis?

A Tryptophan - dopa - dopamine - adrenaline - noradrenaline

B Tyrosine - dopamine - dopa - noradrenaline - adrenaline

C Tyrosine - dopa - dopamine - noradrenaline - adrenaline

D Tysosine - dopa- dopamine - adrenaline – noradrenaline

Explanation C

**Question 39**

Which drug-effect match is incorrect?

A Phenytoin - gum hypertrophy

B Ethosuximide - hirsutism

C Diazepam- ataxia

D Carbamazepine - blood dyscrasias

Explanation A

Phenytoin causes gum hyperplasia. In the prescribed texts, it is not clearly stated, but ethosuximide can cause hirsutism

**Question 41**

A patient receiving multiple drugs for parkinsonism develops urinary retension, mydriasis and confusion. Which of the following drugs may be to blame?

A Tolcapone

B Pramipexole

C Levodopa

D Benztropine

Explanation D

These benztropine side effects are typical antimuscarinic: mydriasis, delirium, flushing, lack of sweating (remember: blind as a bat, mad as a hatter, dry as a chip, red as a beet).

Levodopa: GIT upset, arrhythmias, dyskinesias, behavioral disturbance, on-off phenomena.

Tolcapone: hepatotoxicity.

Pramipexole: nausea and vomiting, postural hypotension and dyskinesias

**Question 43**

Which of the following cholinoceptor blocking drugs is the least absorbed by the brain?

A Ipratropium

B Benztropine

C Atropine

D Scopolamine

Explanation A

Ipratropium is a quaternary amine-charged- and therefore poorly taken up by the brain and are relatively free-at low doses-of central nervous system effects. The other drugs are tertiary amines and are able to be taken up by the brain at lower doses.

**Question 44**

Select the correct statement regarding L-Dopa.

A Dyskinesias occur in 80% of patients receiving L-dopa therapy for long periods B Carbidopa given with L-dopa worsens GIT side effects

C Levodopa stops the progression of parkinsonism

D It is a precursor to tyrosine

Explanation A

L-dpoa is an immediate precursor of dopamine. L-dopa is rapidly absorbed from the samll intestine, but its absorption depends on the rate of gastric emptying and the pH ofthe gastric contents. Food will delay the appearnace of L-dopa in the plasma. Adding carbidopa will reduce GIT side effects. (only 20%will suffer as opposed to 80% without carbidopa)1-3% enters the brain unaltered, but this number will be higher if given with dopa decarboxylase inhibitor. Concomitant administration of a peripheral dopa decarboxylase inhibitor (carbidopa) may reduce the daily requirement of levodopa by approximately 75%. L-dopa causes a positive Coombs test. L-dopa has a half life of between 1-3 hours but when administered with carbidopa, the plasma half lie is longer. Suddenly stopping L-dopa will cause tremor. This side effect part of the neuroleptic malignant syndrome which may occur on abrupt stopping of the drug. L-dopa does not stop the progression of parkinsonism but its early initiation will lower mortality.

**Question 45**

Regarding stemetil, which of the following statements is correct?

A It can cause neuroleptic malignant syndrome

B It has anti-emetic effect through serotonin antagonism

C It can cause serotonin syndrome

D It can cause malignant hyperthermia

Explanation A

Stemetil is prochlorperazine: gives dopamine (D2) receptor blockade, especially dopaminergic receptors in CTZ (chemoreceptor trigger zone) of the medulla. Also has anticholinergic, alpha blocker and NA channel blocking effects. Indications: anti emetic, migraines, not for psychotic episodes. Side effects: muscarinic (anticholinergic) blockade : dry mouth,/urinary retention, constipation, loss of accommodation, flushed (remember :red as a beet, mad as a hatter, blind as a bat, dry as a crisp). Alpha blockade: orthostatic hypotension. Another life threatening side effect is :Neuroleptic malignant syndrome (A high fever, stiff muscles, confusion, irregular pulse or blood pressure, tachycardia, sweating, arrhythmias.

**Question 46**

Which of the following drugs is not used in the treatment of glaucoma?

A Alpha blocker

B Cholino-mimetic agents

C Carbonic anhydrase inhibitor

D Beta blocker

Explanation A

Direct acting cholinomimetics (Pilocarpine) and Indirect acting cholinomimetics (Physostigmine): constricts ciliary and iris circular muscle = Decrease IOP

Prostaglandin analogues (Latanoprost): Relax ciliary muscle and modulate extracellular matrix = Increase uveoscleral outflow tract = Decrease IOP

Beta-adrenoreceptor antagonists (Timolol): Block B adrenoreceptors on ciliary muscle = Decrease aqueous secretion = Decrease IOP

Alpha-2 adrenoreceptor agonists (Brimonidine) decreases aqueous secretion and Non selective alpha agonist (adrenaline) increases uveoscleral outflow tract = Decrease IOP

Carbonic anhydrase inhibitors (Acetazolamide): Decrease HCO3 formation and aqueous secretion = Decrease IOP

**Question 47**

Regarding pralidoxime, which of the following statements is correct?

A It regenerates acetylcholine

B It regenerates succinylcholine

C It regenerates acetylcholinesterase

D It regenerates acetylcholine receptors

Explanation C

Pralidoxime is used to reactivate acetylcholinesterase inhibited by organophosphates. It is only effective if given before irreversible binding of the OP and the acetylcholinesterase has occurred. Re-establishment of enzymic function rapidly reverses the nicotinic and muscarinic effects of OP poisoning. It is used concurrently with Atropine. Atropine is usually administered prior to pralidoxime and the effects at muscarinic receptor are synergistic. Atropine is only effective at muscarinic receptors and not at nicotinic receptors

**Question 48**

Regarding SSRI's, which of the following statements is correct?

A They have more pronounced side effects than TCA's

B They are effective in obsessive compulsive disorder

C They usually have short half-lives

D They are the treatment of choice in bipolar disease

Explanation B

A. Lithium Carbonate is the drug treatment of choice in bipolar, especially the acute manic episodes and relapse prevention. B. Due to their high plasma protein binding, they usually have long half-lives. C. Side effects of SSRI are usually less and better tolerated than those of TCAs. D. SSRIs are indicated in major depression, obsessive-compulsive disorder (OCD), Body dysmorphic disorder (BDD), posttraumatic stress disorder (PTSD), premenstrual dysphoric disorder (PMDD), panic disorder and social phobia (social anxiety disorder).

**Question 49**

Regarding diazepam, which of the following statements is correct?

A It is an enzyme inducer

B It should not be used in convulsions of unknown origin

C It has a half life of 4 hours

D It is metabolised to oxazepam

Explanation D

Diazepam has a half life of 20-40hrs. It is used for any seizure disorder. In contrast to barbiturates, benzodiazepines do not change hepatic drug metabolizing enzyme activity with continuous use.

Benzodiazepines are widely used as sedative hypnotics

They bind to the GABA-a receptor in the CNS. This receptor functions as a chloride ion channel is activated by the inhibitory neurotransmitter GABA. Benzodiazepines appear to increase the efficiency of GABAergic synaptic transmission. The benzodiazepines do not substitute for GABA but appear to enhance GABA’s effect allosterically without directly activating GABA-a receptors or opening the associated ion channel. There is an increase in the frequency of channel opening events

Benzodiazepines cross the placenta. If given during the predilvery period, they may contribute to the depression of neonatal functions. They are detectable in breast milk and may exert depressing effects in the nursing infant

**Question 50**

Dantrolene is used in malignant hyperthermia. Which of the following statements best describes it's mechanism of action?

A It is a succinylcholine antagonist

B It has an antipyretic through prostaglandin inhibition

C It causes hypothermia through muscle relaxation

D It decreases calcium release from sarcoplasmatic reticulum

Explanation D

Dantrolene has a spasmolytic function outside the CNS. It reduces skeletal muscle strength by interfering with excitation–contraction coupling in the muscle fiber. Dantrolene interferes with the release of activator calcium via the sarcoplasmic reticulm calcium channel, possible by binding to the same receptor used by ryanodine. Malignant hyperthermia results in massive calcium release, massive muscle muscle contraction, hyperthermia and lactic acid production. Triggers are often general anaesthesia and neuromuscular blockers. Dantrolene is used to stem the calcium release

**Question 51**

What is the earliest and most frequent neurological sing of an acute overdose of Lithium?

A Hyperreflexia

B Tremor

C Confusion

D Sedation

Explanation B

In acute Lithium overdoses, neurological symptoms, if they develop, are delayed reflecting slow redistribution into the CNS. The earliest and most frequent neurological sign is tremor. Other CNS neurotoxic symptoms rarely progress beyond tremor provided adequate lithium excretion is maintained.

Source: Toxicology Handbook, Murray et al

**Question 52**

With the MAOI tranylcypromine, which drug will be least problematic?

A Propofol

B Phenylephrine

C Ephedrine

D Pethidine

Explanation A

Tranylcypromine is a MAOI, which will inhibit the catabolism of dietary amines-prevents breakdown of tyramine in the gut. When foods containing tyramine (cheese, tap beer, soy products and dried sausage) are ingested, the patient may develop a hypertensive crisis. The mechanism is poorly understood but is thought that tyramine displaces noradrenaline from the storage vesicles and enhance peripheral noradrenergic effects, including raising blood pressure dramatically. Similarly drugs with sympathommimetic properties may cause significant hypertension when combined with MAOIs. Over-the-counter preparations that contain pseudoephedrine and phenylpropanolamine are contraindicated in patients taking MAOIs. Pethidine is associated with serotonin syndrome when given with the MAOI drug group

**Question 53**

Which is true regarding the group of antipsychotics

A Haloperidol cause the most anticholinergic side effects

B Aripiprazole is an example of an atypical antipsychotic

C Antagonism of all the dopamine receptors play a role in the action of antipsychotic drugs

D Chlorpromazine causes the most extrapyradimal (EP) toxicity

Explanation B

The antipsychotics have antipsychotic properties as well as extrapyramidal (EP) toxicity, sedative action and hypotensive and anticholinergic effects. These side effects were traced to the blocking effects of alpha, 5-HT2, H1 receptors and muscarinic receptors

It seems that there is no demonstrable antipsychotic effect after blocking any other receptor than the D2 (dopamine). D1, D3, D4 receptors have been tested with no antipsychotic effects.

Haloperidol, a butyrophenone, is the most widely used antipsychotic. It has the highest EP toxicity relative to its antipsychotic effect. Piperazine, a phenothiazine, has high EP as well. Thioridazine, a phenothiazine, has the greatest anticholinergic side effects (anti muscarinic).

Atypical antipsychotics: clozapine, asenapine, olanzapine, quetiapine, paliperidone, risperidone, sertindole, ziprasidone, zotepine and aripiprazole. They have less EP effects.

Chlorpromazine has the greatest affinity for the alpha-receptor and thus causes hypotension.

**Question 55**

Which receptors do the tricyclic antidepressants NOT block?

A Histamine receptors

B Serotonin receptors

C Dopamine receptors

D Noradrenaline receptors

Explanation C

TCA block the following receptors:

Noradrenaline, histamine, serotonin, muscarininc, alpha receptors. They also block sodium channels and in overdose lead to ventricular tachycardia and fibrillation.

Note: The MCQ option may include nicotinic receptors. A web-based search does report that TCA can block these receptors

They do not block dopamine receptors. The MCQ may offer GABA receptors- according to current web sources- they do antagonize the GABA receptor

**Question 56**

Which neurotransmitter in NOT stored in preformed secretory granules?

A Histamine

B Acetylcholine

C Serotonin

D Noradrenaline

Explanation D

Note: Difficult question. Not sure of the answer. A closer look at Histamine reveals that it is a neurotransmitter and a neuromodulator and in most tissues histamine is sequestered and bound in granules (vesicles) in mast cells or basophils

Looking through Ganong:

Norepipherine: is sequestrated into presynaptic vesicles

Ach: is transported into a storage vesicle. By definition, Ach is a neurotransmitter of the parasympathetic nervous system

Serotonin: is concentrated in vesicles. It is also found in the brainstem where cell bodies synthesise, store and release it

Histamine: It seems to be more of a stimulant of sensory nerve endings via H1, rather than being released form vesicles. Histamine is sequestrated into vesicles of mast cells, rather than vesicles of nerve endings. H3 agonists induce the release of ACH, amine and peptide transmitters (rather than acting as vesicle bound neurotransmitters themselves)

Extra: it may be noradrenaline as noradrenaline is stored as dopamine, and then converted to noradrenaline once inside the actual vesicle. I will let you decide

**Question 57**

Antipsychotics exert their function by antagonising which receptor?

A D3

B D4

C D1

D D2

Explanation D

It seems that there is no demonstrable antipsychotic effect after blocking any other receptor than the D2 (dopamine). D1, D3, D4 receptos have been tested with no antipsychotic effects. Most of the newer antispychotics agents and some of the traditional ones have a higher affinity for 5-HT2A receptor than D2, suggesting an important role for the serotonin system in the aetiology of schizophrenia and the action of these drugs.

**Question 58**

Which dopaminergic systems are important for the understanding of schizophrenia

A Mesolimbic-mesocortical pathway

B Medullary-periventricular pathway

C Tuberoinfundibular pathway

D Nigrostriatal pathway

Explanation A

Mesolimbic-mesocortical pathway= behaviour and psychosis

Nigrostriatal pathway= coordination of voluntary movement

Tuberoinfundibular pathway= inhibits prolactin form the anterior pituitary

Medullary-periventricular pathway= ?eating behaviour

Incertohypothalamic pathway= regulates the anticipatory motivational phase of copulatory behaviour in rats

**Question 59**

Regarding Phenobarbitone, which is CORRECT?

A 20-30% of Phenobarbitone is excreted unchanged in the urine

B Is effective for absence seizure activity

C Has a pKa of 7.2

D It enhances GABA mediated opening of the Ca channel

Explanation A

Phenobarbitone is the oldest of the current anti-seizure medications available. Due to its side effects, it is considered the first choice of anti-seizure medication only in infants. pKa is similar to that of plasma pH=7.4. Mechanism of action is through enhancement of inhibitory processes and diminution of excitatory transmission. At higher doses it suppresses high frequency repetitive firing in neurons through an action on Na conductance. It also enhances GABA receptor mediated prolonged opening of the Cl channel. Finally it plays a role in suppression of glutamate-mediated excitation. It is used in the treatment of partial and generalized seizures, but there is no evidence for its use in the management of absence seizures. All barbiturates are metabolised in the liver and then excreted in the urine. With the EXCEPTION of phenobarbitone (20-30%), only insignificant quantities of barbiturates are excreted unchanged in the urine

**Question 60**

Regarding neuroleptic malignant syndrome: All are true except:

A It may occur after months on a stable drug regimen

B Specific treatments include cooling, bromocriptine and dantrolene.

C The syndrome characteristically develops over 60 mins and is usually fully blown by 4 hours

D Clinical features may include mutism, dysarthria, dystonia, incontinence and delirium

E Results from blockade of dopaminergic neurotransmission in the basal ganglia and hypothalamus

Explanation C

Neuroleptic malignant syndrome (NMS) is a life threatening neurologic emergency associated with the use of neuroleptic agents. The aetiology of NMS remains controversial. Although a central deficiency of dopaminergic neurotransmission at nigrostriatal, mesolimbic and hypothalamic-pituitary pathways appears pivotal. The syndrome develops in 0.02-2.5% of people taking neuroleptic medication. The onset of NMS usually occurs over 24-72 hours. It presents with a triad of CNS, neuromuscular and autonomic changes.

CNS: Altered mental state (in 82% of patients) agitated delirium with confusion rather than psychosis. Catatonic signs and mutism can be prominent. Progression to stupor and eventual coma.

Neuromuscular: Increased tone with ‘lead-pipe’ rigidity, generalised bradykinesia or akinesia – Mutism and staring- Dysarthria – Dystonia and abnormal postures – Abnormal involuntary movements – Incontinence

Autonomic instability: Hyperthermia – Tachycardia – Hypertension – Respiratory irregularities – Cardiac dysrhythmias

 Management: Attention to ABC with rapid sequence intubation if coma or hyperthermia >39.5 degrees celcius. Detect and correct hyperthermia with continuous core temperature monitoring from 38.5 and RSI with neuromuscular paralysis above 39.5.

Dantroline is indicated for severe muscle rigidity and fever. Bromocriptine is a dopamine agonist and can be given in moderate to severe cases to improve autonomic instability and fever. Hypertension and tachycardia may be initially treated with a parental vasodilator such as GTN or nitroprusside. Any agent with dopamine antagonist effects should be avoided.

**Question 61**

Which of the following drug drug clases interact dangerously with Monoamine Oxidase Inhibitors (MAOI)

A Selective Serotonin reuptake inhibitors (SSRI)

B Tetracyclic antidepressants

C 5 HT2 antagonists

D Tricyclic antidepressants

Explanation A

MAOIs are associated with a sever drug interaction when combined with SSRIs. Life threatening serotonin syndrome can develop. The serotonin syndrome is due to overstimulation of the 5-HT receptors in the central gray nuclei and the medulla. Symptoms range from mild to lethal and include a triad of cognitive (delirium and coma), autonomic (hypertension, tachycardia and diaphoreses) and somatic (myoclonus, hyperreflexia and tremor) effects. Most SSRI antidepressants should be discontinued for at least 2weeks before starting a MAOI. Fluoxetine, because of its long half-life, should be discontinued for 4-5weeks. Conversely, an MAOI must be discontinued for at least 2 weeks before starting a serotonin agent

Note: There is a potential for drug interaction with all antidepressants, but the most serious of these involve the MAOIs and to a lesser extent the TCAs

**Question 62**

Sodium Valporate inhibits the metabolism of all of the following drugs EXCEPT?"

A Phenytoin

B Lamotrigine

C Carbamazapine

D Phenobarbitol

Explanation B

Sodium valproate (SV) inhibits the metabolism of phenobarbitol, phenytoin and carbamazepine, leading to higher steady state concentrations of these agents. SV dramatically decreases the clearance of lamotrigine.

Clearance and metabolism are two separate concepts

**Question 63**

Which of the following pharmacokinetics of Lithium is CORRECT?

A Volume of distribution is 2.0L/Kg

B Bioavailability is <50%

C Plasma half life is 30hrs

D It is not metabolized

Explanation D

Lithium is rapidly absorbed, and plasma conc. peak within one-half to three hrs following oral administrations.

Gastrointestinal absorption of lithium carbonate tablets or capsules appears to be virtually complete (95% to 100%).

The absorption of sustained-release lithium products is more variable, and ranges from (60% to 90%). Lithium solutions appears to be rapidly and completely absorbed and plasma conc. peak within 60 min(30min-2Hrs).

The usual volume of distribution for lithium is approximately (0.7 L/kg).

T1/2=20hrs, no plasma protein binding

It is NOT metabolised and excreted virtually entirely in the urine

**Question 64**

Which of the following drugs reduce the clearance of lithium?

A Aspirin

B Thiazide

C Clozapine

D Paracetamol

Explanation B

Renal clearance of lithium is reduced by 25% with thiazide diuretics and the dose may need to be reduced by a similar amount. A similar reduction occurs with the newer NSAIDS. There is no issue with Aspirin however. Paracetamol is also safe. All neuroleptics with the possible exception of clozapine may produce more severe extrapyradimal side effects when combined with lithium

**Question 68**

Which pharmacological agent is best prescribed for motion sickness

A 5-HT3 receptor blockers

B Anti-muscarinic agents

C Anti-histamines

D Dopamine 2 blockers

Explanation B

Certain vestibular disorders respond to antimuscarininc drugs (and to antihistaminic agents with antimuscarinic effects). Scopolomine is one of the oldest remedies for seasickness and is affective as most other newer agents.

**Question 69**

Which of the following analgesic medications is relatively contraindicated in patients who have a history of seizure activity?

A Indometacin

B Tramadol

C Morphine

D Codeine

Explanation B

Tramadol-central acting analgesia, mechanism of action-blockade of serotonin reuptake. Toxicity includes association with seizures and the drug is relatively contraindicated in patients with a history of epilepsy and with use of other drugs that lower the threshold for seizures. Another serious risk is the development of serotonin syndrome, especially if combined with a SSRI antidepressant

Note: In Australia the most common drugs causing toxic seizure are venlefaxine, bupropion, tramadol and amphetamines

**Question 71**

Which side effect is most severe with chlorpromazine?

A Dry mouth

B Hypotension

C Extra pyramidal side effects

D Nausea and vomiting

Explanation B

Chlorpromazine has strong anti alpha and 5HT2A effects, followed by anti dopamine 2 and 1. Clinical potency is low, extrapyramidal toxicity is moderate. Hypotensive action is high. Sedative action is also high. Other anti alpha effects include failure to ejaculate and impotence.

**Question 72**

Which of the following metabolites of benzodiazepines is NOT active?

A Lorazepam

B Diazepam

C Alprazolam

D Triazolam

Explanation A

Diazepam is metablised into oxazepam (an active metabolite)

Alprazolam and triazolam are metabolised into alpha-hydroxy metabolites (active)

Chlordiazepoxide is metabolised into desmethylchlordiazepoxide (active)