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Pharmacology for National Board Examination

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PHARMACOLOGY

**FOR NATIONAL BOARD
EXAMINATION**

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INTERNATIONAL DENTAL STUDIES

UNIVERSITY OF THE
PACIFIC

Arthur A. Dugoni
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ANS

Cholinergic

Cholinergic Agonist

- Choline Esters**
 - Aceylcholine
 - Methacholine
 - Carbacol
 - Bethanechol
- Alkaloids**
 - Pilocarpine
 - Arecoline
 - Muscarine
 - Cevimeline

Anticholinesterase

- Reversible**
 - Physostigmine (acts centrally & Peripherally)
 - Neostigmine (direct Ach activity at NMJ)
 - Neostigmine
 - Pyridostigmine
 - Edrophonium
- Irreversible**
 - Malathion
 - Isoflurophate
 - Sarin
- Donezepil (Cholinesterase inhibitor)**
 - Treatment of Alzheimer's disease

Anti - Cholinergic

Muscarine Receptor Antagonist

- Natural**
 - Atropine (Tertiary amine) - Mydriatic
 - Can enter brain
 - Hyoscine (scopolamine) - CNS Depressant
 - Motion Sickness
 - Pre-Anesthetic
- Semi Synthetic**
 - Lpratropium
 - Tiotropium
- Synthetic**
 - Mydriatic - Cyclopentolate
 - Tropicamide
 - Anti Secretory.- Propantheline - for diarrhea
 - Glycopyrolate - ↓Saliva
 - Vesico Selective - Oxybutynine
 - Antiparkinson - Trihexyphenidyl
 - Benzotropine Mesylate
- Others**
 - Amityrptiline
 - Pralidoxime (Cholinesterase reactivator)

Nictonic Receptor Antagonist

- Neuro Muscular Blocker**
 - (NMJ Skeletal Muscle)
 - Depolarising - Succinylch. (Non Competitive)
 - Non Depolarising - Tubocurare (Competitive)
- Ganglionic Blockers**
 - Mecamylamine
 - Hexamethonium

Adrenergic

Direct (Interacts with Receptors)

1. Adr. $\alpha 1, \beta 1, \beta 2$
2. NA - $\alpha 1, \alpha 2, \beta 1$
3. Phenyl ephrine - $\alpha 1, \alpha 2$
4. Methoxamine, Isoprenaline - $\beta 1, \beta 2$
5. Clonidine, Methyl dopa - $\alpha 2$
6. Albuterol (Salbutamol)
 - Terbutaline
 - Salmeterol (Long Acting)
 - Aminophylline

Mixed

- Dobutamine - $\alpha 1, \beta 1$
- Dopamine - $d1 = d2 > \alpha 1, \alpha 2, \beta 1, \beta 2$
- (Delta Mechanism)

Indirect

- Amphetamine
- Ephedrine
- TCAS
- Cocaine
- MAOIS
- Tyramine

Anti-Adrenergic

α Blocker

- Non equilibrium**
 - Phenoxybenzamine (Non Selective)
- Equilibrium (Competitive)**
 - Non Selective - Phentolamine
 - $\alpha 1$ Selective - prazosin, doxazosin (Cardio-Selective)
 - $\alpha 2$ selective - Yohimbine, Mirtazapine

β Blockers

- Non Selective**
 - Betaxolol- to treat glaucoma
 - Propranolol
 - Pindolol (Intrinsic Sympathomimetic Activity)
- Cardio-Selective ($\beta 1$)**
 - Atenolol
 - Metoprolol
 - Acetabutolol (Intrinsic Sympathomimetic Activity)
 - Esmolol

$\alpha 1, \beta 2, \beta 2$ blockers

- To Treat heart failure
- Carvedilol
- Labetalol

Neuronal Depleting Agents

- Reserpine
- Guanethidine
- Metyrosine

Important Points:

- * **Methyl dopa** - False Neurotransmitter → taken up by storage vesicle → released with NE → ↓Sympathetic activity
- * **Clonidine** - ↓sympathetic activity
- * **Pressor action of Nor Epinephrine** - Activation of baroreceptors → Stimulates Vagal reflex → ↓Heart rate
- * **Orthostatic Hypotension** - Most likely cause of transient unconsciousness in dental office.
 - Anti hypertensive (Alpha1 blockers)
 - Anti-parkinson drugs
 - Centrally acting (clonidine, Methyl dopa)
 - Direct vasodilators
 - Narcotics
 - Phenothiazines
 - TCAS

Small, Non - Myeli. (pain and Temp.) affected first followed by touch, pressure, skeletal muscle tone (motor)

ANESTHETIC

Barbiturate - No analgesic effect
- Small Therapeutic window

Local Anesthesia

General Anesthesia

Amides (CONHCH₂)

- i+caine**
- Metabolism in Liver**
 - Except Articaine
 - which is metabolized by serum esterases.
- Lidocaine**
 - Dealkylation - Amino Terminus
 - Hydrolysis - Amide Bond
 - Hydroxylation- Aromatic Ring
 - Metabolite: 4 Hydroxylidine
 - Infill - 60 min duration of action
 - Inferior Alv. Block - 90 Min. duration of action
 - 64.3 % Protein Bound
- Mepivacaine (3% - Carbocaine)**
 - Less vasodilator effect.
- Bupivacaine longest duration of action** (95.6 % protein bound)
- Prilocaine 4% less Vasodilation**
 - Metabolised to Orthotoluidine
 - Causing Methemoglobinemia (Decrease O₂ carrying capacity)
 - Half toxic then Lido but methmo. so not used in pt. with Hypoxia
 - EMLA eutectic mixture - cream Inc. absorption (Lydo 2.5% + Prylo 2.5%)
- ADR**
 - Opioids - Inc. toxicity of LA
 - Allergy - Methylparaben (preservative)
 - N Metabisulphate

which is preservative for Vaso constructor.
↓
Common in patient with history of asthma
↓
(Airways Hyper active due to sulphites)

Others

- Diphenhydramine**
 - Given when allergic to both amides and esters
 - Tetrodotoxin (from blowfish)**
 - Saxitoxin (From algae)**
 - Dyclonine Hydrochloride (ketone linkage, topical)**
 - Quinoline - Centburicidine**
 - short acting - procaine**
 - Intermediate - Lidoca. (B)
 - mepiva.
 - priloc. (B)
 - Long - Bupiva.
 - Ethido. (b)
 - Tetra.
- * B - Safer in pregnancy

Esters (COOCH₂)

- Metabolism - Plasma (Pseudo cholinesterase)
- Not used in dentistry due to inc. incidents of allergy
- Procaine** metabolised to PABA (Allergic compound)
 - Dec. effectiveness of sulphonamides
- Benzocaine** - no amino terminus
 - does not become charged
 - Dec. water solubility
 - used tropically
- Cocaine - naturally occurring Vasoconstrictor**
 - Blocks dopamine in brain
 - inhibits - uptake of catecholamines
- Piperocaine**
 - Though i+caine, it is an Ester type of LA (Exceptional)

Intravenous agents

- Barbiturates (for Induction)**
 - No Analgesic effect
 - Small therapeutic window
 - Ultra short acting - thiopental (Pentothal)
 - (Most lipid soluble, - Methohexital (Brevital)
 - Rapidly reads brain and redistribute in tissues)
- BZD - Diazepam (Valium)**
 - Midazolam (versed)
 - Lorazepam (Ativam)
- Neuroleptanalgesic + Anesthesia** (Droperidol + fentanyl) + N₂O₂
- Others**
 - Propofol (Hypnotic, Veso dilator)
 - Ketamine - Dissociative Anesth.
 - Blocks NMDA (Glutamate) receptors
 - Give Diazepam along with it to prevent Hallucination
 - Etomidate

Nitrous Oxide - CNS depressant
(combined gases - 3-5 lit/per min.
30 to 50 % usually used)

- No less than 30% O₂,
- 100% O₂ given at the end of the procedure to prevent diffusion Hypoxia.
- Rapid onset = 5 Min., Rapid recovery = 5 min.
- Blood gas solubility coefficient = 0.47
- main effect - relaxation, sedation
- First symptom of onset - tingling of hands
- Stored at pressure - 750 psi
 - Steel (blue) cylinders - N₂O₂
 - Green tanks - O₂
- ADR**
 - Nausea (Most Common)
 - Abortions, contraindicated in 1st trimester of pregnancy
 - Interfere with Methionine synthase, dec. Vita. B12
 - Diffuse in air containing cavities
 - Bone marrow depression

Important Points:

- Non ionized, free base (lipophilic) penetrates tissue membranes
 - ↓ PKa → ↑ Ph → more free base
 - Physiologic Ph - 7.4 5 - 20 % LA is free based form. (It is enough to cause anesthesia)
 - Inflammation → ↓ Ph → LA not effective
 - PKa = Ph → ionized form/proton attached / H+Atom = Non ionized form
- * 1 ML 2% LA with 1:1, 00, 000 epinephrine contains 20 ML lidocaine and 0.01 mg epinephrine
Maximum dose lidocaine with epinephrine - 300 mg
- 7 mg / Kg - Adult (without epinephrine = 4mg / Kg)
- 4.4 Mg / Kg - child
- 1 ML 4% LA (articaine) with 1:1, 00, 000 epinephrine contains 40mg articaine and 0.01 mg epinephrine
Maximum dose Articaine - 7mg/ Kg in both adult and child

- ↑ LA in body
 - Cemitidine (Inhibits liver microsomal enzymes)
 - (Dec. LA clearance by - Opioids
 - 30% or More) - β blockers (↓ Cardiac Output - therefore ↓ Liver blood flow)
 - ↓ LA in body (Hepatic drug metabolising drug inducers) - Phenobarbital
(↑ LA clearance) - Phenytoin
- *Pentolamine Mesylate (Oraverse) - α₁, adrenergic receptor blocker
- Vaso dilation
- 50% ↓ Time for sensation to be restored
- 1/2, cartridge (0.2 mg) oraverse subcutaneous given if 1/2 cartridge anesthetic was administered

DRUGS ACTING ON CNS

Anti - Anxiety

I. Benzodiazepines

- Potentiates action of GABA
- Induces sleep
- Amnesia- Skeletal muscle relaxation

* Classification:

1. GABA - BZ - Zolpidem
(Omega-1 Subunit, Anti-insomnia, short half life, no addiction)
- Eszopiclone
- Zaleplon
2. Hypnotics
(to over come insomnia)
- Flurazepam
- Triazolam
- Temazepam
3. Pre - op. sedation - Midazolam (Versed)
4. Tranquilizer - Diazepam (Minor),
- Chlordiazepoxide
Calming effect - Alprazolam
- Lorazepam

* Duration of action

- Mida (shortest)
- Triazo, Alpra (Intermediate)
- Lora (Least lipid solu),
Diaz. (Longest)

} α - hydroxylation
i.e. Rapid metabolism

* ADR / Contra Indication

1. Never be taken with alcohol
2. Active metabolites
3. Anti-Fungal Inhibits CYP3A4 responsible for metabolism of Triazolam.
4. Diazepam
- contraindicated in acute narrow angle glaucoma
- Anti-cholinergic,
- Thrombophlebitis (Propylene glycol in IV mixtures)
- High lipid solubility therefore enters brain

* BZD antagonist is Flumazenil

II. Buspirone

5HT_{1a} serotonin receptor agonist partially
- it has only anti-anxiety action

III. Barbiturates-Sedative- Hypnotic, to treat insomnia

- i. Short acting - Secobarbital, Pentobarbital
- ii. Intermediate acting- Amobarbital, Butobarbital (Day time sedation, Suppress REM)

IV. Agents used in pediatric dental patients

- i. Chloral hydrate (pro drug)
- Active metabolite - Trichloroethanol
- Sedative + Hypnotic (most commonly used)
- 500 mg/ 5 ml solution,
- Dose 50 mg / kg (maximum - 1g)
- Contraindication: Displace warfarin from its protein binding sites
- ii. Meperidine (Narcotic)
- iii. Hydroxyzine (Primarily antihistaminic)
- iv. BZD - Midazolam, Diazepam

Anti Depressant

1. Tricyclic Anti- Depressant

- Inhibit neuronal reuptake of NA and serotonin in brain.
- To treat unipolar disorder (depression)

- i) Amitriptyline
 - ii) Doxepin
 - iii) Imipramine
- * ADR - Amitri. - Anticholin.
- Orthostatic Hypotension

2. Selective Serotonin reuptake Inhibitors (SSRIS)

- i). Fluoxetine (Prozac)
- Longest half life
- it is second generation anti-depressant
- ii). Citalopram - to treat generalized anxiety / panic attacks.
- iii). Sertraline

3. To treat bipolar disorder

(Manic depressive syndrome)

- i. Lithium salt
- Dec. degradation of Inositol tryprophate which is 2nd messenger within CNS
- ii. Carbamazepine - blocks NA + channels
- iii. Valproic acid - blocks NA +, CA²⁺ channels
- iv. Neuroleptic / - Phenothiazine
Anti psychotic / - Chlorpromazine
Major Tranquilizer - Haloperidol

4. MAO inhibitors (3rd line agents)

Contraindicated with Epinephrine, indirect acting sympathomimetic, meperidin

ADR: Hypotensive crises

V. Serotonin and NA reuptake inhibitors

- Desipramine

* ADR - Anticholinergic effect

VI. Miscellaneous

1. Mirtazepine - Alpha₂ - NA antagonist.
 2. Bupropion - NA /Dopamine reuptake inhibitor
 3. Trazodone - Serotonin reuptake inhibitor
 4. St Johns Wort (herbal) - Dec. Serotonin reuptake
- * ADR:
Induce Cyt. P450 therefore rapid metabolism of
- Cyclosporin,
- Indinavir,
- Midazolam,
- Nifedipine.

Anti psychotic/major tranquilizer

1. 1st generation / Typical

(Treat positive, but not negative symptom)
Antagonist of D₂ receptor

- i. Phenothiazines - Chlorpromazine
- ii. Butyrophenones - Haloperidol (potent dopamine antagonist)
- iii. Thioxanthenes.

*ADR - Extra pyramidal syndrome (Parkinson like movements, muscles spasm of orofacial region)
- Tardative Dyskinesia (uncontrollable movements)
- Anticholinergic effects.

2. 2nd generation

Treat both positive and negative symptoms
- Antagonist of D₁, D₂, D₄, D₅, 5H₂ (major action) receptor

- i. Clozapine } Prolactin sparing
- ii. Arpiprazole }
- iii. Risperidone }

* Ari: Dopamine system stabilizer
- D₂ + 5HT_{2A} antagonist
Cloza - specific for limbic receptor, not for striated muscle receptor
i.e. Dec. EPS & TD

* ADR:

- INC QT Interval,
- Convulsion,
- Arrhythmia,
- Orthostatic hypotension

Generalized Seizures

- Petit mal (absence)
- Myoclonic
- Atonic
- Tonic- clonic (Grand mal)

H1 receptor - Allergic reaction
H2 receptor - Gastric acid secretion

Anti Epileptic

1. Barbiturates

- Long acting
- Phenobarbital
- Mephobarbital
- Primidone (Bind to GABA Cl transmission threshold for electric stimulation of motor cortex, does not abolish abnormal discharge)

Primi -metabolized to Phenobarbital and Phenylethylmalonamide which are anticonvulsants)

- * Contraindication -
- Intermittent porphyria
- Hydantoins
- Phenytoin - to treat tonic clonic (INC. refractory period)

Blocks NA + Channels)

ADR: Gingival hyperplasia

3. GABA Analogs

- Valproic Acid
- Gabapentin
- Lamotrigine
- Topiramate

4. Succinimides - to treat Petit mal seizures

- Ethosuccimide

5. BDZ

- Diazepam to treat status epilepticus
- Clonazepam (Bzd Inc. No. of CL- Channels)

6. Miscellaneous

- Carbamazepine
- Prophylaxis for partial seizures (Involves 1 part of brain) to treat tonic clonic and trigeminal neuralgia.

Angina - Pain due to occlusion of coronary arteries

Heparin binds with antithrombin III at Xa and then at IIa (Thrombin) factor sites

Coronary Artery disease narrowing of blood vessels

CARDIOVASCULAR SYSTEM DRUGS

Anti-Anginal

1. Dilate coronary blood vessel

i. Nitro Glycerin - dilate coro. artery
Dilates mostly veins

ADR - orthostatic hypotension

Headache

(most effective for acute episodes)

1st drug of choice

ii. Amyl Nitrite

- inhalation only

acts in 10 seconds

acts only for 3 to 5 minutes

- oxidizes - Hb to met-Hb which

binds cyanide keeping it in peri.

circulation and prevent access

to tissues.

*ADR - fainting

- pounding headache

- abused

iii. Calcium channel blockers

(Coro. and peri. vasodilator)

- Nifedipine

- Verapamil

- Diltiazem

*ADR - Gingival hyperplasia

iv. Non-Nitrate vasodilator

- Dipyridamole

2. Dec. cardiac rate and force

i. B-blockers - Propranolol

To Treat Congestive Heart Failure

i. Digitalis - Digoxin

(Bradycardia, +ve inotropic effect

by inhibition of

NA +-K+-ATPase enzyme

↓
Inc ca ion influx)

*ADR:

i) Digoxin + B blocker - heart block

ii) Inc. digoxin toxicity - Clarith.,

- Eryth.,

- Tetracy.,

- Thiazides,

- Loop diuretics,

iii) Thyroid replacement therapy inc.

dose requirement of digoxin.

II. ACE Inhibitors

III. Diuretics

Anti-Arrhythmics

(inc. refractory period of cardiac muscle)

I. Vaughan - williams classification system

1. class I NA ch. blocker

- IA - Inc. A - P

- Quinidine

- Procainamide

- IB - Dec. AP (Dec. cardiac excitability)

- Lidocaine

- Mexiletine

- Tocainide

- IC - No effect on AP

- Flecainide

- Propafenone

ii. Class II - B-Blocker

- Propranolol

iii. Class III - K ch. blocker

- Amiodarone

(Most potent and broad spectrum,

blocks NA, B, CA channels as well)

- Sotalol

- Ibutilide

iv. Class IV- CA Ch blocker

- Verapamil

II. Miscellaneous

i) Adenosine

ii) Digoxin- Dec. AV conduction

* USES:

1. Quinidine - atrial fibrillation

2. Lidocaine - Ventri. arrhy.

3. Flecainide - wide range

4. Propafenone

- Ventri. arr. and supra ventri. tachcar.

5. b - blocker - Ventri. rate

iii. Verapamil

- for suppression of paroxymal

supraventricular tachycardia

stemming from AV node

*ADR: -

1) Torsade de pointes

(type of ventricular tachycardia)

- Procainamide

- Quinidine

2) Cinchonism (deafness)

- Quinidine

Anti-Coagulants

I. Heparin

- Inc. Bleeding Time

- 16000 Daltons

i) Low Molecular Weight

(sub-cutaneous)

- Prevent DVT

- Enoxaparin

- Fondaparinux

iii) Direct Thrombin Inhibitors

- Bivalirudin

- Argatroban

II. Oral Anti-Coagulant

i) Warfarin - Interfere With

Factor 2,7, 9,10 Production

ii) Anisindione

III. Platelet Aggregation Inhibitors

Prevents Activation Of

Coagulation Pathway

i) Traditional

- Aspirin (irreversible)

- Dipyridamole

ii) ADP - Induced Platelet

Fibrinogen Binding Inhibitor

- Clopidogrel (irreversible)

iii) Platelet Glycogen IIb/IIIa Inhibitors-

(reversible, intravenous

Prevents Cardiac ischemia)

- Abciximab

- Eptifibatid

- Tirofiban

IV. Platelet reducing agents

1. phosphodiesterase III inhibitor

- Anagrelide

- Cilostazol

V. Thrombolytic agents

- Alteplase

- Streptokinase

* Antidotes

1. Heparin - Protamine

2. Warfarin - Vitamin K

* Thrombin - Ca2+, Thromboplastin,

factors 5, 7 (shortest half life), 10

* $INR = \frac{PT \text{ time in patient}}{\text{standard PT time}} \times \text{constant}$

1 = Normal = 12 seconds

INC. INR = INC Anti-coagulant effect

INR = 3 (upper limit for safe oral surgery)

* Anti-coagulant do nothing to dec. BP.

Anti-Hyperlipidemic Drugs

I. HMG-COA reductase inhibitor

- Statins (Cholesterol is not produced)

II. Fibric acid derivative

- INC Catabolism of VLDL

- Gemfibrozil

III. Bileacid sequestrants

- (INC diversion of cholesterol to Bile

acid synthesis Dec Intra cellular

stores of Cholesterol)

- Cholestyramine

IV. Selective Cholesterol absorption

- Inhibitor

- Ezetimibe

V. Others

- Nicotinic acid: Inhibites Lipolysis

(Niacin)

VI. Combination

- Statin + Nicin

- Statin + Eze.

*ADR

1. Statin - Breakdown of skeletal

muscle

* Erythromycin increases statin

capability to cause this effect.

VII. Garlic (herbal)

- Dec. Cholesterol

- Dec. Platelet Aggregation

VIII. Chaumomile (herbal)

- Contains Coumarin

Anti Hypertensive agents

I. ACE inhibitor

(Peripheral vasodilation, INC. urinary

volume excretion

- Lisinopril

II. Angiotensin II receptor blocker

- Losartan

III. α -Blocker - Dilate arterioles and veins

IV. β -Blocker - Dec. cardiac output

V. Ca Channel blocker - Dec. Calcium

entry into vascular smooth muscle,

i.e. Vasodilation

VI. Centrally acting adrenergic drugs

(Dec. sympathetic outflow i.e. Vasodilation)

- Clonidine

- Methyldopa

VII. Gingo biloba (herbal)

- Peripheral artery vasodilation

VIII. Neuronal blocker

(for severe hypertension)

- Guanethidine

IX. Drugs used in acute hypertension

(emergency)

1. Oral - clonidine, Captopril, Labetalol

- Nifedipine

2. Paraentral - Na nitroprusside

(Direct - Niro glyserine

Vasodilator) - Trimethapan

(Hydralazine - Diazoxide

and minoxidil - Hydralazine

are peripheral

vasodilator)

X. Diuretics

1. Thiazides - Hydrochlorothiazide

- Indapamide

- Metolazon

2. Loop diuretics - Furosemide

3. Potassium sparing

- i. NA channel blockers

(negative potential Dec. K and

H+ ion secretion)

- Triamterene

- Amiloride

ii. Aldosterone antagonist

- Spironolactone

- Eplerenone

4. Osmotic diuretics (act on proximal tubule)

- Mannitol

- Glycerin

- Urea

5. Carbonic Anhydrase Inhibitors

- Acetazolamide

Bacteriostatic - Broad Spectrum
Macrolides,
Clinda,
Sulpho

ANTI INFECTIVE

In viral infection: If Absolute Neutrophil Count(ANC),
less than 1000/mm³, then antibiotics recommended

Antibiotics

Agents affecting cell wall

I. β -lactam

1. Penicillin (6 - Aminopenicillamine acid
{ L-Cysteine & L-Valine})

Thiazolidine ring

||

B lactam Ring
{ 3C + 1 nitrogen}

1. Penicillin G (Original)
- Acid unstable, Paraentral
- Benzathine (IM)
2. Penicillin VK - preferred for
Non penicillinase gram positive
over ampicillin as VK is narrow spectrum
3. Extended spectrum
1. Ampicillin (oral / IV)
Ampicillin + Sulbactam (UNASYN) -
best against gram negative
2. Amoxicillin (High oral absorption)
Amoxicillin + Clav. (AUGMENTIN)
3. Carbenicillin - for pseudomonas infection
4. Broad spectrum (paraentral)
Piperacillin, Ticarcillin
5. Penicillinase resistant (excreted in bile)
Naf, Oxa,
Cloxa, Dicloxa - Protected B lactum ring
* ADR / contraindication
i. Hypersensitivity, skin rash - delayed reaction
ii. Provenecid - Inc. Peni. level
iii. Ampicillin, Amoxycillin,
- Dec. Gi flora - Inc. Steroid excretion
therefore Dec. oral contraceptive effect
iv. Amox: Inc. Methotrexate level
v. Penicillinase excreted by bacteria opens
B-lactum ring
- Blocked by augmentin and UNASYN.
- 2) Imipenem (Carbapenem)
-Imi + Cilastatin = to treat nosocomial infection.
- 3) Aztreonam (Mono bactum) - para-enteral
Against aerobic gram negative rods
- 4) Cephalosporins
Binds to transpeptidase that build cell wall
Generations
1st- Cephalexin, Cephradine
2nd- Cefaclor, Cefuroxime
3rd- Cefixime, Ceftriaxone
4th- Cefepime (against pseudomonas)
5th- Ceftobiprole(against nosocomial pneumonia)
**10% allergic to penicillin are also allergic to
cephalosporin.**
ADR- Hypersensitivity
II) Vancomycin (Intravenous)
against staph, strepto, clost. difficile
ADR- Ototoxicity, Red man syndrome
III) Bacitracin - ADR: Nephrotoxicity
IV) Cycloserine

Agents effecting protein synthesis

1. Broad spectrum

I. Tetracycline

- Against local
Aggressive periodontitis
- Anug,
- Acne,
- Gonorrhoea,
Short action - tetracycline
Intermediate - Demecloxy
long - minocy., doxycy.

In Pt. allergic
to penicillin

* contraindicated in children upto 8 years,
pregnant women
ADR:
I) Fanconi syndrome (certain substance
absorbed by kidney are released)
ii) Super infection
iii) Photosensitivity reaction
iv) Hepatotoxicity
v) Tetra + Peni. (Static + cidal) cancel each
other due to opposing mechanism of action
vi) Absorption inhibited by Al^{3+} + Ca^{2+} + Fe^{2+}
mg³⁺ (form chelation products)
vii) INC. action of coumarin anti-coagulants
due to dec. vit K sources
viii) Teeth - greenish brown

II. Chloramphenicol

* ADR
INC. action of coumarin anti coagulant
Due to dec. vitamin K
affect Bone marrow
grey baby syndrome
Clari, } against *H. influenzae Pylori, mycobact. avium*
azithro, } (concentrated within macrophages)
erythro - against gram positive
*ADR inhibits metabolism of
seldane (terfenadine), digoxin
erythromycin - GI effects
Clari., erythromycin - inc. QT- Arrhy. (Torsade de pointes)
iii. Aminoglycosides
- Against aerobic, gram negative bacteria
- Gentamycin (most commonly used)
- Amikacin, Tobramycin, Streptomycin
- Neomycin (topical), Kanamycin
* ADR:
- Curare like effect (neuromuscular weakness)
- Ototoxic
- Nephrotoxic
- Fanconi's syndrome (gentamycin)
4. Clindamicin
Against gram positive and anaerobic gram negative (bacteroids fragilis)
*ADR:
- Diarrhea,
- Pseudomembraneous colitis } Over growth of
clostridium difficile
5. Linomycin

Agents affecting Biosynthetic pathway

1. Sulfonamides

- Sulfo. and PABA structural similarities

Compete
↓
Inhibit PABA
↓
Inhibit folic acid
↓
Inhibit growth
* Not used in dentistry due to less
effect against oral pathogens
Bactrim
(Trimethoprim + Sulfamethoxazole)
ADR - Hypersensitivity

2. Fluoroquinolones

- Ciprofloxacin - inhibits DNA
* ADR: Nausea, Headache

3. Metronidazole

- Alters bacterial DNA

Anti-Malarial (Parasitic disease)

1. Mefloquine
- Against all four
malarial species

2. Atovaquone

+
Proguanil
= Malarone

3. Sulfadoxine

+
Pyrimethamine
= Fansidar

Anti-Protozoal

1. Nitazoxanide

- Against Giardia (interfere with
electron transfer reaction)

2. Atovaquone

- Against pneumocystitic carinii

3. Eflornithine

Against meningoencephalitic
stage of brucei (sleeping sickness)

4. Furazolidone

- Treat diarrhea against Giardia and
Vibrio cholera

5. Metronidazol (Synthetic)

- Against trich. vaginalis
- Anaerobic bacteria (anti-bacterial)
* Not to be used in pregnancy.

Anti-Tubercular Combination used to avoid resistance

1. Isoniazide (H)

- Interfere with Biosynthesis

2. Streptomycin (S)

- Suppress RNA synthesis

3. Rifampin (R)

prevent mycolic acid incorporation

4. Ethambutol (E) (Bacteriostatic)

prevent mycolic acid incorporation

5. Pyrazinamide (Z)

* Static (E) + Cidal (HRZS)
- used against dividing organisms.

Anti fungal (Bind to ergosterol in cell wall to weaken the wall)

I. Topical

1. Dissolve & Swallow
- Clotrimazole (Troche)
- Nystatin (Oral suspension)
2. Cream/Ointment
- Amphotericin B } Cream
- Ketoco
- Nys - Ointment

II. Systemic

- Ampho - IV
- Ketoco
- Fluco
ADR: Ampho Kidney toxicity
* Also used to treat angular
cheilitis as it is limited to
C. Albicans

Anti-viral

I. Herpes Labialis

- (Topical Only)
Inhibit viral DNA synthesis
2. Docosanol cream
3. Lysine
4. Valacyclovir

II. Anti-HIV drugs

1. Nucleosidase
2. Didanosine
3. Zidovudine
4. Protease Inhibitors
- Indinavir
5. Non-nucleoside Reverse Transcriptase
Inhibitors
- Delavirdine
- Nevirapine
- Adefovir (Nucleotide analog)

III. Against influenza virus

1. Neuraminidase inhibitors (To treat acute cases)
- Oseltamivir
- Zanamivir
2. Acyclovir
- Inhibits DNA synthesis
3. Inhibits replication (for prevention)
- Amantadine
(interfere with viral M2 protein
required for uncoating)
- Rimantadine (less side effects)

DRUGS TO TREAT CANCER

I. Aromatase Inhibitor

1. Exemestane - Irreversibly prevent conversion of androgen to estrogen
 2. Letrozole
- * Both are given in treatment of breast cancer.

II. Monoclonal Antibody

- Trastuzumab
- Binds to Human epidermal growth factor receptor 2 protein (HER - 2)
- To treat Metastatic breast cancer

III. Colony Stimulating factor

1. Darbopoetin alpha
2. Pegfilgrastin - stimulates neutrophils
3. Sargramostin - used for myeloid reconstitution.

IV. Chemotherapeutic Drugs

1. Alkylating Agents - forms covalent alkylbonds to nucleic acids
- N7 position of guanine is common binding site.
 - i. Nitrosoureas - Mechlorethamine
mustards - Cyclophosphamide
- Chlorambucil (chr. lymphocy. leukemia)
 - ii. Nitrosoureas - carmustine
 - iii. Busulfan - chr. myelogenous leukemia
 - iv. Cisplatin
 2. Anthracyclines - destroy DNA
- Daunorubicin
 3. Antibiotics - Dactinomycin
 4. Anti-estrogen - Tamoxifen
 5. Anti-metabolites -Methotrexate
- 5 - Fluorouracil
- 6 - Mercaptopurine
(* Attack the cell in "S" phase)
 6. Anti - microtubular - Paclitaxel
 7. Gonadotropin Hormone releasing antigen
- Leuprolide
 8. Vinca Alkaloids - Mitotic spindle poisons
- Vinblastine
- Vincristine
- * ADR -
- Mucositis - most common with 5 - fluoro, metho, doxorubi.
- All blood counts are low
- Alopecia - 1 to 2 weeks after treatment
- Nutritional deficiencies
- Teratogenic

V. Asparaginase

- Deprives Tumor cells of amino acids

VI. Interferons

- Boosts the immune system
- Induce Gene transcription
- ↓ Cell growth and differentiation

1. 1 grain = 65 mg
 1 ounce = 30 g or 30 ml
 1 Kg = 2.3 Lbs

1 Teaspoon = 0.166 ounces
 3 Teaspoon = 1 Tablespoon
 48 teaspoon = 1 cup/glass

Hs = at bedtime
 Prn = As needed
 Ac = before meals
 Pc = After meals
 Sig = Label
 Centigrade = (_____ x 2 +32) Farenheit

2. Shy - Drager syndrome - chronic orthostatic hypotension
 3. Pain threshold = lowest level of pain a patient will detect

4. Dec. NA → angiotensinogen → Renin → Angiotensin I → ACE → Angiotensin II → Aldosterone → Inc. NA
 (Kidney) (Lungs (Potent Vasopressor))

5. Leukotriene modifiers - Leukotriene receptor antagonist
(To treat asthma) - Montelukast
 - Zafirlukast

Leukotriene synthesis inhibitors / 5 - Lipoxygenase inhibitor - Zileuton

6. Insulin - ↓ Blood glucose by ↑ Conversion to glycogen and fat
 - ↓ protein synthesis

Type 1 diabetes mellites are devoid of insulin production by beta cells of pancreas

Anti-Diabetic agents / hypoglycemics

Oral (for non-insulin dependant / type 2 diabetes)

1. alpha glucosidase and alpha amylase inhibitors - Acarbose (Delays glucose absorption) - Miglitol
2. Biguanides - Metformin (↓ Hepatic glucose production)
3. Meglitinides (Stimulates release of insulin)
4. Sulphonylureas - (Close K channels in cell membranes, produce more insulin, ↑ sensitivity of target organs)
 -1st generation - Tolbutamide (Binds to proteins in blood, they can be dislodged by other medications that bind to same proteins. Activity ↑ rapidly, ↓ Blood sugar)
 -2nd generation - Glipizide
5. Thiazolidinediones - Rosiglitazone (↑ sensitivity of muscle and liver by improving control of glycemic utilization)

7. Anti-Rheumatic Agents

*TNF is a pro inflammatory cytokine produced by macrophages and lymphocytes.

- i. TNF α inhibitors - Etanercept
 - Infliximab - Monoclonal Antibody
 - Adalimumab - Monoclonal Antibody
- ii. Gold Injections - ↓ Prostaglandin production
- iii. NSAIDS
- iv. Glucocorticoids - Prednisone } Also used for Osteoarthritis
- v. Methotrexate

Insulin

1. Rapid acting
 -Insulin asparte
 -Insulin glulisine
 -Insulin lispro
2. Short acting
 -Insulin regular (Humulin R) (30%)
 Fast onset (30 to 60 minutes)
3. Intermediate acting
 -NPH (Humulin N) (70%)
 Long duration of action (10 to 16 hours)
4. Long acting
 -Insulin detemir
 -Insulin Glargine

} Humulin = 70/30 Mixture

8. Salivary Substitute

- i. Over the counter - oral balance Half Tsp 5 Times/day
- ii. Anethole trithione - 25 Mg 3 times / day.
- iii. Sodium Carboxymethylcellulose 0.5 % Aq. Solution
- iv. Cholinergics

9. Anti-parkinson drugs (Parkinson - ↑ cholinergic activity, ↓ Dopamine in brain)

- ADR: Dyskinesia
- i. Levodopa + Carbidopa ↓ 75% Levodopa dose)
 (ADR - sympathomimetic) (Dec. Peripheral Decarboxilation of levodopa)
 - ii. Bromocriptine, Pergolide - Dopamine Agonists
 - iii. MAOI
 - iv. Amantadine - ↑ Dopaminergic responses
 - v. Anti-cholinergics
 - vi. Anti-depressant
 - vii. Anti-histaminic

10. Agents having effect on bone

- i. Bisphonate drugs - to treat Paget's, Osteoporosis, prevent hypercalcemia of malignancy
 - Zoledronic acid, Causes Osteonecrosis
 - Pamidronate } (Oral - 0.06%, IV - 10% chances)
- ii. Blocks bone resorption
 - Bisphonates
 - Selective Estrogen Receptor Modulators - Raloxifene
 - Calcitonin
- iii. Inc. calcium absorption
 - PTH
 - Vitamin D (1, 25 Dihydroxycholecalciferol - it is active form)

11. Alcohol treatment

- Disulfuram - Inhibits aldehyde dehydrogenase
 - Metronidazol - Inhibits aldehyde dehydrogenase
- Drugs synergistics with alcohol - Diazepam
 Meperidin
 Pentobarb.
 Chlorproma.

* Ethanol - ↓ ADH, ↓ Excitatory Nerve pathway

12. Aluminum Hydroxide: Potent anta-acid- It dec. Neutralizing capacity.

13. Syncope management - head not more than 10% below body
 Hyper ventilation syndrome - O2 not needed
 COPD - 100% O2 not given

14. Growth hormone - ↓ Carbohydrate utilization

15. Gout management

- i. ↓ Inflammation (acute) - Colchicine - Oral
 NSAIDS - most common (indomethacin)
- ii. ↓ uric acid production (Chronic) - Allopurinol
- iii. ↑ uric acid clearance - Probenecid
 - Sulfinpyrazone

16. Caffeine is the only approved OTC stimulant

Tea - 40 - 110 Mg caffeine

17. I.Skeletal muscle relaxants / Spasmolytics (acts in CNS or in skeletal muscle cells)

- i. Acute- Cyclobenzaprine
 - Methocarbamol
- ii. Chronic -Baclofen - stimulates GABA b receptors } Acts in spinal cord
 - Diazepam
 - Tizanidine
 - Carisoprodol - used to treat acute TMJ pain
- iii. ↓ Nocturnal leg cramps - Quinine

II.Peripheral acting muscle relaxants

- Dantrolene - use - UMN associated spasm, Malignant Hyperthermia
- Pancuronium

18. To Treat ADHD (3 to 5 years of age, M:F - 10:1)

- Amphetamine
- Methyphenidate
- Atomoxetine (Non stimulant)
- Modafinil (CNS stimulant, ↓ GABA action)

19. Anti-Diarrheals

- Opiate - Loperamide
 - Diphenoxylate - Requires prescription
- Anti-secretory - Bismuth Subsalicylate
- Absorbent - Attapulgit

20. Anti-emetics

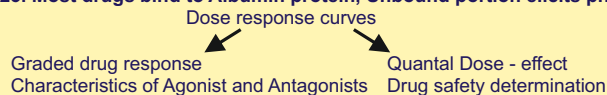
- I. Anti-dopaminergic - Phenothiazine, Benzamide
- ii. Anti-cholinergic
- iii. Anti-histaminic
- iv. Serotonin 5HT3 receptor antagonist - Ondansetron

21. Substance	Treatment
I. Mercury - ↑ Saliva is toxic effect	British Anti - Lewisite (BAL) / Dimercaprol Penicillamine
Half life - 55 days	British Anti - Lewisite (BAL) / Dimercaprol
ii. Lead	Penicillamine EDTA
	Penicillamine
iii. Copper / Wilson's disease / Hepatolenticular Degeneration	Deferoxamine
iv. Iron	100 % Oxygen
v. Carbon monoxide	Sodium Nitrite
vi. Cyanide	Sodium Thiosulfate

22. Neurotransmitters - Dendrite receives the signal

- I. Aminoacids: Glutamate (Excitatory)
 - GABA (g-amino-butyric acid)
 - Glycine
- ii. Amines - Catecholamines - Dopamine (D1-Activates Adenyl cyclase, D2 - Inhibits Adenyl cyclase)
 - Nor - Epinephrine
 - Epinephrine
 - Serotonin
 - Histamine
 - Acetylcholine
- iii. Neuropeptides - Hormones

23. Most drugs bind to Albumin protein, Unbound portion elicits pharmacological effect



24. Tacromilus, Cyclosporin - Immunosuppressant agent

25. Alefacept - Monoclonal Antibody - To treat Psoriasis

26. Migraine medications

- (Cranial vessel constriction → ↓Neuropeptide Release → ↓trigeminal Pain pathway)
- I.Serotonin 5HT1D receptor agonist - Triptans
- ii. Ergotamine
- iii. Midrin (65 mg Isometheptene + 100 mg Dichloralphenazone + 325mg Acetaminophene)
- iv. Methylsergide - Blocks Serotonin 5HT2 receptors (prophylaxis)

27. Thyroid medications

- Thyroid Supplements - T4 (Slow onset of action, Cumulative)
- Thyroid Suppressant - Methimazole, Propylthiouracil
- * LA with epinephrine should not be used in patients with hyper thyroidism as these patients are sensitive to sympathomimetic agents (i.e. Epinephrine)

28. NRT

- I. Nicotine -1.Patch (Most common) - 15mg, 21mg
- 2.Gum (Faster delivery) - 2mg, 4mg
- 3.Lozenge - 2mg, 4mg
- 4.Nasal Spray - Fastest
- 5.Inhaled - absorbed by mouth(10mg Nicotine when inhaled,delivers 4mg into systemic blood)
- ii. Anti-Depressant - Bupropion - for reducing craving
- iii. Nicotine receptor agonist - Varenicline

29. Herbal

- i. Immune stimulator - Echinacea
 - Ginseng
- ii. To treat enlarged prostate - Saw Palmetto

30. Route

- | | Onset |
|---|---|
| 1. Inhalation | Within 5 Min. |
| 2. IM | 5 Min. |
| 3. Subcutaneous | 15 Min. |
| 4. Patch | 15 Min. (Released over 12 - 24 Hrs period) |
| 5. Oral (Most Unpredictable, least effective) | 30 Min. (Passes 1st to liver, absorbed best from Duodenum) |
| 6. Topical | Not for systemic administration |
| 7. IV | 100 % Bio-availability |
- * IM - Uniform absorption, Rapid absorption from Aqueous solution
 - Young children - Anterior Thigh - 1/4th inch Needle penetration
 - Adult - 1 inch Needle penetration

31. Terms

- I. Competitive antagonism - response achieved by ↑ dose of agonist
- ii. Tolerance - ↓ responsiveness
- iii. Additive effect - no enhancement of potential (Sum of individual drug)
- iv. Synergistic response - Greater than sum of individual action
- v. ↓ EC50(Dose causing 50% maximum effect) - ↑ potency

32. Hepatic metabolism (Not a method of elimination)

- I. Phase I reactions (occurs in liver, Microzomal enzyme/P450 system)
- Oxidation reaction - Most common, oxygen in the form of hydroxyl group is attached to drug molecule
- ii. Phase II reactions
- Conjugation - results in polar water soluble compound,
- Mechanism: Couples drug with an acid present in cell.

33. Physiological receptors - Drug on interaction with receptor → Drug does not create effect → But modulates intrinsic cell functions

- i. Enzymes - cell surface protein Kinases
- ii. Ion channels - Alters membrane potential
- iii. G protein - coupled receptors - 2nd Messengers like Cyclic AMP are produced
- iv. Cell nucleus - for steroid hormones

34. Mechanism of drug transfer across biological membrane

- I. Passive
 - i. Simple diffusion - Non-ionized are lipid soluble - Moves across lipoprotein membrane (Resorption favors highly lipid soluble agents)
 - ii. Filtration - Molecular weight 60,000 or less - filtration across capillary membranes
- II. Active / carriers
 - i. Drugs transported to region of ↑ concentration by carriers
 - ii. Facilitated Diffusion - driving force - concentration difference
- III. Osmosis - membrane is permeable only to solvent.

35. Scheduled drugs - All have potential for abuse

* Drug Enforcement Agency authorization number (DEA) for II & III prescription

I (Not for medicinal use) <ul style="list-style-type: none">- Heroin- LSD- Mescaline- Marijuana	II (Prescription Required) <ul style="list-style-type: none">- Morphine- Methadone- Cocaine- Straight Codeine- Oxycodone- Pentobarbital	III (Prescription Required) <ul style="list-style-type: none">- Analgesic + Codeine compounds	IV <ul style="list-style-type: none">- Diazepam- Chloral Hydrate	V <ul style="list-style-type: none">- Medications that contain small amount of codeine
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36. Therapeutic Index = $\frac{LD50}{ED50}$ → Greater → Safer

Therapeutic Window = range between lowest therapeutic concentration and beginning of toxicity

37. Prescription

- I. Superscription - patients name, age, address, date
- II. Inscription - Drug name, dose
- III. Subscription - Direction to pharmacist
- IV. Transcription / Signa - Direction to patient
- V. Signature - Signature of Prescriber.

38. Clinical testing

- Phase I - In lab
- Phase II - In diseased patients
- Phase III - General Population