pharmacology
Team 438

MED438
KING SAUD UNIVERSITY

Reviewed by Razan AlRabah & Ibrahim AlDakhil

Neuropsychiatry Block

Pharmacology Team 438

Summary

★ Starred lectures are more likely to come in SAQ

Table of contents:

Team Leaders:

May Babaeer Zyad Aldosari

This Summary was done By:

Reem AlGarni Yasmeen AlMousa

Sara AlFarraj Nujud AlAbdullatif

Deana Awartani Reema AlSerhani

Nouf AlShammari

Lecture (1): Drugs related to balance

Drug	M.O.A	Uses	ADRs	C.I
Vestibular Suppressants				
Anticholinergics				
Hyoscine	-Inhibits firing in vestibular nucleus neurons -Reduce the velocity of vestibular nystagmus	1-motions sickness 2-sedation	-Dry mouth -Blurred vision -sedation	—
Benzodiazepines				
Lorazepam **Clonazepam** **Diazepam**	binding to **BZ receptors** in the brain⟶ **enhance GABA** action on the brain ⟶reduction of neural excitability. (Mentioned in Anxiety lecture)	-Management of acute vertigo (small doses) -Minimize anxiety and panic w/ vertigo	-Dependence -Impaired memory - Increased risk of falling (ataxia)	-**pregnancy⟶ (Fetal depression).** -Breast feeding⟶ **(neonatal depression).** - Dose reduction **in Liver disease & old people** (Mentioned in Anxiety lecture)
Betahistine				
Betahistine *(Structural analog of Histamine)*	**1**-Weak H1 receptor agonist: local vasodilation and increased permeability (reverses endolymphatic hydrops) **2**-Potent H3 receptor antagonist: Increases local conc. of histamine in inner ear	Ménière's syndrome	-Headache -Nausea -GIT side effects -Hypersensitivity	-Pheochromocytoma - bronchial asthma -History of peptic ulcer -Hypersensitivity reactions
Antiemetics				
Phenothiazines				
Prochlorperazine	1-Blocks **dopamine** receptors at CRTZ **2-Antiemetic** 3-Antipsychotic + some sedation 4-Some vestibular suppression	One of the best antiemetic drugs used in vertigo	—	—

Lecture (1): Drugs related to balance

Drug	M.O.A	Uses	ADRs	C.I
Antiemetics				
Antihistamines				
Dimenhydrinate	**1-Block H1** receptor in CRTZ **2-** Sedation **3-** Weak **anticholinergic** effect **4-** Decrease excitability in the labyrinth and blocks conduction in the vestibular-cerebellar pathways	- Vertigo -Prevention of nausea & vomiting associated motion sickness	-Sedation -Dizziness -Anticholinergic side effects	- Glaucoma -Prostatic enlargement
Dopamine Antagonists				
Metoclopramide **Domperidone**	**1-**Block dopamine D2 receptors in the CRTZ, resulting in potent **central** antinausea & antiemetic action **2-**Some sedation **3-**Potent gastroprokinetic effect	Esophagogastric reflux	-Restlessness or drowsiness -Extrapyrimidal manifestations on prolonged use	—
Prophylactic Treatment				
Calcium Channel Blockers				
Cinnarizine	**1-**selective K+ & Ca^{2+} channel blockers **3-**Inhibits K+ currents (Lessens vertigo and motion induced nausea by dampening the over-reactivity of the vestibular hair cells) **2-** Antihistamine, antiserotonin, antidopamine	Treatment of **nausea** and **vomiting** associated with: 1-Motion sickness 2-Vertigo 3-Ménière's disease	1-Sweating 2-Headache 3-Drowsiness 4-Muscle Rigidity and tremors	1-Parkinsonism 2-Car drivers

Drugs Inducing Vertigo

A- Vestibular toxins

(Altering function)

1- Drugs altering fluid and electrolyte balance:
Diuretics

2- Drugs altering vestibular firing (neural depressant)
Anticonvulsants, antidepressants, sedative hypnotics, alcohol, & cocaine

B- Mixed ototoxins

(Altering structure)

Aminoglycosides:
-**gentamicin**: induces apoptosis by **evoking free radicals** —> mitochondrial pathway
-**neomycin**: induces apoptosis by **activating caspases**—> death receptor pathway.

(Altering function)

Quinine, choloroquine, quinidine / nitrogen mustard / loop diuretic / NSAIDS / tobacco
-Decrease local blood flow —> biochemical changes —> decrease electromechanical transduction —> decrease firing of impulse

Lecture (2): Drugs acting on Eye

	Drug	Actions	Uses	ADRs	C.I
Cholinergic agonist					
direct					
	Methacholine	- Meiosis - **Contraction** of ciliary muscles → **Increase aqueous outflow** through trabecular meshwork → **decrease IOP**	-induction of miosis in surgery. **-open angle glaucoma.**	- Diminished vision (myopia) -Headache	–
	Carbachol				
	Ach				
	Pilocarpine		**-open angle glaucoma.**		
Indirect					
reversible	Physostigmine		**-Glaucoma.** -Accommodative esotropia → **echothiophate + physostigmine**. -In lice infestation of lashes.→ **physostigmine**. **Both direct and indirect:** -Counteract action of mydriatics. - To break iris-lens adhesions.		
	Demecarium				
Irreversible	Isofluorophate				
	Echothiophate				
Cholinergic antagonist					
Natural Alkaloids	Atropine	**- Passive mydriasis** **-Cycloplegia.** **- Increased IOP.** - Decreased lacrimal secretion → sandy eye.	-To prevent adhesion in uveitis & iritis. - Funduscopic examination. - Measurement of refractive error.	_	-angle closure glaucoma.
	Scopolamine				
Synthetic atropine	Homatropine				
	Cyclopentolate				
	Tropicamide				

Lecture (2): Drugs acting on Eye

Drug	M.O.A	Uses	ADRs	C.I
Adrenergic agonists				
Selective α2 agonists				
Apraclonidine	-↓**production** of aqueous humor.	**-open angle glaucoma** -prophylaxis against IOP spiking after glaucoma laser procedures.	-bradycardia. -hypotension.	–
Selective α1 agonists				
Phenylephrine	-active mydriasis **(without Cycloplegia)**.	-fundoscopic examination. -prevent adhesion in uveitis & iritis. -Decongestant in minor procedures. allergic hyperemia of eye.	-↑ In BP.	-patients with narrow angle.
Non-selective agonists (α1 , α2 , β1 , β2)				
Dipivefrin (pro-drug of epinephrine)	-↑ uveoscleral **outflow** of aqueous humor.	-eye drops → in **Open angle glaucoma.**	- Headache. - Arrhythmia. -↑ In BP.	-patients with narrow angle.
Epinephrine				
β Blockers				
Selective β1 (cardio-selective) **Betaxolol**	-↓ **production** of aqueous humor.	**-Open angle glaucoma.**	-Ocular Irritation.	**Advantage:** -Can be used in patients with **hypertension & ischemic heart disease.** -Betaxolol is **not** causing bronchospasm
Non-Selective **Carteolol**				
Timolol				

Lecture (2): Drugs acting on Eye

Prostaglandin analogues

Drug	M.O.A	Uses	ADRs	C.I
Latanoprost **Travoprost**	-↑ uveoscleral aqueous **outflow**.	**-open angle glaucoma.**	-Pigmentation of the iris (heterochromia iridis)	–

Carbonic anhydrase inhibitors

Drug	M.O.A	Uses	ADRs	C.I
Acetazolamide **Dorzolamide**	- ↓ **production** of aqueous humor by blocking Carbonic anhydrase enzyme	**-open angle glaucoma.**	Myopia, malaise, anorexia, GI upset, headache, Metabolic acidosis, & renal stone.	- Sulfa allergy - Pregnancy - Digitalis users.

Osmotic agents

Drug	M.O.A	Uses	ADRs	C.I
Mannitol (I.V)	- Can rapidly ↓ **IOP by ↓ vitreous volume** prior to anterior surgical procedures.	-only in **acute situations** to temporarily reduce high IOP. (Closed Angle Glaucoma)	-Diuresis, circulatory overload, pulmonary edema, heart failure, & CNS effect: seizures, and cerebral hemorrhage.	-heart failure.
Glycerol (Orally)				-diabetic patients Causes: hyperglycemia

Anti-inflammatory drugs

Corticosteroids

Drug	M.O.A	Uses	ADRs
Systemic: **Prednisolone, Cortisone**	- Inhibition of arachidonic acid release from phospholipids **by inhibiting phospholipase A2.**	**-posterior** uveitis. - optic neuritis.	**- Glaucoma, cataract, increase IOP.** - Skin atrophy. -Secondary infection. -Delayed wound healing.
Topical: **Prednisolone, Dexamethasone, Hydrocortisone**		**-anterior** uveitis. - severe allergic conjunctivitis. -scleritis. -prevention of corneal graft rejection.	

NSIAD

Drug	M.O.A	Uses	ADRs
Flurbiprofen	**- COX (cyclo-oxygenase) inhibitor.**	**-Pre-operatively** to prevent miosis during cataract surgery.	- Stinging, sterile corneal melt & perforation.
Diclofenac		**-postoperative** inflammation. - mild allergic conjunctivitis. - mild uveitis.	
Ketorolac		-Cystoid macular edema **after** cataract surgery.	

Lecture (3): Alcohol & the Brain

Pharmacokinetics	Metabolism
• Ethanol crosses all biological membrane including **placenta & CNS** • **Acute** alcohol consumption **inhibits** **CYP450 2E1** ,↓ metabolism of other drugs taken concurrently as (**warfarin**, **phenytoin**). • **Chronic** alcohol consumption **induces** liver microsomal enzyme **CYP450 2E1**, which leads to significant increases in ethanol metabolism (Tolerance) & metabolism of other drugs as **warfarin** (Drug interactions).	1. Ethanol is converted to **Acetaldehyde** via [***alcohol dehydrogenase*** **(Cytosolic Enzyme) in case of ACUTE consumption**] or [CYT-p450 2E1 **(Microsomal Enzyme) in case of CHRONIC consumption**] 2. Acetaldehyde is converted to Acetate via ***aldehyde dehydrogenase*** [in both acute and chronic]

"Acute acetaldehyde toxicity" characterized by **nausea, vomiting, dizziness, headache, vasodilatation and facial flushing**

Mechanism of action of alcohol: Alcohol is a CNS depressant

Acute alcohol: Enhancement of the effect of **GABA** on its receptor & Inhibition of **glutamate** action on **NMDA** receptors.	**Chronic alcohol:** Up-regulation of **NMDA** receptors & Down regulation of **GABA** receptors Leading to **alcohol tolerance & withdrawal symptoms**

Chronic alcoholism associated syndromes:

Systemic: CVS: Hypertension,cardiomyopathy | **Endocrine**:Hypoglycemia & ketoacidosis,Hypogonadism | **Liver:**Hepatic cirrhosis

Fetal Alcohol Syndrome (FAS) Irreversible Prenatal exposure to alcohol causes congenital malformation • Microcephaly • Impaired facial development • Congenital heart defects • Physical and mental retardation.	**Wernicke-Korsakoff Syndrome:** It is a combined manifestation of 2 disorders: 1. Wernicke's Encephalopathy 2. Korsakoff's psychosis **Cause: Thiamine (vit. B1) deficiency** **TREATMENT: Thiamine + dextrose-containing IV fluids**

Alcoholism Tolerance in Chronic Consumption is Due to

Metabolic tolerance: due to induction of **liver microsomal enzymes e.g. CYP450**	**Functional tolerance:** due to **change in CNS sensitivity**

Drugs Used in case of:

Management of Alcoholism Withdrawal: • **Benzodiazepines**(Diazepam,lorazepam) **best choice** • Acamprosate • Fluoxetine • Clonidine and Propranolol	**Prevent alcohol relapse:** **Disulfiram:** **MOA:** inhibits hepatic **aldehyde dehydrogenase** →increase blood level of **acetaldehyde,** this induces the symptoms of Acute acetaldehyde toxicity

Lecture (6): Central NTs

NT	Function	Diseases associated with its level
NE	Alertness, Arousal	↑ Mania + Anxiety | ↓ Depression
Serotonin	Mood, Sleep, Appetite	Depression, Anxiety, Schizophrenia
Dopamine	- Nigrostriatal pathway: control movement. - Mesolimbic & mesocortical pathway: cognition and emotion - Tuberoinfundibular: related to endocrine system	↓ Parkinson's | Schizophrenia
Ach	Learning, Memory	↑Parkinson's | ↓ Alzheimer's
Glutamate	Excitatory NT	↑ Epilepsy
GABA	Inhibitory NT	↓ Epilepsy, Anxiety

Lecture (5): General Anesthetics

Drug	Uses	Drug	Uses
Pre-Anesthetic medications			
opiates eg.Morphine	Induce analgesia	Anticholinergics e.g Hyoscine	Prevent secretion of fluids into the respiratory tract
Sedatives & anxiolytics e.g Diazepam	Relieve anxiety	Antihistamines e.g Diphenhydramine	Allergic reactions
Antiemetics e.g metoclopramide & prochlorperazine	Post surgical N&V	H2-receptor blockers e.g Ranitidine	Reduce gastric acidity
Thiopental (Barbiturates)	Smooth induction	**Adjunct to general anesthesia:** Neuromuscular blockers e.g **succinylcholine, vecuronium & atracurium**	-Facilitate intubation. -suppress muscle tone.

MOA of General anesthetics: **Enhance the action of GABA A and glycine on receptors** leading to **Greater entrance of chloride ion** → hyperpolarization → thus **decrease neuronal excitability.**

Drug	Features	ADRs or Disadvantage
Inhalation Anesthetics		
Halothane	- Non irritant **(used in children**) -Potent anesthetic, weak analgesic	-Slow induction and recovery -Sensitization of Heart to catecholamines -Hepatotoxicity -Malignant Hyperthermia **C.I = Pheochromocytoma**
Enflurane	- Metabolized to fluoride -Better muscle relaxation, Better analgesic properties	-Pungent (less induction -**Not for pediatrics**) -Airway irritation -CNS stimulation (Epilepsy-like seizure "abnormal EEG") **C.I = seizure disorders & Renal failures**
Isoflurane	-No nephrotoxicity & hepatotoxicity - No sensitization of the heart or arrhythmia	Pungent (**Not for pediatrics**)
Sevoflurane	-Better smell & No airway irritation (**used in children**) -little effect on HR	-
Desflurane	- Less metabolized - low boiling point (special equipment)	-Pungent odor -Airway irritation
Nitrous oxide	-Potent analgesic **Uses=** Outpatient anesthesia (Dental procedures) -balanced anesthesia -Neuroleptanalgesia -Delivery	- Diffusion hypoxia, Nausea & vomiting -Inactivation of B12 → megaloblastic anemia -congenital anomalies w\ repeated exposure -Leukopenia(chronic use) **C.I=** Pregnancy , Pernicious anemia, Immunosuppression

★ All Inhalation anesthetics are **CONTRAINDICATED IN HEAD INJURIES** because they ↑ICP

Lecture (5): General Anesthetics

Drug	Characters	Uses	ADRs	C.I
Intravenous Anesthetics				
Ultrashort acting barbiturates				
Thiopental Methohexital	-Rapid onset of action (1min) - Short duration (15-20 min) - Potent anesthetic **- ↓ ICP**	**- in head injury** -Induction in major surgery - Alone in minor surgery	-CVS collapse - Respiratory depression - Precipitate porphyria attack - Hypersensitivity reaction	COPD & severe hypotension (hypovolemic & shock patient)
Non barbiturates				
Propofol	**- ↓ICP** - Antiemetic action	-head injury	-Hypotension (↓PVR) -involuntary movements	-
Etomidate	-Minimal CVS and respiratory depressant effects	-	-Involuntary movements during induction -Postoperative nausea & vomiting -Adrenal suppression	
Benzodiazepines				
Midazolam Diazepam Lorazepam	Anxiolytic and amnesic action	-Induction of general anesthesia. -Alone in minor procedure (endoscopy). **-In balanced anesthesia (Midazolam).**	Respiratory depression	-
Ketamine				
Ketamine	-Dissociative anesthesia (Analgesic activity Amnesic action) -Potent bronchodilator	- asthmatic patient - can be used in children - Hypovolemic, shock, & elderly patients	-Postoperative hallucination vivid dreams & disorientation & illusions -Increases plasma catecholamine levels→ **↑ICP** → Risk of hypertension and cerebral hemorrhage -↑ BP & cardiac output → (↑central sympathetic activity)	-Head injuries -CV diseases (hypertension & stroke)
Opiate drugs				
Fentanyl Alfentanil Sufentanil Remifentanil	Potent analgesia (not anesthetic)	[Neuroleptanalgesia (Fentanyl+Droperidol) **C.I= parkinsonism**] Neuroleptanesthesia (Fentanyl + Droperidol + nitrous oxide) Cardiac surgery (morphine + nitrous oxide)	-Respiratory depression, bronchospasm (wooden rigidity) -Hypotension -↑ICP -Urinary retention -Prolongation of labor & fetal distress	-Head injuries -Pregnancy -Bronchial asthma Chronic obstructive lung diseases -Hypovolemic shock (Large dose only)

Lecture (7,14): Drugs for Epilepsy

Drug	M.O.A	Uses	ADRs	C.I
Class: 1st Generation				
Fosphenytoin Parenteral form of phenytoin **(IV & IM)**	-Blockade of **Na+** & **Ca2+** influx into neuronal axon. -Inhibit the release of glutamate -Potentiate the action of GABA	1.**Partial** and **generalized** tonic-clonic seizures 2.**Not** in absence seizure. 3.In **status epilepticus**, given IV.	-**Gum(gingival) hyperplasia** -**Folic acid deficiency (Megaloblastic anemia)** -**Vit D deficiency (Osteomalacia)** -Teratogenic effect	-Pregnancy
Phenytoin (orally) Enzyme inducer				
Carbamazepine (Orally only) Enzyme inducer (including its own)		1.**Drug of choice in partial seizures** 2.Tonic-clonic seizures(1ry & 2ry generalized) 3.**Not** in absence seizures -**Other uses:** 4.Bipolar depression, 5.Trigeminal neuralgia	-Hypersensitivity reactions. -Drowsiness , ataxia, headache. & diplopia. -**Hyponatremia & Water intoxication** -**Teratogenicity**	
Ethosuximide (Orally)	**Inhibits T-type Ca2+ channels in thalamocortical neurons.**	**Drug of choice in absence seizures**	-**Drowsiness**, fatigue, **hiccups**, headaches.	-
Sodium Valproate (Broad spectrum antiepileptic) **(Orally, IV) Enzyme inhibitor**	-Blocks activated **Na+** channels -**Enhances GABA synthesis & reduces degradation** -Suppress glutamate action -**Blocks T-type Ca2+ channels**	**Effective in all forms of epilepsy include absence and photosensitive epilepsy** **Other uses:** -Bipolar disorder and mania -Prophylaxis of migraine **-Lennox-Gastaut syndrome**	-**Weight gain** (↑ appetite) -Transient hair loss, with re-growth of curly hair -**Thrombocytopenia** -**Hepatotoxicity** -**Teratogenicity** (neural tube defect)	**-not used with aspirin or coumadin**"warfarin" (+Bleeding) -pregnancy

Lecture (7,14): Drugs for Epilepsy

Drug	M.O.A	Uses	ADRs	C.I
Class: 2nd Generation				
Topiramate (Orally) **No effect** on microsomal enzymes	-Blocks **Na+** channels -Potentiates the inhibitory effect of GABA	1.Alone for, partial,generalized tonic-clonic, & ***absence seizures***. **2.Lennox- Gastaut syndrome**	**-Psychological or cognitive dysfunction** **-Weight loss** -Sedation, Dizziness, Fatigue **-Urolithiasis** -Paresthesias (abnormal sensation)	-kidney stones
Lamotrigine (Orally) **No effect** on microsomal enzymes	-Blockade of **Na**+channels -Inhibits excitatory amino acid release (glutamate & aspartate)	1.As **add-on** therapy or as **monotherapy** in partial seizures. 2.**Lennox- Gastaut syndrome**	**-Influenza-like symptoms** -Skin rashes (may progress to **Steven – Johnson Syndrome**) -Somnolence -Blurred vision -Diplopia -Ataxia	–
status epilepticus (IV)		**LORAZEPAM / DIAZEPAM**		
safe in pregnancy (monotherapy is **better** than combo)		**LAMOTRIGINE** / levetiracetam		

Lecture (8): Drugs for Schizophrenia

Class	Drug	MOA	Uses	Characteristics
Typical	Chlorpromazine Thioridazine	Block dopamine receptors	**Both classes:** **-Schizophrenia (main use)** **-Acute mania** **-Manic-depressive illness** (during manic phase) **For Atypical:** -**Refractory cases** of schizophrenia **-Reduce risk of recurrent suicidal behavior in patients with schizophrenia**	**-Nonselective** -Treat positive symptoms -**Many** side effects
	Haloperidol			
	Thiothixene			
Atypical	Clozapine	Block dopamine and serotonin receptors		-**1st line of treatment** -**More** selective -**Treat both positive/negative symptoms** (thus helps in the treatment of emotional blunting and anhedonia) -**Less** side effects
	Risperidone			
	Olanzapine			
	Quetiapine			
	Ziprasidone			
	Cariprazine			

Specific ADRs for Atypical drugs

Drug \receptor blockade	Main ADRs
Clozapine D_4 and $5HT_2$	• **Agranulocytosis** • **Seizures** • Myocarditis
Olanzapine D_1 - D_4 and $5HT_2$	• Postural hypotension • Weight gain (**O**besity) • Sedation
Quetiapine D_1 - D_2 and $5HT_2$	• Sedation • Hypotension • Sluggishness
Cariprazine D3 receptor	• Has positive impact on the cognitive symptoms of schizophrenia "advantage"
Risperidone D_2 and $5HT_2$	• Postural hypotension • Weight gain (**O**besity) • QT prolongation **(contraindicated in cardiac patient with QT prolongation)**
Ziprasidone D_2 and $5HT_2$	• Dizziness & drowsiness • Akathisia • Headache • Weight gain (**O**besity) **•Increased mortality in elderly with dementia-related psychosis**

Lecture (8): Drugs for Schizophrenia

Pharmacological actions and ADRs for Both

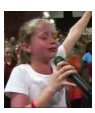
Action	Effect	Mechanism	ADR
CNS	**Antipsychotic:** • Produce emotional quieting and psychomotor slowing • Decrease hallucinations, delusions and agitation	Blockage of dopamine receptors in mesolimbic system	• Sedation, drowsiness, fatigue **Haloperidol** (typical), **Risperidone** (atypical)
	Extrapyramidal symptoms: • Abnormal movement such as tremors, parkinsonism & Tardive dyskinesia	Blockage of dopamine receptors in nigrostriatal system	• **Early:** Parkinson's syndrome • **Late:** **-Tardive Dyskinesia** **-Neuroleptic Malignant syndrome**
	Endocrine: • Galactorrhea • Amenorrhea • Gynecomastia • Impotence	Prevent dopamine inhibition of prolactin release from pituitary → hyperprolactinemia	• Same as the effects
	Metabolic: • Changes in eating behavior and weight gain	Blockage of dopamine receptors in periventricular (medullary) system	• Same as the effects
	Antiemetic effect : • Effective against drug and disease-induced vomiting **(not motion sickness)**	Blockage of dopamine receptors in the CTZ of the medulla	—
ANS	**Anticholinergic effect:** • Blurred vision • Dry mouth • Urinary retention • Constipation	Blockage of muscarinic receptors	• Same as the effects **Chlorpromazine** (typical), **Clozapine** (atypical)
	Antiadrenergic effect: • Postural hypotension • Impotence • Failure of ejaculation	Blockage of a-adrenergic receptors	• Same as the effects **Chlorpromazine** (typical), **Thioridazine** (typical)
Others	**Temperature regulation:** • May decrease body temperature	Heat loss as a result of vasodilatation (a-blocking) **OR** due to central effect	• Obstructive Jaundice • Retinal deposits (**thioridazine**) • Granular corneal deposits • Agranulocytosis (**clozapine**) • Seizures(**clozapine**)
	ECG changes • Prolongation of QT interval		
	Antihistamine effect: • Sedation due to H1 receptor blockade		
	Quinidine-like actions (Block Na channels, antiarrhythmic effect)		

Lecture (9):Drugs used in Management of Pain

Drug	M.O.A	Uses	ADRs	C.I
Opioids				
Agonist				
Morphine μ (Can cross placenta) Actions -↓ cough reflex & respiration -Mioses -release Histamine -↑Pressure in biliary tract	**1- Binding to presynaptic opioid receptors coupled to Gi:** →↓ AC & cAMP →↓voltage gated Ca2+ channels → reduce release of neurotransmiter → ↓ excitatory transmitter **2-Binding to postsynaptic receptors:** → ↑ opening of K+ channels (hyperpolarization) →↓ neuronal excitability	-Pain control (Severe cases: In cancer pain, severe burns, trauma, Severe visceral pain) -Pulmonary edema -Myocardial ischemia -Non-painful conditions e.g Heart Failure -Pre-anesthetic medications	**-TOLERANCE & DEPENDENCE** -Itching -Constricted Pupil -Sedation -Respiratory Depression -Constipation -Hypotension on long term use -Nausea & vomiting	-Elderly -Head injury "↑ICP" -Patients taking MAOIS -Pancreatic pain & Biliary\renal colic -Infants,neonates, or during childbirth -bronchial asthma or impaired pulmonary function
Codeine μ		-Mild and moderate pain (systemic) -Cough -Diarrhea	Dependence less than morphine	-
Tramadol μ -less potent than Morphine -inhibit NE & 5HT		-Mild to moderate acute and chronic visceral pain -During labor - Rescue therapy in headache & migraine (Mentioned in headache & migraine Lecture)	**- Seizures** -Nausea - Dry mouth - Dizziness - Sedation - Less ADRs on respiratory and CVS	**-Epileptics**
Pethidine (meperidine) K -Atropine-like action (smooth muscle relaxant) -no cough suppressant effect		-As in morphine but **not in cough and diarrhea** -Better preanesthetic medication -in obstetric analgesia (no decrease in respiration) **-Best choice in severe visceral pain; renal and biliary colics** (smooth muscles relaxant)	-Tremors, convulsions, hyperthermia, hypotension. -Blurred vision, dry mouth, urine retention -Tolerance and addiction	-
Fentanyl μ **more potent than pethidine and morphine**		-Analgesic supplement during anesthesia -Induce and maintain anesthesia in poor-risk pts (stabilizing heart) - in combination with Droperidol (antipsychotic) as NEUROLEPTANALGESIA - In cancer pain and severe postoperative pain	**-Respiratory depression** (more serious than morphine) -CV effects are less -Bradycardia may still occur	-
Methadone μ		**-To treat and control opioid withdrawal**	-In non-addicts, it causes tolerance and dependence but not as severe as that of Morphine	-

Lecture (9):Drugs used in Management of Pain

Drug	M.O.A	Uses	ADRs
Opioids			
Antagonist (ANTIDOTES)			
Naloxone (Pure opioid antagonist) **Naltrexone**	Competitive antagonists that bind to the opioid receptors with **higher affinity** than agonists but do **not activate the receptors**	-Used to treat and reverse respiratory depression caused by opioid overdose -Reverse the effect of analgesia on the respiration of the new born baby	-Precipitates withdrawal syndrome in addicts



مساحه للفضفضه
اطلقوا العنان لما في داخلكم

Lecture (4,10): Drugs for Depression

Drug	M.O.A	Uses	ADRs	C.I or +ve
Tricyclics (TCAs)				
Imipramine **Amitriptyline** **Clomipramine** (More potent on 5HT) **Desipramine** **Nortriptyline** (More potent on NE)	Block **reuptake pumps for both 5HT and NE** by competing for binding site of the transport protein	- Depression - Anxiety w\depression (mentioned in Anxiety lecture) - Panic attack **-Imipramine** because is used for treatment of **nocturnal enuresis** in children and geriatric patients -Chronic neuropathic pain	**-TCA block :** **α1**→Postural hypotension. **M1**→blurred vision,urine retention. **H1**→Sedation. and **5HT2.** -Sexual dysfunction -Narrow therapeutic index (↑VD & protein bound)	**C.I:** -Glaucoma & enlarged prostate -Seizure disorder -manic-depressive illness **(if given alone)** "should be given combo w\lithium salts"
MonoAmine Oxidase Inhibitors (MAOIs)				
Phenelzine **Tranylcypromine** (Non selective Irreversible)	**Inhibition of MAO enzyme** which is responsible for catabolism of monoamines (NE -5HT-DA) There is 2 type of MAO: A (for NE & 5HT) B (for DA)	**-Only used for refractory cases**	-Antimuscarinic effects -Postural hypotension. -Sedation. -sleep disturbance. -Weight gain. **Specific for Phenelzine:** **Sexual dysfunction** **Hepatotoxicity**	-
Moclobemide (Selective MAO-A reversible)				**special advantage** for Moclobemide is that, No cheese reaction "tyramine" occurs with its use.
Selective Serotonin Reuptake Inhibitors (SSRIs)				
Fluoxetine **Paroxetine** (STRONG enzyme **INHIBITORS**) **Citalopram** **sertraline** (Weak enzyme **INHIBITORS**) **Escitalopram**	-Selective 5HT reupatake inhibitors -Have **no** effect on NE or mAch, H, a1 receptors.	-Depression -first line of treatment for most anxiety disorders (mentioned in Anxiety lecture) **-Eating disorders:** **-bulimia nervosa (Fluoxetine)** **- Anorexia nervosa** **-premature ejaculation (+5HT2A)**	-Changes in appetite -Sexual dysfunction: delayed ejaculation -Drowsiness with Fluvoxamine -Discontinuation syndrome	**Advantages over TCA and MAOI:** -Lacks cardiovascular and anticholinergic side effects -they do not cause 'cheese' reaction
Norepinephrine and Dopamine Reuptake Inhibitors (NDRI)				
Bupropion	**UNIQUE MOA:** **NE and DA reuptake inhibitor**	**SMOKING CESSATION** (reduces the severity of **nicotine craving)**	**Seizures**	**ADVANTAGES:** -No sexual dysfunction -No weight gain. -No orthostatic hypotension.

Lecture (4,10): Drugs for Depression

Drug	M.O.A	Uses
Noradrenergic and specific Serotonergic Antidepressants (NaSSA)		
Mirtazapine	**- α2 receptor antagonist.** **-Blocks 5HT2A , 5HT3** and thus reduces side effects of sexual dysfunction and anxiety. - Blocking **5HT2C** →weight gain & **H1** →Sedation	**Preferred in CANCER patients because:** 1- It improves appetite, ↑ **body weight** 2- ↓ nausea & vomiting 3- Sedation 4- Less sexual dysfunction 5- **Has no anti-muscarinic effect.**
Serotonin-2A Antagonist and Reuptake Inhibitors (SARI)		
Trazodone, Nefazodone	-**Blocks 5HT uptake selectively** **-5HT2A antagonists reduces** the risk of anxiety, sedation or sexual dysfunction -**stimulates 5HT1A receptors**	-
Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs)		
Venlafaxine	-Selective **5HT** and **NE uptake blockers** without α1, M1 cholinergic or H receptor blocking properties	-Depression -Anxiety
NE Selective Reuptake inhibitors (NRIs)		
Reboxetine	**Block only NET** (norepinephrine transporter)	**SAFE TO COMBINED WITH SSRIs**

Lecture (11): Drugs for Parkinsonism

Drug	M.O.A	Uses	ADRs	C.I
Dopamine precursor				
Levodopa & Carbidopa (Orally on **EMPTY** stomach)	- Is converted into dopamine via dopa decarboxylase (DC) **peripherally and centrally**. - **L-dopa is usually given combined with DC inhibitors** (**carbidopa**)to prevent **peripheral** conversion. **-Benefits of the combo:** Lower the dose and increase availability in CNS -Have Short duration which cause fluctuation lead to Dyskinesia	-all types of parkinsonism in (bradykinesia & rigidity) **except** those associated with antipsychotic drug therapy.	CNS effects: -depression -delusion -hallucination -Insomnia Peripheral effects: -N & V -cardiac arrhythmia (withdraw the drug) -mydriasis -Orthostatic hypotension -**Dyskinesias**	-Psychotic patient -Glaucoma (due to mydriatic effect) -Patients with history of melanoma -cardiac arrhythmia --- **Limitation:** -Dyskinesia -Wearing-off effect - on-off phenomenon
Dopamine agonist				
Bromocriptine (Ergot Derivatives)	-D2 agonist	-Little use for Parkinson's disease **-galactorrhea** **-Infertility in women.**	-Similar to L-dopa but with **Less prominent** Dyskinesias	-Peripheral vascular disease**(with ergot only)** -Psychosis -Recent myocardial infarction
Pramipexole (Non-Ergot Derivatives)	-D3 agonist -Free radicals scavenger (Antioxidant)	initial therapy or with L- dopa For Parkinson's disease		
Dopamine release				
Amantadine	**-Inhibits dopamine reuptake & increase DA release** -an **antagonist** at **muscarinic & NMDA** receptors	-L-dopa resistance. **-early stages** of parkinsonism or as an **adjunct to levodopa** therapy.	**-livedo reticularis** -dopamine like side effects -Anticholinergic effect	-Anti cholinergics -History of seizures or heart failure

Lecture (11): Drugs for Parkinsonism

Drug	M.O.A	Uses	ADRs	C.I
MAO-B inhibitors				
Selegiline	-**selective irreversible inhibitor of MAO-B** **P.K:** **Neuroprotective effect**: **-Antioxidant** **-Anti-apoptotic.**	Adjunctive to levodopa + carbidopa in **later-stage** parkinsonism to: -↓ the required dose of levodopa -Delay the onset of **dyskinesia** and motor fluctuations.	At high doses: -may **inhibit MAO-A** → (hypertensive crises) -insomnia	co-administered with: -TCA (hypertensive crisis) -SSRI (hyperpyrexia, delirium, coma) -Food restriction "**low tyramine diet**" is required (hypertensive crisis)
COMT Inhibitors Inhibitors				
Entacapone	-Acts **peripherally** to inhibit COMT enzyme.	**adjuvant** to L-dopa + carbidopa to: -Decrease fluctuations -Improve response **-Prolonged the ON-Time**	-L-dopa side effects -Orange discoloration of urine	–
Tolcapone	**-Peripheral** and **central** COMT inhibitor		–	
Anticholinergic Drugs				
Benztropine	**-Central** muscarinic antagonist. -It has **modest** anti-parkinsonian action	-Improve tremor & rigidity but have little effect on bradykinesia -Provide benefit in **drug-induced parkinsonism** (due to **antipsychotics**). -early stage of the disease or adjunct to L-dopa therapy.	-Cycloplegia -Mydriasis -Dry mouth -Urinary retention -Constipation At high doses: -Confusion,Delirium & Hallucinations -Trihexyphenidyl may cause withdrawal symptoms in high doses.	-Prostatic hypertrophy -Glaucoma -Intestinal obstruction
Trihexyphenidyl				

Lecture (12): Drugs for Meningitis

Drug	M.O.A	Spectrum & uses	P.K	ADRs
Inhibitors of cell wall synthesis (B-LACTAMS)				
Penicillins **Penicillin G**	Inhibit bacterial cell wall synthesis (bactericidal)	Narrow (+ve Only)	-B-lactamase sensitive	- Hypersensitivity -diarrhea - Nephritis -Super-infections -High dose in renal failure —> seizure
Aminopenicillins: **Amoxicillin** **Ampicillin**		-Broad -**Not active against *pseudomonas aeruginosa***	**given with b- lactamase inhibitors:** 1-Amoxicillin + clavulanic acid 2-Ampicillin + sulbactam **Combo intended to:** prevent hydrolysis by the enzyme and extend spectrum	
Cephalosporin (3rd Gen) **Ceftriaxone** **Ceftazidime** **Cefotaxime**		-Highly effective against **Gm -ve bacilli** **-Ceftazidime—> against P. Aeruginosa** -Used for treatment of meningitis cause by pnemococci, meningococci, H. Influenzae - highly resistant to B-lactamase	-	
Carbapenems **Imipenem**		-wide spectrum -resistant to most B-lactamases	-inactivated by **dihydropeptidase** to a nephrotoxic metabolite, so given **combo** with **dihydropeptidase inhibitor(cilastatin)**	
Other inhibitor of cell wall synthesis				
Vancomycin	Cell wall inhibitor (bactericidal)	**- Narrow (+ve bacteria)** -used against (MRSA) -used in combo with 3rd gen cephalosporins for meningitis caused by penicillin resistant pneumococci	-poorly absorbed orally, only given orally to treat **GIT infections** cause by *clostridium difficile* **(pseudomembranous colitis)** - given IV for meningitis	-ototoxicity -nephrotoxicity -phlebitis at site of injections -**histamine** release leading to: 1-**red man** or **red neck syndrome** 2-**hypotension**
Aminoglycosides				
Gentamicin	-Inhibit protein synthesis (30 S subunit) -Bactericidal	Exclusive for aerobic Gram -ve bacteria	I.V	-Ototoxicity & Nephrotoxicity -Neuromuscular blockade

Lecture (13): Anxiety and Panics

Drug	M.O.A	Uses	ADRs	C.I
Benzodiazepines (FAST ONSET OF ACTION)				
Agonist				
Triazolam & Oxazepam *(short act)* **Lorazepam Alprazolam Temazepam Estazolam** *(Intermediate act)* **Diazepam Chlordiazepoxide Flurazepam** *(Long - IV only)*	binding to **BZ receptors** in the brain→ **enhance GABA** action on the brain → chloride channels opening → hyperpolarization →reduction of neural excitability. --- **Actions**: They have Anxiolytic action and CNS depressant action	**1- Anxiety disorders:** -severe anxiety -GAD -OCD -Panic attack w/ depression: **Alprazolam.** **2- Sleep disorders (Insomnia):** Triazolam, Lorazepam, Flurazepam. **3-Treatment of epilepsy:** Diazepam, Lorazepam **4- In anesthesia:** ●Pre-anesthetic medication (diazepam) ● Induction of anesthesia (Midazolam, IV) **5- Alcohol withdrawal syndrome:** (diazepam)	**-Tolerance & dependance.** **-withdrawal symptoms**:(rebound insomnia, anorexia, anxiety, agitation, tremors, convulsion). -**Respiratory & cardiovascular depression** *in large doses only (toxic effect)* -cognitive impairment **-motor ataxia** -anterograde amnesia -**Hangover**: (excess sedation,drowsiness, confusion)	-**pregnancy→ (Fetal depression).** -Breast feeding→ **(neonatal depression).** - Dose reduction is recommended **in Liver disease & old people**
Antagonist				
Flumazenil (IV)	Selective **benzodiazepine receptor antagonist**, bind competitively to GABA receptor replacing BDZ	Benzodiazepines overdose (**antidote**)	Can ***precipitate withdrawal symptoms*** in benzodiazepines addicts	
5HT-1A Agonist (DELAYED onset)				
Busprione (Orally)	Acts as a partial agonist at brain 5HTA1 receptors **pre-synapticaly inhibiting 5HT release.** **Actions: Anxiolytic only**	As **anxiolytic** in mild anxiety & **GAD**	-GIT upset, dizziness, drowsiness -**Not** effective in *severe* anxiety/panic disorders	-Pregnant women -breastfeeding -Old people (>65) ● Dose reduction in liver disease, elderly

Lecture (13): Anxiety and Panics

Drug	M.O.A	Uses	ADRs	C.I
Monoamine oxidase inhibitors (MAOIs)				
Phenelzine	blocking the action of MAO enzymes	**Reserved** for patients who have not responded / intolerant of other treatments.	-Dry mouth -constipation -diarrhea -restlessness -dizziness	Require dietary restriction of fermented foods that contain **tyramine** (**hypertensive crisis**)
selective serotonin reuptake inhibitors (SSRIs) (DELAYED onset)				
Fluoxetine (Orally)	Blocking uptake of 5-HT	**Considered** the **first line of treatment** for **most anxiety** disorders (panic clinical disorder, OCD, GAD, PTSD, phobia) because they have low risk of **dependency**	-Nausea, diarrhea -Sexual dysfunction -weight gain -Sleep disturbance or insomnia -Dry mouth -Seizures *Increase in anxiety symptoms, insomnia or headache in the first days of treatment may ↓ compliance	
Tricyclic Antidepressant (DELAYED onset)				
Doxepin Imipramine Desipramine	Reducing uptake of **5HT & NA.**	1.Used for **anxiety** esp: w/**depression**. 2. Panic attacks.	**-Atropine like actions** (dry mouth, blurred vision, tachycardia, urinary retention) **-α-blocking activity** (Postural hypotension). -Sexual Dysfunction	-Benign hypertrophic prostate. -Glaucoma. -seizures. -w/MAOI (mentioned in Antidepressant lecture)
Beta blockers				
Propranolol Atenolol	blocking **peripheral sympathetic** system →Reduce somatic symptoms of anxiety	performance or social anxiety.	-Decrease BP -Slow HR	**caution in** -asthma -cardiac failure -peripheral vascular disorders
Second generation (FAST ONSET BUT slower than BDZ)				
Pregabalin	Modulates calcium channels in CNS, **↓Ca++ influx** modulates release of NTs	- treatment & prevention of relapse of GAD **(1st line as SSRIS).** - Epilepsy & neuropathic pain.	-dizziness & somnolence -Withdrawal symptoms may occur but less severe than benzodiazepines.	-

Lecture (15): Headache & Migraine

Class	Drugs
Acute Attack (Rescue Therapy)	
Analgesic	1. **NSAIDs: buprofen**, **Naproxen:** for **mild to moderate** attack with **no** nausea & vomiting. 2. **Non-opioid** μ (mu) agonist: **tramadol** (it also inhibit 5-HT reuptake)
Antiemetics	**1. Dopamine Antagonists:** ★ **Domperidone**: Increases the Gastro-prokinetic →↑absorbtion of abortive therapy ● **Phenothiazines** (**Promethazine**): Has a **sedative** effect. **2. 5HT3 antagonists** ● **Ondanseteron , Granisetron:** For severe nausea and vomiting. **3. H1 antagonist** ● **Meclizine, diphenhydramine:** Has anti-histaminic+ sedative + Anti-cholinergic effects.

Drug	M.O.A	Uses	ADRs	C.I
Acute Attack (Abortive Therapy)				
Ergots				
Ergotamine tartarate rare clinical use due to severe adverse effects may worsen Nausea & vomiting **Dihydroergotamine (DHE)** preferred in clinical setting. **I.V, good with vomiting**	**-Non-Selective**, -Partial agonism at 5HT1 receptors (5HT1B\1D)→ ↓ release of vasodilating peptides ↓ excessive firing of nerve endings -Partial agonist α-adrenoceptors→ Vasoconstriction (peripherally, not desirable)	-only used to abort the attacks, **EXCEPT** DHE can be given for severe, recurrent attacks NOT responding to other drugs	-cold and numbness of limbs -Anginal pain (coronary spasm) - Arrhythmia -Prolong use : **-rebound headache** -paraesthesia	★ -Pregnancy -Peripheral and coronary vascular diseases -Hypertension -prophylaxis of migraine -Liver and kidney diseases -in concurrent use with **triptans**
Triptans				
Sumatriptan Subcutaneous → peaks after 2 **min** (**good with vomiting**) **Zolmitriptan** **Naratriptan**	**Selective** Agonism at 5-HT1: inhibit the release of vasoactive peptides, promote vasoconstriction, and block pain pathways in the brainstem **-No α1, α2, β –adrenergic, dopamine or muscarinic receptors.**	-frequent, moderate or infrequent but severe attacks **-cluster headache**	same as ergot but **better tolerated:** -Vasospasm -Ischemic heart -Angina -Arrhythmias **-Zolmitriptan:** Chest & neck tightness, Coronary vasospasm & Somnolence	-Cerebrovascular disorders -Peripheral vasospastic diseases -Renal or hepatic impairment - uncontrolled hypertension. -History of ischemia **-In concurrent use with ergots or MAOIs, lithium, SSRIs.**

Lecture (15): Headache & Migraine

Class	Drugs
Preventive Therapy	
Anti-epileptics	Block Na+ channel & augment GABA at GABA-A receptors e.g **Topiramate, Valproic**
Antidepressants	TCA; **amitriptyline** and **nortriptyline**
Antihypertensives	B-blockers; **propranolol (COMMONLY USED)**

migraines a day or less and need rapid relief:

Triptans are often a better choice

Pregnant woman

paracetamol or **intranasal**[1] **sumatriptan** and or **diphenhydramine**, **meclizine** are **safe**.

headache episodes lasting 2 or 3 days

DHE is often the optimal choice because it has longer **T1\2**

Menstrual migraine

Frovatriptan (very long t\12) twice per day beginning two days before the anticipated onset of menstrual migraine and continuing for six days.

★ For **extremely fast relief within 15 min** "emergency". **injectable Sumatriptan** is the **only choice**.

★ If expected **re-dosing is needed** & / or **recurrence of headache** →**Naratriptan**, **frovatriptan**, have slower onset, fewer side effects, and a lower recurrence rate.

Drug Interactions

Class\ Drug	Interactions
TCAs	• TCA are strongly bound to plasma protein→compete for **(Aspirin and Phenylbutazone)** plasma protein binding site • CYP-450 inducers **(Barbiturates)** • CYP-450 Inhibitors **(Oral contraceptives, Antipsychotics, and SSRIs)** ↑risk of toxicity • **Co administration w\ MAOI→ cause hypertensive crisis.**
MAOIs	• **Pethidine:** MAOIs interact with the **opioid receptor agonist (pethidine)** which may **cause severe hyperpyrexia, restlessness, coma, hypotension.** • **Levodopa: mania** and **hypertensive crisis**. • **Amphetamine and Ephedrine:** Indirectly acting **sympathomimetic** → accumulated monoamines→ **hypertensive crisis.** • **Co administration w\ TCAs→ cause hypertensive crisis.** • **Co administration w\ SSRI→Serotonin syndrome.** • **Cheese reaction "Tyramine" →hypertensive crisis.**
L-dopa	• Nonselective MAOIs • Pyridoxine
Benzodiazepines	• **CNS depressant=** e.g alcohol & antihistamine → increase their effect **(Additive effect)** • **CYT P450 inhibitors =**e.g. cimetidine & erythromycin, ↑t\12 of BDZ • **CYT P450 inducers=**e.g phenytoin & rifampicin, ↓t\12 of BDZ
Buspirone	• **CYT P450 3A4 inhibitors =** e.g. verapamil, diltiazem , ↑ buspirone level • **CYT P450 3A4 inducers=**e.g. Rifampin , ↓ buspirone level. • **MAOIs** (increase BP)
Ziprasidone	• **Shouldn't** be used **with** any drug that **prolongs QT interval** • Activity decreased by **carbamazepine (CYP3A4 inducer)** • Activity increased by **ketoconazole (CYP3A4 inhibitor)**
Alcohol	• **Acetaminophen** + alcohol = risk of **hepatotoxicity** • **NSAIDs** + alcohol = risk of **major GI bleed** or an **ulcer** • **Narcotic drugs (codeine and methadone)** + alcohol = risk of **respiratory and CNS depression**

THE END

CONGRATULATIONS !!!!
you have done so much for the pharmacology in this block
and we believe that your hard working will pay off.
Good luck and ACE THE EXAM FUTURE DOCTORS !

Some SAQ Qs

Q1: A patient came to the clinic with phobia and anxiety and depression.

What is the drug should be prescribed ?
Fluoxetine
What is the MOA?
Selective serotonin inhibitors : bind to SERT-> block 5HT transport -> increases 5HT in the synapse.
Mention 4 ADRS:
1- GIT symptoms : nausea , vomiting
2- sexual dysfunction : loss of libido , delayed ejaclation
3- changes in appetite
4- anxiety and tremors (if combined with other antidepressants)

Q2: A patient came to the clinic with phobia and anxiety and depression.(Refractory case)

What is the drug should be prescribed?
Moclobemide
What is the MOA?
Selective MAO-A inhibitor
Mentions 4 ADRS:
1- postural hypotension
2- sleep disturbances
3- Weight gain
4- Antimuscarinic effects

Q3: A patient came to the clinic with Bulimia nervosa or Depression.

What is the drug should be prescribed ?
Fluoxetine
What is the MOA?
Selective serotonin inhibitors : bind to SERT-> block 5HT transport -> increases 5HT in the synapse.
Mention 4 ADRS:
1- GIT symptoms : nausea , vomiting
2- sexual dysfunction : loss of libido , delayed ejaclation
3- changes in appetite
4- anxiety and tremors (if combined with other antidepressants)

Q4: A cancer patient with depression.

What can be prescribed for his depression?
Mirtazapine
What is the MOA?
a2 receptor agonist , blocks 5HT2A and 5HT3
Mention 2 side effects :
Sedation and weight gain

Q5: A patient with depression and wants to stop smoking?

What drug should be prescribed?
Bupropion
What is the MOA ?
Potency as NE and DA reuptake inhibitor
Mention advantages:
1-No sexual dysfunction
2- No weight gain
3- No orthostatic hypotension
ADRs:
seizures

Q6: A patient with cluster headaches or menstrual migraine

What drug should be prescribed ?
Sumatriptans - Frovatriptan
Mention the MOA:
Selective 5HT1 receptor agonists, inhibit the release of vasoactive peptides, promote vasoconstriction, block pain pathways in the brainstem
Mention 3 ADRs:
1- vasospasm
2- arrhythmia , angina, ischemic heart
3- mild pain and burning sensation at the site of injection
Mention 4 contraindications:
1- history of ischemia
2- cerebrovascular disorders
3- peripheral vascular diseases
4- uncontrolled hypertension

Q6: Patients with severe migraine not responding to other drugs .

What drug can be used?
Dihydroergotamine
Mention the MOA:
Non-selective partial 5HT1 receptor agonist, decrease release of vasodilating peptides
and excessive firing of nerve endings. And decrease vasodilation & stretching of the pain endings
Mention 4 ADRs:
1- GI upset
2- anginal pain due to coronary spasm
3- rebound headache on prolong use
4- paraesthesia
Mention 4 contra indication:
1- pregnancy
2- peripheral and coronary vascular diseases
3- hypertension
4- liver and kidney diseases

Q7: A patient with schizophrenia showing leukopenia.

What antipsychotic drugs was he using?
Clozapine
Mention the mechanism of action:
Blocking D4 and 5HT2 receptors
Mention other adrs :
1- seizures
2- myocarditis
3- excessive salivation during deep sleep