MED437
KING SAUD UNIVERSITY

Pharmacology
Team 437

Drugs of Neuropsychiatry Block

Drugs of Neuropsychiatry Block

Medication affecting the balance system

Drug	Key point	contraindication
Vestibular suppressants		
Anti-cholinergics (Hyoscine)	- Inhibit firing in vestibular nuclear neurons - Reduce the velocity of vestibular nystagmus. **Uses:** sedation - motion sickness. **ADRs:** Dry mouth. - Blurred vision. -sedation.	-
Benzodiazepines (Lorazepam, Clonzepam, Diazepam)	Enhance the effect of GABA receptors **Uses:** acute vertigo. (small dosage) **ADRs:** Dependence. - Impaired memory. Drowsiness	-
Betahistine	**MOA:** 1-**Weak** histamine H1 receptor **agonist**, 2- **potent** histamine H3 receptors **antagonist** → increase serotonin **Uses:** Meniere's disease **ADRs:** Headache -Nausea. -GIT upset	- Pheochromocytoma - Bronchial asthma. - History of peptic ulcer.
Anti-emetics		
Phenothiazines (Prochlorperazine)	**MOA**: - Blocks D2 receptors at CRTZ. Antipsychotic, some sedation & antiemetic. **Uses**: - one of the best antimetics in vertigo	
Anti-histamines (Dimenhydrinate)	- Block H1 receptors in CRTZ - sedative effects + weak anticholinergic effects -↓ Excitability in the labyrinth & blocking conduction in vestibular-cerebellar pathways **Uses: Vertigo** - **Motion sickness**. **ADRs:** - Dizziness - Anticholinergic side effects.	- Glaucoma - Prostatic enlargement
Dopamine antagonists (Metoclopramide, Domperidone)	**MOA**: - Block **D2 receptors in the CRTZ** of the medulla - Potent gastroprokinetic effect. **ADRs:** Restlessness or drowsiness - **Extrapyramidal manifestations** on prolonged use.	-

Drugs of Neuropsychiatry Block

Drug	Key point	contraindication
Prophylactic: K and Ca+2 channel blockers		
Cinnarizine	**-MOA**: selective ca channel blocker - Anti-histamine, Anti serotonin and Anti-dopamine, inhibits K+ currents. **- Promotes cerebral blood flow** **-Uses**:to **prevent** vertigo attacks **-ADRs:** Headache, muscle rigidity and tremor, Sweating, Drowsiness	- Parkinsonism - Car drivers
Drugs inducing vertigo		
vestibular toxins		
Diuretics (loop)	Altering fluid & electrolyte balance	-
Anticonvulsants Antidepressants Sedative hypnotics Alcohol, Cocaine	**Altering vestibular firiings (**neuronal depressant)	-
mixed ototoxins;Alter function and structure (affect balance and hearing)		
Aminoglycoside; 1-kanamycin 2-streptomycin	**Alter structure**	-
3-Gentamycin	Alter structure, induce apoptosis by **evoking free radicals > Mitochondrial pathway**	-
4-Neomycin	Alter structure, induce apoptosis by activating caspases > **death in receptor pathway**	-
Quinine, Chloroquine Quinidine, Nitrogen mustard Loop diuretics, NSAIDs, Tobacco	- **Alter function,**	-

Drugs of Neuropsychiatry Block

Drugs acting on the eye

Drug	Key point	contraindication
Cholinergic		
Agonist		
Direct: Carbachol, methacholine, pilocarpine, Ach	**Uses:** - Glaucoma (both types) - **Pilocarpine**: drug of choice in Open Glaucoma - Counteract action of mydriatics	-
Indirect: **1- Reversible :** Physostigmine, demecarium **2- Irreversible:** Echothiophate,Isoflurophate	**Uses:** - Glaucoma (both types) - Counteract action of mydriatics	
Antagonists		
Natural alkaloids: Atropine ,Scopolamine (hyoscine) **Synthetic atropine substitutes:** Homatropine, Cyclopentolate, Tropicamide	**Actions:** - Passive Mydriasis, Cycloplegia, sandy eye **Uses:** - Funduscopic examination - prevent adhesion in uveitis & iritis - Measurement of refractive error	- Glaucoma
Adrenergic		
Non-selective agonists		
Epinephrine, Dipivefrin	**Uses:** open angle glaucoma (eye drops) **M.O.A:** Mydriasis (without cycloplegia). **ADRs:** arrhythmia, elevated BP	Patients with narrow angles as they may precipitate closed angle glaucoma.
Selective α1 agonists		
Phenylephrine	**Action:** Active mydriasis (without cycloplegia) **Uses:** prevent adhesion in uveitis & iritis, Decongestant (minor allergic hyperemia) **ADRs:** increased BP	Patients with narrow angles as they may precipitate closed angle glaucoma.

Drugs of Neuropsychiatry Block

Drug	Key point	C.I
Selective α2 agonists		
Apraclonidine (eye drops)	**Uses:** - Open glaucoma - Prophylaxis against IOP Spiking after glaucoma laser procedures. **ADRs:** Bradycardia, hypotension.	-
β blockers		
Non-selective: timolol, carteolol **Selective β1:** Betaxolol	**Uses:** open angle glaucoma. **Advantages:** can be used in patients with hypertension & ischemic heart disease.	-
Carbonic anhydrase inhibitors		
Acetazolamide (oral)	**M.O.A:** ↓aqueous humor production. **Uses:** Open angle glaucoma	- Sulpha allergy - Pregnancy -Digitalis users.
Dorzolamide (topical)		
Prostaglandin analogues		
Latanoprost (preferred, less ADRs)	**M.O.A:** increase uveoscleral aqueous outflow **Uses:** open angle glaucoma, replaced beta blockers. **ADRs:** pigmentation of the iris	-
Travoprost		
Osmotic agents		
Mannitol (I.V)	- Rapidly lower IOP - **used only in acute situations to temporarily reduce high IOP**	Heart failure due to fluid overload
Glycerol (Orally)		-
Anti-inflammatory		
NSAID		
Flurbiprofen	**Uses:** pre-operatively to prevent miosis during cataract surgery.	-
Diclofenac	**Uses:** postoperatively inflammation	
Ketorolac	**Uses:** cystoid macular edema	

Drugs of Neuropsychiatry Block

Drug	Key point	C.I
Corticosteroid		
Topically: Prednisolone Dexamethasone Hydrocortisone	**Uses:** anterior uveitis, severe allergic conjunctivitis, scleritis, prevention and suppression of corneal graft rejection. **Ocular ADRS:** Glaucoma	-
Systemic: prednisolone cortisone	**Uses:** posterior uveitis, optic neuritis	-
Drugs causing corneal deposits		
Amiodaronen & chloroquine	- Causes optic neuropathy & Retinopathy - Pigmented deposits of the cornea	
Digitalis	Ocular disturbances & chromatopsia with overdose. (objects appear yellow).	
Phenothizines	Brown pigmentary deposits in the cornea, conjunctiva & eyelid	
Steroids	Cataract formation, elevated IOP & glaucoma.	
Ethambutol	Optic neuropathy characterized by gradual progressive vision loss.	
Sildenafil	Causes a bluish haze & causing light sensitivity.	
General Anesthetics		
Inhalation Anesthetics		
Methoxyflurane	-The most potent **ADRs:**,slow induction & recovery.	-
Halothane	**ADRs:** Sensitization of heart to catecholamines, **Hepatotoxicity , Malignant hyperthermia**	-
Enflurane	**ADRs**:Epilepsy-like seizure-abnormal EEG	-
Isoflurane	-less potent, rapid induction & recovery	-
Sevoflurane	**-Better smell, No airway irritation**	-

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General Anesthetics

Drug	Key point	contraindication
Inhalation Anesthetics		
Desflurane	**ADRs:Pungent odor ,Airway irritation**	-
nitrous oxide.	-The least potent anesthetic,rapid induction & recovery,Potent analgesic. **ADRs**:Diffusion hypoxia, Nausea and vomiting. **Inactivation of B 12 ⟶ megaloblastic anemia**, Abortion - Congenital anomalies	pregnancy (uterine relaxant).
Intravenous Anesthetics		
Ultrashort acting barbiturates : -Thiopental - Methohexital	**ADRs:** **-CVS collapse** and respiratory depression	-
Hypnotic (Non Barbiturate) : -Propofol	**use:** -Antiemetic action **ADRs:** CVS and respiratory depression, Excitation (involuntary movements)	CVS and respiratory depression
Benzodiazepines : -Midazolam -Diazepam -Lorazepam	Slow induction and recovery	
Etomidate	**ADRs:** Minimal CVS and respiratory depressant effects,Adrenal suppression.	-
Dissociative anesthesia: -Ketamine	**Use:** is the drug of choice in hypovolemic & shock patient. **ADRs**: (vivid dreams, hallucination)	-
Opiate drugs: -Fentanyl -Alfentanil -Sufentanil - Remifentanil	**- Potent analgesia.** **Use:-** Neuroleptanalgesia:used for diagnostic procedures (Fentanyl + Droperidol). -Neuroleptanesthesia (Fentanyl+Droperidol+ nitrous oxide). **ADRs**:bronchospasm ,(wooden rigidity). Respiratory depression	Head injuries. ,Pregnancy,bronchial asthma,Chronic obstructive lung

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Schizophrenia

Drug	Key point	contraindication
Typical		
Chlorpromazine	Antihistamine,Anticholinergic and Antiadrenergic effects **ADRs**: postural hypotension Failure of ejaculation,impotence, Atropine like actions, obstructive jaundice	
Thioridazine	**ADRs**: postural hypotension Failure of ejaculation, impotence Retinal deposits	
Haloperidol	**ADRs**: sedation drowsiness fatigue	
Atypical		
Clozapine	Anticholinergic effects **ADRs: Agranulocytosis - Seizures**	
Risperidone	**ADRs: postural hypotension** **QT prolongation** **sedation**	patients with long QT interval
Olanzapine	**ADRs: increase salivation,** weight gain	
cariprazine	**has higher affinity at D3 receptor.**	
Quetiapine	**ADRs**: **sluggishness,** weight gain	
Ziprasidone	**ADRs: Akathisia**, weight gain,prolong QT **increase mortality in elderly patients with dementia-related psychosis**	Drug interactions: should not be used with any drug that prolongs QT interval **-Activity decreased by carbamazepine(CYP4A4 inducer)** **-Activity increased by ketoconazole antifungal(CYP3A4 inhibitor)**

Drugs of Neuropsychiatry Block

Drugs used in Depression (Old)

Drug	Key point	contraindication
Tricyclics (TCAs) and Tetracyclics		
Imipramine, **Nortriptyline, Trimipramine**, Clomipramine, Protriptyline, Desipramine, **Amitriptyline** (and Tetracyclic drugs: Amoxapine, Maprotiline)	-block reuptake pumps for both 5HT (serotonin) and NE , So ↑ conc. of NE & serotonin. -Imipramine is used for treatment of nocturnal enuresis ADRs:-atropine-like action, Weight gain, sexual dysfunction	-manic-depressive illness
Monoamine Oxidase inhibitors		
Moclobemide(Selective Act on MAO-A) Phenelzine and Tranylcypromine (Non- selective mostly in labs not for patients,Irreversible)	-atypical depression where phobia and anxiety are prominent symptoms. -ADRs:Postural hypotension -Specific ADRs for (Phenelzine): Sexual dysfunction،Hepatotoxicity **-Moclobemide has No cheese reaction occurs with its use.**	**Drug interaction:** -when you use it with (Levodopa or Amphetamine or Ephedrine or TCAs) it will cause hypertensive crisis -MAOIs & SSRIs: Serotonin syndrome.

Drugs used in Depression (New)

NRIs		
Reboxetine	-**Block only NET** -Safe to combine with SSRIs	-
SSRI		
Fluoxetine, Fluvoxamin, Citalopram, Escitalopram, Sertraline, Paroxetine	-they do not cause 'cheese' reaction. USES: -premature ejaculation (5-HT2A) -bulimia or Anorexia nervosa (Fluoxetine) ADRs: Sexual dysfunction, delayed ejaculation,	-should not be used in combination with MAOIs because of the risk serotonin syndrome

Drugs of Neuropsychiatry Block

Drug	Key point	contraindication
NaSSA		
Mirtazapine	-α2 receptor antagonist = ↑NE ↑5HT, **Preferred in cancer patients**,reduces sexual dysfunction(Blocks 5HT2A) and anxiety(Blocks 5HT3)	-
SARI		
Trazodone, Nefazodone	-affect only serotonin -5HT2A antagonists = less sexual dysfunction	-
SNRIs		
Venlafaxine	- It is used primarily for the treatment of depression, generalized anxiety disorder, and social anxiety disorder in adults.	-
NDRI		
Bupropion	-No sexual dysfunction -No weight gain [No 5HT effect] USES: -smoking cessation -ADR: Seizures	-
Antiepileptic drugs		
Anti-Epileptic Drugs 1st Generation		
Phenytoin	**MOA**: -Blockade Na^+ & Ca^2**, i**nhibit the release of excitatory release GABA. -**USE**: partial and generalized tonic-clonic ,status epilepticus IV -**(ADRs):** Gum hyperplasia,Hirsutism,Acne ,megaloblastic anemia,osteomalacia.	-
Carbamazepine	.**MOA:**-Blockade of Na^+ & Ca^{2+} **,**Inhibit the release of excitatory transmitters**,**release GABA. **Use**: Drug of choice in partial seizures. -Other uses:Bipolar depression and Trigeminal neuralgia. -**ADRs:** Hyponatremia and water intoxication	absence seizures.

Drugs of Neuropsychiatry Block

Drug	Key point	C.I
Anti-Epileptic Drugs 1st Generation		
Sodium Valproate	**MOA**: -Blocks Na^+ channels **,** enhances GABA synthesis, reduces degradation & Blocks T-type Ca^{2+} channels. **Use**:Bipolar disorder ,mania Prophylaxis of migraine and Lennox-Gastaut syndrome. all typesof epilepsy -**(ADRs):** Thrombocytopenia ,Transient increase in liver enzymes & Hepatotoxicity and Teratogenicity.	aspirin or Coumadin
Ethosuximide	**MOA**-Selectively Inhibits T- type Ca2+ channels in thalamo-cortical neurons. **use**: in Absence seizures	-
Anti-Epileptic Drugs 2nd Generation NO EFFECT on MICROSOMAL ENZYME		
Topiramate	MOA: block Na channels , inhibitory effect of GABA -Food has no effect on absorption - Has no effect on microsomal enzyme. - **Usse**: alone for partial, generalized Tonic-Clonic, and absence seizures and Lennox-Gastaut syndrome. -**ADRs** Urolithiasis,weight loss	-
Lamotrigine	**MOA**: -Blockade of Na+ channels**.**Inhibits excitatory release. **-Use**: As add-on therapy or as monotherapy in partial seizures,generalized tonic-clonic seizure ,Lennox-Gastaut. **ADRs:** Skin rashes	-
Anti-Epileptic used in status epilepticus(I.V)		
Lorazepam **Diazepam** **Phenytoin** **FosPhenytoin** **Sodium Valproate** **phenobarbital**	**They all used in status epilepticus BUT Lorazepam Diazepam they are the drug of choice**	

Drugs of Neuropsychiatry Block

Drugs used in management of pain

Drug	Key point	contraindication
Natural		
Morphine	**P.D**. Respiratory depression Depression of cough reflexes Pin point pupil (miosis) →Diagnostic feature of opioid addiction. **Use:** Control pain (but not renal colics/biliary colics, acute pancreatitis), Acute pulmonary edema ,Myocardial ischemia ,Non painful conditions to relieve stress **ADRs:** C r I n c s, constipation itching , Constricted pupil, CVS: ↓ blood pressure, (↓ both diastolic and systolic)	-Head injury (↑ ICP) -With MAOIs -Bronchial asthma & impaired pulmonary function . -Elderly -Renal/Biliary colic & pancreatic pain. - infants, neonates or during childbirth
Opioid antagonists		
Naloxone	**Use:** Treatment and reverse of respiratory depression caused by opioid overdose. - To reverse the effect of analgesia on the respiration of the new born baby.	-
Naltrexone	Very similar to naloxone but with **longer duration** of action [t1⁄2=10h].	
Opioid agonists		
Tramadol	- Inhibits NE and 5HT reuptake **Use:** Mild to moderate acute and chronic visceral pain. - During labor it does not inhibit respiration **ADRs:** Less ADRs on respiratory and CVS, Seizures	Not use with epileptics
Codiene	- Less dependence than morphine **Uses:** Mild & moderate pain	

Drugs of Neuropsychiatry Block

Drug	Key point	contraindication
Opioid agonists		
Pethidine (mepridine)	- More effective k(kappa) agonist. - Has atropine-like action **Use:** Better preanaethetic medication. - in obstetric analgesia (no decrease in respiration) - Used in severe visceral pain; renal and biliary colics **ADRs**: Tremors, convulsions, hyperthermia, hypotension	-
Fentanyl	**Use**: Analgesic supplement during anesthesia - Induce and maintain anesthesia in poor-risk pts (stabilizing heart) - in combination with Droperidol as NEUROLEPTANALGESIA. - In cancer pain and severe postoperative pain **ADRs**: Respiratory depression (most serious)	-
Methadone	**Use:** to treat and control opioid withdrawal	-
Meningitis		
Penicillin (inhibit bacterial wall synthesis by inhibiting the peptidoglycan layer of bacterial cell wall " bactericidal")		
penicillin G	**Narrow spectrum** (gram +ve) , given **IV** **B-lactamase sensitive (penicillinase sensitive)** **ADRs**: Hypersensitivity,nephritis	Renal failure
Aminopenicillins ampicillin and amoxicillin	**Wide/extended spectrum** **given by** IV or IM **Amoxicillin** is better absorbed from the gut and not affected by food **inactivated by B-lactamase enzyme.** **combinated with B-lactamase inhibitors:** **Amoxicillin-clavulanic acid** **ampicillin--sulbactam** **ADRs:** same as penicillin G	

Drugs of Neuropsychiatry Block

Drug	Key point	contraindication
Cephalosporins (inhibit bacterial cell wall synthesis) " bactericidal"		
Ceftriaxone, Ceftazidime & Cefotaxime	Effective on gram -ve bacilli and anaerobic microbes. given **IV** **Highly Resistant to B-lactamases** **Ceftazidime** against **P. aeruginosa** treatment of bacterial meningitis caused by pneumococci, meningococci and H.influenzae **ADRs**: **Thrombophlebitis ,**Allergy, super infections	Renal failure
Carbapenems (Inhibits bacterial cell wall synthesis "bactericidal")		
Imipenem	**Wide spectrum** ,given **IV** Effective on pseudomonas aeruginosa. Resistant to most β lactamases. **combined with cilastatin** **ADRs:** seizure in high doses with renal failure , Patients allergic to **penicillins**	Renal failure
Aminoglycosides (Bactericidal Inhibit protein synthesis (30s subunit)		
Gentamicin	**given by IV** (Not absorbed orally) **ADRs:** **-Ototoxicity .** **-Nephrotoxicity.** **-Neuromuscular blockade (** high dose**)**	-Patient with **myasthenia gravis** -Combinated with muscle relaxant
Vancomycin(Inhibits bacterial cell wall synthesis "bactericidal")		
Vancomycin	**Narrow spectrum** on gram +ve **given by IV** (in meningitis) **given by Orally** (in GIT infection by C.difficile.) Used Against Methicillin resistant S.Aureus (MRSA). **ADRs:** Ototoxicity. , **Nephrotoxicity**. -**Histamine release (Red man syndrome) ,** Hypotension.	-

Drugs of Neuropsychiatry Block

Drugs used for Parkinsonism

Drug	Key point	contraindication
Drugs that increase dopaminergic activities (DA precursors)		
Levodopa (L-dopa)	- 1st line treatment. -Is converted into dopamine via **dopadecarboxylase** (DC) -L-dopa is usually **combined** with **carbidopa** or benserazide to (↓effective levodopa dose,Increase availability of L-dopa to CNS,↓ side effects of L-dopa) -Short duration of action lead to fluctuation of plasma concentration . -**ADRs:**Dyskinesia ,Anorexia,postural hypotension, Cardiac arrhythmias, Mydriasis.	Psychotic patient Glaucoma Patients with history of melanoma. With High proteins meals
Dopamine receptor agonists		
Ergot derivatives		
Bromocriptine	-**D2** agonist .Is given **orally** -Used for the treatment of : Parkinson's disease ,Hyperprolactinemia(galactorrhea),**Infertiliy in women.** -**ADRs:**similar to L-dopa (**Confusion**, **hallucinations**, **delusions**)	-**Psychosis** -Peripheral vascular disease. -Recent myocardial infarction.
Non ergot derivatives		
Pramipexole	-**D3** agonist . -Has the advantage of being free radicals scavenger -**ADRs:**similar to bromocriptine	similar to bromocriptine
COMT Inhibitors		
Entacapone	- Acts **peripherally** to inhibit COMT -**ADRs:**Orange discoloration of urine.	
	They Used as adjuvant to L-dopa + carbidopa to: - Decrease fluctuations - Improve response - Prolonged the ON-Time	
Tolcapone	- Acts **Peripheral** and **central** COMT inhibitor	

Drugs of Neuropsychiatry Block

Drug	Key point	contraindication
Monoamine oxidase-B (MAO-B) inhibitors		
Selegiline	**- It is a selective irreversible inhibitor of MAO-B.** **-**may have Neuroprotective effect (due to Antioxidant activity) -**later**-stage parkinsonism -**ADRs:**inhibit MAO-A ⟶ (hypertensive crises) ,insomnia	Should **NOT** be co-administered with: - Tricyclic . - SSRI -Food restriction "low tyramine diet" is required .
Anticholinergic Drugs		
Benztropine **Trihexyphenidyl**	-Central muscarinic antagonist. -Provide benefit in drug-induced parkinsonism (due to antipsychotics). -Improve tremor & rigidity. -Used during **early** stage -**ADRs:**Constipation,Cycloplegia, mydriasis, dry mouth, urinary retention	-Prostatic hypertrophy -Glaucoma -**Intestinal obstruction**
Amantadine		
Amantadine	**-** Antagonist at muscarinic receptors -↓ the reuptake of DA. -Useful in the **early** stages -**ADRs: Ankle edema, and livedo reticularis,**Restlessness and hallucinations , anticholinergic effects	
Drugs used in anxiety and panic disorders		
5HT1A agonists (5-hydroxytryptamine)		
Buspirone	M.O.A: partial agonist at brain 5HT1A receptors, Uses: generalized anxiety disorders Actions: only aniolytic , dosen't impaired memory, dosn't affect driving skills.	- Pregnant women or breast-feeding. - Old people (>65) - Dose reduction is recommended in liver disease.

Drugs of Neuropsychiatry Block

Drug	Key point	contraindication
Selective serotonin reuptake inhibitors (SSRIs)		
Fluoxetine	Acts by blocking uptake of 5-HT, Considered the first line of treatment for most anxiety disorders ADRs: Sexual dysfunction,weight Loss.	
Tricyclic Antidepressants		
Doxepin Imipramine Desipramine	MOA: reducing uptake of 5HT & NE. Uses: in anxiety especially associated with depression, Effective for panic attacks. ADRs: Atropine like actions, Sexual dysfunction, Weight gain.& α-blocking activity.	
Beta Blockers		
Propranolol (non-selective) atenolol	-MOA:blocking peripheral sympathetic system. -Decrease BP & slow heart rate. -Uses:in r social anxiety. - Are less effective for other forms of anxiety.	Should be used with caution in asthma, cardiac failure, peripheral vascular disorders.
Benzodiazepine antagonist		
Flumazenil	- -selective benzodiazepine receptor antagonist. - precipitate withdrawal symptoms in benzodiazepines -Used in benzodiazepine overdose .	-Pregnant women - Dose reduction in liver disease + old people
Benzodiazepines		
Short acting : triazolam , oxazepam . intermediate acting : lorazepam , alprazolam , temazepam , estazolam . Long acting : diazepam , chlordiazepoxide , flurazepam .	- actions :CNS depressants , Anxiolytic action , Sedation , Hypnotic action Skeletal muscle relaxing (diazepam) Anticonvulsant effect (clonazepam, diazepam, lorazepam). -Uses: Anxiety disorders , Sleep disorders , Epilepsy , Anesthesia , Alcohol withdrawal. -ADRs: cognitive and psychomotor,Ataxia, -Tolerance Anterograde amnesia,Sedation, drowsiness Psychological & physical dependence ,withdrawal symptoms: (Rebound insomnia, anorexia, anxiety, agitation, tremors & convulsion). -Respiratory & CVS depression in large doses only (toxic effects).	

Drugs of Neuropsychiatry Block

Alcohol and the brain

Asian populations (including Chinese, Japanese, Taiwanese, Korean) have genetic variation in aldehyde dehydrogenase and Can develop "Acute acetaldehyde toxicity"

In mild-moderate amounts	In severe amounts
CNS depression and CVS depression	Respiratory depression and CVS depression

- Oxidation of ethanol to acetaldehyde via alcohol dehydrogenase (major) or cyt-p450 (CYP2E1) (minor).
- Acute alcohol consumption inhibits CYP450 2E1
- Chronic alcohol consumption induces liver microsomal enzyme CYP450 2E1

Chronic actions of alcohol

Liver	hepatic cirrhosis & liver failure	**CNS**	cerebral atrophy, cerebellar degeneration, and peripheral neuropathy. Wernicke encephalopathy or Korsakoff psychosis* may occur.
GIT	irritation, inflammation, bleeding, nutritional deficiencies	**Hematology**	Hematological disorders & neoplasia.
CVS	Hypertension & myocardial infarction & damage blood vessels	**Endocrine**	gynecomastia & testicular atrophy Hematological disorders, neoplasia.

Chronic Alcoholism Associated Syndromes

Fetal Alcohol Syndrome (FAS): Irreversible	Wernicke-Korsakoff syndrome
	Treated by: Thiamine + dextrose-containing IV fluids

Alcoholism withdrawal symptoms:

Delirium,, tremors, anxiety, agitation, insomnia

Vomiting, thirst

Profuse sweating, severe tachycardia

Vasodilatation , fever

Drugs of Neuropsychiatry Block

To prevent alcohol relapse:

Disulfiram therapy: 250 mg daily, Inhibits hepatic aldehyde dehydrogenase,Disulfiram, induced symptoms render alcoholics afraid from drinking alcohol

Management of Alcoholism Withdrawal

- Benzodiazepines (chlordiazepoxide, diazepam)
- Fluoxetine Avoid excessive dose that causes respiratory depression & hypotension
- Clonidine Propranolol :Clonidine is a_2 agonist presynaptic inhibits the action of exaggerated sympathetic activity
- Acamprosate

Drugs Used in Headache and Migraine

Drug	Key point	contraindication
Abortive Therapy		
1- Ergots (only in SEVERE cases)		
Ergotamine tartarate	**P.K**: worsen the nausea and vomiting associated with migraine. **Use**: to abort the attacks. **ADRs**: Anginal pain, cold and numbness of limbs, Prolong use → rebound headache.	-Pregnancy -Peripheral and coronary vascular diseases. -Hypertension -prophylaxis of migraine -Liver and kidney diseases
Dihydroergotamine (DHE)	**Use**: can be given for severe, recurrent attacks not responding to other drugs) **ADRs:** Same as previous	
2- Triptanes		
Sumatriptan (good for patient with vomiting + safe with Pregnancy)	**Use**: frequent, moderate or infrequent but severe attacks. -In cluster headache (Menstraul migraine: Frovatriptan) **ADRs**:Vasospasm, Ischemic heart; Angina and Arrhythmias (**Zolmitriptan**: Chest & neck tightness, Coronary vasospasm & Somnolence)	-Uncontrolled hypertension -Coronary artery disease -History of ischemia -**In concurrent use with ergots or others inducing vasospasm** -In concurrent use with MAOIs, lithium, SSRIs, → (5HT increased to toxic level) -Renal or hepatic impairment.
Zolmitriptan		
Naratriptan		

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Drug	Key point	contraindication
Frovatriptan	**-Uses:** *If expected re-dosing is needed or recurrence of headache Naratriptan , Frovatriptan should be used . ***In menstrual migraine**	-
Rescue therapy		
Analgesics		
NSAIDs: Aspirin - Acetaminophen ibuprofen, naproxen	-ibuprofen, naproxen Drugs of choice for **mild to moderate attack with no nausea & vomiting.** -Acetaminophen (Paracetamol) safe with Pregnancy.	-
Opioid: tramadol	-Inhibit serotonin reuptake	-
Antiemetics		
Dopamine Antagonists: Domperidone	-Gastro-prokinetic (↑ Absorption, bioavailability of abortive therapy)	-
Phenothiazines: Promethazine	-Dopamine antagonists -Sedation	-
5HT3 antagonists: -Ondanseteron -Granisetron	-for severe nausea &vomiting	-
H1 antagonist: Meclizine diphenhydramine	-Antihistamine, sedation, Anticholinergic -can be used with Pregnant	-
Prevent Recurrence		
Anti-epileptics : topiramate, Valproic	Block Na+ channel & augment GABA at GABA-A receptors	-
Antidepressants	-TCA; amitryptylin and nortryptyline	
Antihypertensives: propranolol	-Ca2+ Channel Blockers Propranolol is commonly used in prophylaxis of migraine attack.	

Repeated drugs

(mentioned in more than one lecture !)

1- Benzodiazepines

Uses:

1- As vestibular suppressants in small dosages for management of acute vertigo (Lorazepam,
Clonzepam, Diazepam)
2- I.V In induction of general anesthesia (Midazolam, Diazepam , Lorazepam)
3- In balanced anesthesia (Midazolam)
4- Alone in minor procedure
5- Pre-anesthetic medication (Diazepam)
6- Anxiety disorders (sever anxiety, GAD, OCD)
7- Panic disorder with depression (Alprazolam)
8- Insomnia (Triazolam, Lorazepam, Flurazepam)
9- Treatment of epilepsy (Diazepam, Lorazepam)
10- Alcohol withdrawal syndrome (Diazepam, Lorazepam, Chlordiazepoxide)
11- As antipsychotic drug (Clozapine)

2- Phenothiazines

Uses:

1- Antiemetics in vertigo
2- Vestibular suppressant action.
3- Schizophrenia

3- Domperidone:

Uses:

1- Anti-emetic
2- Rescue therapy in acute attack of headache

4- Gentamicin

Uses:

1- Meningitis
2- Ototoxic alter the structure (not a use actually:))

5- Chloroquine

1- Ototoxic Altering Function
2- Causes optic neuropathy

Repeated drugs
(mentioned in more than one lecture !)

6- Fentanyl
Uses:
1- Neuroleptanalgesia (Fentanyl+Droperidol)
2- Neuroleptanesthesia (Fentanyl+Droperidol+ nitrous oxide)
3- In cancer pain and severe postoperative pain

7- Imipramine
Uses:
1- Treatment of nocturnal enuresis
2- Used for anxiety especially associated with depression.

8- Fluoxetine
Uses:
1- Antidepressants SSRI
2- First line of treatment for most anxiety disorders

9- Topiramate
Uses:
1- Can be used alone for partial, generalized tonic-clonic, and absence seizures.
2- Lennox- Gastaut syndrome
3- Prevent recurrence of headache

10- Tramadol
Uses:
1- Mild to moderate acute and chronic visceral pain.
2- During labor
3- Rescue therapy in acute attack of headache

11- Propranolol
Uses:
1- Used in performance or social anxiety.
2- Prevent recurrence of headache
3- Inhibits the action of exaggerated sympathetic activity in Management of alcoholism withdrawal

12- NSAIDs
1- Ototoxic Altering Function
2- For mild to moderate attack with no nausea & vomiting. (Ibuprofen, Naproxen)

Alcohol and the brain

- small lipophilic molecule, large Volume of distribution (distributed to all body tissues) & wide absorption level result in a lot of toxic effects.
- In pharmacokinetics the most important are drug-drug interaction in acute & chronic.
- Drug-drug interaction:

  Acetaminophen + alcohol (chronic use): risk of hepatotoxicity ,and also, there is hepatotoxicity due to accumulation of acetaldehyde (more toxic than alcohol).
- Metabolism of:

  -Acute alcohol: inhibit liver microsomal enzymes (CYP450 2E1) à increase concentration of drug in plasma (blood).

  - Chronic alcohol: induces liver microsomal enzymes (CYP450 2E1)--> drug will metabolize very fast Tolerance(due to increase of drug metabolization).
- Genetic variation not that important.
- Mechanism of action (important):

  -Acute alcohol: enhancement the effect of GABA & Inhibition of glutamate receptor (NMDA) action.

  - Chronic alcohol: down- regulation of GABA & up-regulation of NMDA receptors.

  NMDA receptors are responsible for withdrawal symptoms, why? Due to super-sensitivity of glutamate receptors (NMDA) mainly & inhibition of GABA receptors.
- You don't have to know all of pharmacological action like (vasodilation, hypotension & renal function)

  يعني ركزوا من ناحية الفارما واتركوا المعلومات اللوجاك
- Fetal Alcohol Syndrome(irreversible) + Wernicke-Korsakoff syndrome (important)
- Dopamine is neurotransmitter of happiness and alertness, alcohol will increase dopamine and it's one of the reasons of why people will be addicts to alcohol, if there is no enough dopamine in their brain, the addict will be craving for alcohol
- Certain drug used in nicotine craving and in withdrawal symptoms which is Bupropion (new antidepressant it will increase the dopamine)

Alcohol and the brain

- **Alcohol tolerance:**

  -Metabolic tolerance → affect liver microsomal enzymes.

  -Functional tolerance → due to change in neurotransmitters.

- **Management of alcoholism withdrawal (important):**

  -what kind of drugs will be more effective for management of withdrawal symptoms?

  Benzodiazepines as (chlordiazepoxide, diazepam & lorazepam) are preferable drugs.

  - Benzodiazepines used I.V or oral depending on management plan.

  - Benzodiazepines are most important one for management of withdrawal symptoms but also you should memories other drugs such as:

  A) Clonidine: it's alpha 2 adrenergic agonist which will inhibit the release of norepinephrine.

  B) propranolol: used in anxiety (prophylactic).

  C) Disulfiramà induce discomfort symptoms e.g.: vomiting & flushing.

Headache and migraine

- Migraine Causal Theories
- Don't go for details (phases, symptoms & triggers).
- Rescue therapy:

  A) Analgesics.

  B) Antiemetics:

-Dopamine Antagonists (Domperidone) à Gastro-prokinetic → ↑ Absorption & bioavailability of abortive therapy. How it will help in migraine? In migraine there will be decrease in gastric motility and Domperidone will accelerate gastric emptying.

- Meclizine, Domperidone & Ondansetron → we can combine them together to control nausea and vomiting.

- Abortive therapy:

  A) ERGOTS: not safe for patient who have C.V diseases and pregnancy

- MOA:

- Partial agonist 5HT1a receptor → At blood vessels → ↓vasodilation & stretching.

-Partial agonist effect on α-adrenoceptors→ vasoconstriction.

-DHE → used in sever attack that not controlled of other drugs

-Contraindications: Pregnancy, prophylaxis of migraine & cardiovascular diseases.

A) TRIPTANS: selective, safer cause they don't interact with other receptors unlike ergot.

- No α1, α2, β–adrenergic, dopamine or muscarinic receptors

-could be used as rescue therapy with another drug.

- zolmitriptan & naratriptan à nasal spray 2h

- Zolmitriptan ADRs: Chest & neck tightness Coronary vasospasm Somnolence.

- If a patient have given triptans and he still have nausea and vomiting, we should give him domperidone.
- For prevent recurrence: amitriptylin , propranololà best to use

General anesthetics

- Induction, recovery and blood gas
- If we need smooth induction of anesthesia what will we use? We will use Pre - anaesthetic medication such as benzodiazepines & opiates.
- Mechanism of action: all of them are GABA enhancers.
- Inhalation anesthetics:

- Halothane: ADRs→ Hepatotoxicity, Cardiac arrhythmias (heart tachycardia), Sensitizes heart to action of catecholamines → arrhythmias.
- Nitrous oxide:

1- Rapid induction & Recovery due to low solubility.

2- No muscle relaxation, No hepatotoxicity & Weak anesthetic.

3- ADRs: Inactivation of B 12 → megaloblastic anemia.

Halothane	Nitrous oxide
-Slowest in induction & recovery - less MAC & more potent	-Fastest in induction & recovery because it's gas, more soluble and won't increase partial blood pressure - more MAC & less potent

-Enflurane: Epilepsy-like seizure- abnormal EEG, Contraindication patients with seizure disorders.

- Methoxyflurane: it's not used anymore due to it's ADRs.

- Potency: means low cons. of drug to induce analgesia.
- Intravenous anesthetics: الدكتور ركز اكثر على الانهيلايشن

- thiopental (sulfa group): rapid acting, Metabolize slowly → slow recovery , CVS collapse.
- Diazepam & Lorazepam: used for withdrawal symptoms of alcohol.
- Midazolam: Pre - anaesthetic medication.
-Etomidate: Minimal CVS & Adrenal suppression.
- ketamine:

1- - Increases plasma catecholamine levels, - ICP

2- Used in (hypovolemic, shock) patients.

Potent bronchodilator (asthmatics).

- Opiate drugs: Neuroleptanalgesia & Neuroleptanesthesia aren't coming in exam

Depression

Old:

- **MAOIs: Moclobemide is the best because there is no cheese reaction.**
- **TCAs:**

Imipramine:

- Used for treatment of nocturnal enuresis in children.
- ADRs: Anticholinergic, Antihistamine & Anti-adrenergic(alph)--> Postural Hypotension.

- **Common ADRs for all Old antidepressant:**
  sexual dysfunction, nausea, vomiting & Drug-drug interaction.
- **Some TCAs drugs such as: Amitriptyline, Imipramine, Desipramine & Nortriptyline.**
  (الدكتور يقول هذي بعض الادوية من TCAs اعرفوها)

New:

- **SSRIs:**

- MOA→ Selective Serotonin Reuptake Inhibitors.

-Uses: Treatment of premature ejaculation

-ADRs: Sexual dysfunction, nausea, vomiting & serotonin syndrome.

- serotonin syndrome will appear when there is interaction between 2 classes of drugs such as:

- SSRIs + MAOIs

- SSRIs + TCAs

-SSRIs + SARI (Trazodone, Nefazodone)

-SSRIs + SNRIs (Venlafaxine)

- Bupropion & Reboxetine : serotonin syndrome ما يسببون
- Bupropion Can be used for smoking cessation & alcohol addiction.
-Bupropion doesn't cause Sexual dysfunction + no weight loss.
- Reboxetine will block NET, also it's contraindicated in epilepsy.
- Fluoxetine has long action because it's going to be converted to other form.
- NassA:
Mirtazapine→ Preferred in cancer patients because:Less sexual dysfunction (5-HT2 blocking)

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References:

- Doctors' slides and notes.

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