**PH.1.12**

**Calculate The Dosage Of Drugs Using Appropriate Formulae For An Individual Patient Including Children, Elderly & Patient With Renal Dysfunction**.

**CALCULATION 1**

A 35 Years Old Man Was Admitted With H/O Diarrhoea & Vomiting. On Examination He Was Found To Be Dehydrated. He Needs 3 Pints Of Normal Saline. Calculate The Sodium Chloride To Be Used.

( 1 Pint= 500ml) ( Normal Saline = 0.9% Sodium Chloride Solution).

**N1 = N2**

**V1 V2**

**Required Volume (V1) = 3 Pints = 1500 ml N2 = 0.9 G**

**Required Strength(N1) = ? V2 = 100 ml**

N1 = 0.9 G

1500 100 ml

N1 = 0.9 g x 1500

100

= 13. 5 g

**13.5 g Of Sodium Chloride Is Needed .**

**CALCULATION 2**

An Adult Weighing 60 Kg Is To Be Given IV Thiopentone Sodium In Dose Of 5mg/kg. If The Strength Of The Solution Is 2.5 %, What Is The volume Of Drug You Will Use ?.

**N1 = N2**

**V1 V2**

**Required Strength Of Thiopentone sodium ( N1 ) = 5 x 60 = 300 mg N2 = 2.5 g (2500mg)**

**Required Volume (V1) = ? V2 = 100 ml**

300 mg = 2500 mg

V1 100 ml

V1 = 300 X 100

2500 mg

= 12 ml

**Volume Of The Drug Required = 12 ml**

**CALCULATION 3**

Calculate The Dose Of Paracetamol For A Child Aged 4 Years. The Adult Dose Is 500 mg Four Times A Day . Paracetamol Syrup Is Available As 125 mg/ 5 ml.

As Age Of The Child Is Given , The Paediatric Dose Is Calculated using **Young’s Or Dilling’s Formula.**

**Dilling’s Formula**  **= Adult Dose X Age In Years**

**20**

= 500 X 4

20

= 100 mg

**Dose Needed For The Child Is 100 mg Four Times A Day**.

Volume Of Paracetamol Syrup Needed ?.

**N1 = N2**

**V1 V2**

**Required Strength ( N1 ) = 100 mg Given Strength( N2) = 125 mg**

**Required Volume ( V1 ) = ? given Volume ( V2) = 5 ml**

100 mg = 125 mg

V1 5 ml

V1 = 100 X 5

125

= 4 ml

**The Child Needs 4 ml Of Paracetamol Four Times A Day.**

**CALCULATION 4**

Calculate The Dose Of Amoxicillin For A Child Weighing 12 kg Suffering From Acute Tonsillitis, While The Adult Dose Is 500mg Three Times A Day . Amoxicillin Is Available As Powder For Oral Suspension ( 125 mg/5ml ).

As Weight Of The Child & Adult Dose Are Given, Paediatric Dose Is calculated Based On

**Clark’s Formula .**

**Clark’s Formula = Adult Dose X Body Weight In Kg**

**70**

**= 500 mg X 12 kg**

**70**

**= 86 mg (Approx)**

Dose Needed For The Child Is 86 mg Three Times A Day. What Is The volume Of Amoxicillin Suspension Required ?.

**N1 = N2**

**V1 V2**

**Required Dose (N1) = 86 mg Given Strength(N2) = 125 mg**

**Require Volume ( V1 ) = ? Given Volume (V2) = 5 ml**

86 mg = 125 mg

V1 5ml

V1 = 3.5 ml

**The Child Needs 3.5 ml Of Amoxicillin Suspension Three Times A Day.**

**CALCULATION 5**

A Normal Saline Infusion Of 500 ml Is Administered At The Rate Of 40 Drops/ min . How Long Will It Last ?.

Infusion Rate if Only Volume Of The Drug Given :

**Infusion Rate** ( Drops/Min ) = **Volume Of The Fluid X 20 Drops ( 1ml = 20 Drops)**

**Duration In Minutes.**

40 / Min = 500 X 20

? In Min

Duration In Min = 500 X 20

40

= 250 Min = 4 hrs 16 min

**The Infusion Will Last For 4 hrs & 16 min.**

**CALCULATION 6**

Calculate The Infusion Of Dopamine In Drops/min For A Patient Weighing 60 kg Suffering From Cardiogenic Shock . The Required Therapeutic Dose Is 5 mcg /kg/min. The Drug Is Available As

40 mg/ ml In 5ml Ampoule & It Should Be Delivered Through 245 ml Of Normal Saline.

Infusion Rate If Conc Of The Drug & volume Given :

**Infusion Rate ( Drops/ mt ) = Desired Cocentration infusion X Body Wt In kg**

**Conc Of Drug In Solution ( mcg/ml )**

Desired Concentration Infusion = 5 mcg/kg/min

Dopamine Present In 5ml Ampoule = 40 X 5 = 200 mg

Volume To Be Infused = 245 + 5 = 250 ml Of Normal Saline .

Concentration Of Drug In Solution/ ml = 200 mg

250 ml

= 0. 8 mg = 800 mcg/ml

Infusion Rate In Drops/ min = 5 X 60 = 0.375 ml ( 1 ml = 20 drops)

800

= 0.375 ml X 20 Drops = 8 Drops/min.

**Infusion Rate Of Dopamine Is 8 drops/min.**

**CALCULATION 7**

Calculate The Infusion Rate Of Insulin In Drops/Min For A Patient Weighing 70 kg Suffering From Diabetic keto Acidosis. Required Therapeutic Dose Is 0.1 units/kg/hr. The Given Vial Contains

40 units/ml. The Drug Should Be Delivered Through 250 ml Of Normal Saline.

**Infusion Rate ( Drops/ mt ) = Desired Cocentration infusion X Body Wt In kg**

**Conc Of Drug In Solution ( Units/ml )**

Desired Concentration Infusion = 0.1 units/ kg/ hr

= 0.1 units /kg/min

60

Insulin Present /ml = 40 units

Volume To Be Infused = 250 ml Of Normal Saline .

Concentration Of Insulin In Solution/ ml = 40 units

250 ml

= 0. 16 units/ml

Infusion Rate In Drops/ min = 0.1 X 70 = 0.73 ml ( 1 ml = 20 drops)

60 X 0.16

= 0.73 ml X 20 Drops = 15 Drops/min.

**CALCULATION 8**

Calculate The Dose Of Amikacin In A 40 yrs Old Female With Weight 55 kg Having Impaired Renal Function & Serum Creatinine 2.1 mg/L , While The Normal Dose Of Amiikacin Is 15mg/kg/day.

Formula For Calculating Dose In Renal Dysfunction Is :

**Dose In Renal Dysfunction ( RD) = Normal Dose X CL RD**

**CLN  ( Normal )**

Formula For Calculating Creatinine Clearance In Female :

**Creatinine Clearance In Women** = **0.85 X [ 140 -- age In yrs ] X Body Wt**

**72 X Serum Creatinine Conc mg/L**

= 0.85 X [ 140 – 40 ] X 55

72 X 2.1

= 4675

151.2

Creatinine Clearance = 30. 92 ml/ min

Dose Of Amikacin Needed = 15 mg X 30.92 ml/min

120ml/min

= 463.8

120

= 4 mg/kg/day ( Approx)

**Dose Of Amikacin Needed 4 mg/kg/day**

**CALCULATION 9**

If The Clearance (CL ) & The Volume Of Distribution ( Vd ) Of Chloroquine Are 0.75 L/hr/Kg &

220 L/Kg Respectively , What Will Be The Half-life Of The Drug ?. How long Will It Take For The Drug To Achieve Steady State On Repeated Dosing ?.

Clearance (CL) = 0.75 L/Hr/Kg

Volume Of Distribution ( Vd ) = 200 L/Kg

**Plasma Half Life (t ½ ) = 0.693 X Vd**

**CL**

= 0.693 X 200

0.75

= 0.693 X 267 = 185 hrs

t 1/2 = 7 days 7 hrs

Time Taken To Achieve Steady State Conc = 5 x t ½ = 5 X 185 = 925 hrs

= 38 Days & 5 hrs

**CALCULATION 10**

Calculate The IV Loading Dose & Maintenance Dose Of Theophylline For A Woman With 6o kg Weight Suffering From Acute Severe bronchial Asthma. A Target plasma Theophylline Concentration Of 10mg/L Is Desired For Relief . The Clearance & Volume Of Distribution Of Theophylline Are

0.04L/ hr/ kg & O.5 L/Kg Respectively. What Would Be The Oral Maintenance Dose In The Same Person If Bioavailability By Oral Route is 70% ?

Bioavailability By IV = 100 % = 1

Clearance (CL ) = 0.04 L /hr/KG

CL For 60 kg = 0.04 X 60Kg

= 2.4 L /hr/ 60 Kg

Volume Of Distribution ( Vd ) = 0.5 L/Kg = 30 L/60 Kg

Target Plasma Conc ( Tc ) = 10 mg/L

**IV Loading Dose = Target Plasma Conc X Vd**

**Bioavailability**

= 10 mg X 30 L

1

= 300 mg

**IV** **Maintenance Dose = Target Plasma Conc X CL**

**Bioavailability**

= 10 mg X 2.4 L/Hr

1

= 24 mg /Hr

**Oral Maintenance Dose** = 10 mg X 2.4 L/Hr

0.7

= 34 mg/Hr

**PH 1.3**

**Drug Formulations & Drug Delivery System**

**DOSAGE FORMS**

**1.SOLUTION**

**1.Identify & Describe The given Dosage Form :**

Solution For IV Use. Solutions Are Liquid Preparations Containing Soluble Substances Dissolved In Suitable Vehicles.

**2. What Are The Different Types Of Solutions ?. Give 2 Examples Of Each.**

* Solutions For Oral Use : Mixtures, Syrups
* Solutions For IV Use : Normal Saline , 5% Dextrose Solution.
* Solutions For External Use : Lotions, Liniments
* Solutions For Instillation Into Body Cavities : Enema, Ear Drops.

**3. What Is 1% (W/V) Solution ?**

1 g Of Solute Dissolved In 100 ml Of Solvent.

**2. SUSPENSION**

1**. Identify & Describe The Given Dosage Form :**

Suspension For Oral Use. Suspension Is A Liquid Preparation Containing Insoluble Solids Uniformly

Distributed In The Vehicle, With Or Without The Aid Of A Suspending Agent. Suspensions Can Be

Used For Oral, Parenteral & External Administration.

**2. Name Two Suspending Agents ? Why Are They Added In Suspensions**

Gum Acacia, Starch, Methyl Cellulose. Suspending Agents Increase Viscocity Of Vehicle & There by

Prevent Aggregation Of Insoluble Ingredients & Ensure uniform distribution Of Active Ingredients

In The Vehicle.

**3. Advantages & Disadvantages Of Oral Suspensions ?**

Advantages : Quick Absorption, Suitable For Administration To Children

Dis Advantages : Large Bulk, Less Stability

**3. EMULSION**

**1. Identify & Describe The Given Dosage Form :**

Emulsion For Oral Use An Emulsion Is A Heterogenous System Consisting Of Two Immiscible

Liquids, One Of Which is Dispersed As Minute Globules Into The Other With The Help Of An

Emulsifying Agent. Emulsion Can Be Used For Oral, Topical & Parenteral Administration.

**2. What Are The Types Of Emulsion ? Write 2 examples**

**Oil In Water (o/w) Emulsion** : Oil Is Distributed In The Form Of Globules In Water.

Milky White Appearance. Used For Oral & IV Adminisration .

E.g., Milk & Castor Oil Emulsion (Oral), Propofol --IV

**Water-In-Oil Type (w/o) :** Water Is Distributed In The Form Of Globules In Oil. Waxy & Translucent.

Appearance. Used For Topical & IM Depot Administration.

E.g., Cold Cream & Gamma Benzene Hexachloride Emulsion (Topical) ,

IM Depot Testosterone Propionate Injection.

**3. What Are The Advantages & Disadvantages Of Oral Emulsion ?**

Advantages : Masks The Unpleasant Odor, Rapid Absorption

Dis Advantages : Less stability, Large Bulk.

**4. LOTION**

**1. Identify The Given Dosage Form**

Lotion. Lotions Are Liquid Preparations For Application To The Skin Without Friction. They Commonly

Contain Antiseptics, Astringent, And Soothing Medicaments.

**2. Mention 2 Differences Between Lotions & Liniments**

Lotions : Applied Over Skin Without Friction. Antiseptic, Soothing,cooling & Protective In Nature.

Liniments : Applied over Skin With Friction. Analgesic, Counter-irritant, & Rubefacient

**3.Write 2 uses Of Lotions**

--- Lotions Are Used As Protective in Sunburns

---Soothing & Moisturising Agent In Dry,Rough,Scaly & Itchy Skin.

**5. OINTMENT**

**1. Identify & Explain The Given Dosage Form**

Ointment For Application over Skin. Ointments Are Semisolid Prepartions Meant For Topical

Application To Skin Or Mucous Membrane. Used For Local Effects & Systemic Effects By Their

Percutaneous Absorption.

**2. Name & Explain Other Semisolid Preparations For Topical Application**

**Creams** : Semisolid Emulsions Having lighter Consistency, less Greasy, Easier To Spread & Are Quickly

Absorbed By Skin.

**Pastes** : Semisolid Preparation Containing More Solid Particles. They Are Non- greasy, Stiffer &

preferred For Exudative/ Moist Lesions.

**3.Give 2 Examples For Ointment/Creams Applied Topically To Produce Systemic Effects**:

Nitroglycerine Ointment For Relief Of Angina.

Estradiol cream For Relief Of Menopausal Symptoms.

**6.ENTERIC COATED TABLETS**

**1. Identify The Given Doaage Form. Define Tablets.**

Enteric Coated Tablets. Tablets May Be Defined As Solid Dosage Forms Meant For oral

Administration, prepared By Compression/Moulding Of One Or More Medicaments.

**2. Enumerate Different Types Of Tablets:**

Simple Uncoated oral Tablets

Sugar Coated Tablets

Enteric Coated Tablets

Mouth Dissolving Tablets

Dispersible Tablets

Chewable Tablets

Sublingual Tablets

Sustained Release Tablets

Lozenges

**3. What Are The Advantages Of Enteric Coated Tablets ?. Give 2 Examples**

They Resist Dissolution In Gastric Juice & Release The Drug In The Intestine. They Are Employed When

The Drug Is Destroyed By Gastric Acid Or Is Irritant To Gastric Mucosa.

Eg., Enteric Coated Aspirin --- To Prevent Irritation To Gastric Mucosa

Enteric Coated PPI --- To Prevent Degradation By Gastric Acid

**7. SPANSULES**

**1. Identify & Describe The Given Dosage Form:**

Spansules( Sustain Release Capsules ). They Are Hard Gelatin Capsules Filled With Granules With

Specific Formulation To Disintegrate & Dissolve At Different Times & Thereby Providing Uniform

Medication Over A Prolonged Period Of Time.

**2.What Are Capsules? Describe Different Types Of Capsules**

Solid Oral Dosage Forms That Contain One Or More Medicaments Enclosed Within Shells Of Gelatin.

**Hard Gelatin Capsules** : Made Up Of 2 pieces Fit Together –A long Body & A Shorter Cap. Used For

Packing Powders & Granules.

**Soft Gelatin Capsules** : One Piece Capsule . Contains Liquids/Semisolids.

**3. What Are The Advantages Of Sustained Release Capsules ?**

Maintain Consistent Therapeutic Effect For A Longer Time

Less Frequent Dosing

Reduction In Adverse Effects.

**8. SUPPOSITORIES**

1**.Identify & Describe The Given Dosage Form**

Rectal Suppositories. Suppositories Are Solid Dosage Form Intended For Insertion Into body Cavities

Like Rectum, Vagina & Urethra Other Than Mouth.

**2. What Are The uses Of Suppositories?**

To produce Local Action --- Eg., Bisacodyl Rectal Suppository For constipation.

To Produce Systemic Action --- Eg.,Diazepam Rectal Suopository For Febrile Convulsions In Children.

**3. What Is A Pessary?**

It Is Solid Dosage Form Specifically Shaped To Be Inserted Into The Vagina With The help Of An

Applicator. It is intended For Local Action. It Is Also Called A Vaginal Suppository Or Vaginal Tablet.

Eg., Clotrimazole Pessary For Vaginal Candidiasis.

**DRUG DELIVERY SYSTEM**

**1.ROTAHALER WITH ROTACAPS**

**1. Identify & Describe The DDS**

Rotahaler With Rotacap. It Is A Device That Delivers The Drug Present In The Rotacaps To The lungs By

Inhalation. A Rotacap Contains Single Dose Of The Drug To Be Administered.

**2 . What Are its Advantages?**

--- No Propellant & hence No Environmental Risk.

---Portable, Easy To Use & Less Cost

---Being Transparant has Added Advantage Of Allowing Patients To See Whether Has fully Inhaled

The Drug.

**3. What Are Its Disadvantages?**

--- Can Be Used Only By Children ≥ 6yrs who Could Generate Sufficient Inspiratory Flow Rate

Required For Inalation.

--- Capsule Soften & Do Not Break In Humid weather

--- Only Single Dose Can Be given Each Time.

**TRANSDERMAL DRUG DELIVERY SYSTEM ( TDDS)**

**1. Identify The DDS & Describe With Examples**

Transdermal Patch. It Is An Ahesive Patch Which Permits Absorption Of Drug Through Skin & Deliver It

Into Systemic Circulation At Controlled Rate.

Eg., Nitroglycerine Patch For Relief Of Angina

Scopolamine Patch For Motion Sickness

Estradiol patch For Postmenopausal Osteoporosis.

**2. What Are Its Advantages?**

---Bypass First Pass Metabolism & Hence Increased Bioavailability.

---Produces Sustained Drug Level.

---More Convenient & Improved Patient Compliance

**3. What Are Its Disadvantages?**

--- Local Irritation & Erythema

--- Cannot Be Used To Deliver Polar Drugs.

**PH 1.8 IDENTIFY & DESCRIBE THE MANAGEMENT OF DRUG INTERACTIONS**

**IN THE FOLLOWING CASE SCENARIOS**

1. **A 35 Year Old Male, Type I Diabetes Mellitus On Insulin Was Treated With Propranolol As A Prophylactic Therapy For Migraine.**
2. Explain The Potential Drug Interaction In This Patient:

Propranolol Blunts the Recognition Of Hypoglycemia & Delays Recovery From Insulin Induced Hypoglycemia. Propranolol A Non—Selective β—Blocker Blocks β2  mediated Glycogenolysis & Neoglucogenesis In Liver & Aggravates Insulin Induced Hypoglycemia.

It Also Suppresses The Warning Signs Of Hypoglycemia Like Tremors, Tachycardia, Palpitation, Sweating Mediated Through Sympathetic Stimulation By blocking β—Adrenergic Receptors.

1. How Will You Manage ?

Patient Can Be Prescribed Selective β1 --blockers Like Metoprolol/ Atenolol Or Calcium Channel Blocker Like Flunarizine As Prophylactic Drug Therapy. These Drugs Are Less

Likely To Blunt Symptoms & Delay Recovery From Hypoglycemia.

1. **A 65 Year Old Male Was Complaining Of Pain In Both Knee Joints For Which Diclofenac Twice Daily Was Prescribed By His Physician . He Was A Known Hypertensive Well Controlled With Enalapril 10mg/day. When He Came For Review After 3 Weeks, his BP Was 160/100 mm Hg.**
2. Comment On The Possible Drug Interaction. Explain The Reason For Raised BP.

Dicofenac A NSAID Reduces The Antihypertensive Effect Of Enalapril By Blocking The production Of Vasodilator & Natriuretic PG Production In Kidney. This Results In Increased BP.

Hyperkalemia Produced By Combination Of NSAID & ACE—I Can Produce Marked Bradycardia Leadinng To Syncope especially In Elderly & In Patients With Hypertension, DM, & IHD.

1. What Is The Interaction Of NSAID With Other Antihypertensives ?

NSAIDS Attenuate The Antihypertensive Effect Of ACE –I, ARB, Diuretics & β –blockers.

They Are Less Likely To Attenuate The Antihypertensive Effect Of Calcium Channel Blockers & Centrally Acting Antihypertensives Whose Actions Are Unrelated To Renal/Extra Renal Production Of PG.

1. **A 30 Year Old Female Patient Was Prescribed Erythromycin 500mg Qid For Upper Respiratory Infection. She Was A Known Case Of Bronchial Asthma Maintained On Salbutamol Inhalation & Oral Theophylline 300mg Three Times A day. After 5 Days She Presented With Restlessness, Irritabilitty, Insomnia & Palpitation.**
2. How Would You Explain These Signs & Symptoms:

The Signs & Symptoms Are Due To Increased Plasma Level Of Theophylline Causing CNS Stimulation. Erythromycin Inhibits hepatic Metabolism Of Theophylline By Inhibiting Microsomal CYP 3A4 .

1. What Is The Line Of Management ?

The Dose Of Theophylline Should Be Reduced Or Erythromycin Should Be Stopped & Replaced

By Azithromycin Or β—Lactam Antibiotics Like Ampicillin/Amoxicillin.

4**) A 45 Year Old Male Patient Was On Isosorbide Dinitrate 10mg bd For Angina. A Quack Prescribed T.Sildenafil For Erectile Dysfuction. The Patient Fainted At Home & Was Rushed To The Hospital. On Examination The Patient Was Dyspnoeic With Pulse Rate 115/mt & BP 80/60mmHg .**

1. Explain The Potential Drug Interaction In This Patient**:**

Sildenafil Potentiate The Vasodilator Action Of Nitrates Producing Dangerously Low BP Resulting In Severe Hypotension, MI & Death. Sildenafil Retard The Degradation Of cGMP By Inhibiting PDE—5 . ↑ In cGMP Results In Vascular Smooth Muscle Relaxation & Increased Blood Flow To Corpora Cavernosa Causing Penile Erection .

1. What Advice Will You Give To The Patient ?

Administration Of Sildenafil Is Contraindicated In Patients With IHD & In Those Receiving Organic Nitrates.The Patient Is Advised Not To Take Sildenafil.

**5. A 30 Year Old Female Was Diagnosed As Having Pulmonary TB And Was Put On First Line Anti—tubercular Drugs ( RMC + INH + EMB + PZ ). She Has Been On Oral Contraceptive Pill Since 2 Years.**

a) Comment On Possible Drug Interaction In This Patient:

OCP Are Fixed Combination Of Estrogen & Progesterone. Rifampicin Is A Microsomal Enzyme Inducer Which Enhances The metabolism Of OCP resulting In Decreased Effect Of OCP. This May Result In Failure Of Contraception/ Breakthrough Bleeding And Spotting.

b) How Would You Manage ?

OCP With Higher Dose Of Estrogen + Progesterone Should Be Used Or Couples Should Use

Other Mode Of Contraception.

**6.** **A 40 Year Old Female Had Been On Lithium Carbonate 300mg Daily Since 3 Years For Maniac**

**Depressive Illness. Recently She Was Diagnosed As Having Stage I Hypertension For Which She**

**Was Prescribed Hydrochlorothiazide 25mg Daily. 4 Weeks Later She Came To The Emergency**

**Department With severe Tremors, Ataxia, Muscle Rigidity, Nystagmus And Hyperreflexia.**

1. Explain The Reason For The Above Signs And Symptoms:

The Above Signs And Symptoms Are Due To Increased Plasma Level Of Lithium.

Hydrochlorothiazide Is A Thiazide diuretic Which Cause Sodium Loss By Inhibiting Na+  Cl--

Co-Transporter In DCT. Lithium Being A Monovalent Cation is Handled By The Kidney In The Same

Way As Na+ . Hence Na+  Loss By Diuretics Promote Reabsorption Of Lithium In PCT.

b) How Will You Manage ?

Lithium And diuretics ( Furosemide,Thiazides) Are Not Given Together. The Woman Should Be

Prescribed Other Anti-hypertensives Like Ca2+  Channel Blockers. ACE-I And ARBs Also Cause

Lithium Retention.

**7. A 30 Year Old Female, Known Epileptic Was Well Controlled With Sodium Valproate. She Was Prescribed Ciprofloxacin With Paracetamol For Enteric Fever. After 4 Days She Developed Seizures.**

1. Comment On The Possible Drug Interaction:

Paracetamol ( NSAID ) Augment Displacement Of GABA from Its Receptors By Ciprofloxacin (Quinolones) . This Reduces Seizure Threshold And Precipitate Seizures In Epileptic Patients.

1. Name 2 Drugs That Precipitate Seizures In Epileptics:

Methyl Xanthines --- Theophylline, Aminophylline

CNS Stimulants --- Cocaine , Amphetamine

Opioids --- Tramadol

Anti tubercular Drug --- INH

Tricyclic Antidepressants ---Imipramine, Clomipramine,Amitriptyline

Atypical Anti psychotics --- Clozapine,Olanzapine

**8. A 35 Year Old Obese Female Was On Warfarin Therapy For Deep Vein Thrombosis . She**

**Developed Pelvic Infection For Which She Was Given Amoxicillin + Clavulanic acid . On The 4th**

**Day She Started Bleeding PV And Passing Dark Urine. INR Was 5.6.**

a) What Is The Reason For Raised INR & Bleeding Symptoms ?

Warfarin Is An Oral Anticoagulant Which Acts By Inhibiting Hepatic Synthesis Of Vit K Dependent

Coagulation Factors (II,VII,IX,X). Amoxicillin + Clavulanic Acid Is Extended Spectrum Penicillin. It

Causes Inhibition Of Gut Flora Resulting In Reduction In Synthesis Of Vit K. Therefore ↓ In Vit K

Level Enhances Warfarin Toxicity And Increases INR.

b) How Will You Manage ?

Reduction In Warfarin Dose And INR Monitoring

**9 . A 30 Year Old Female Was Diagnosed To Have Urinary Tract Infection . Urine Culture Showed**

**Growth of E.Coli Organisms Sensitive To Ampicillin. The Physician Prescribed Ampicillin +**

**Probenecid**.

a) Why Did The Physician Prescribe Probenecid ?

Ampicilin A B –lactam Antibiotic, Is Excreted Unchanged By Tubular Secretion Through Organic

Anion Transporter In The PCT. Probenecid Competitively Bocks OAT And Inhibits The Excretion Of

Ampicillin Resulting In Higher Plasma Concentration And Prolonged Half life. The Advantage Is

Reduced Dose And Reduced Frequency Of Administration.

b) Give 2 Examples Wherein Probenecid Is used For Similar Purpose:

Amoxicillin + Probenecid

Ceftriaxone + Probenecid

Cefuroxime + Probenecid

**10. A 40 Year Old Alcoholic Was Treated With Metronidazole 400mg Thrice Daily For Amobic**

**Dysentry. He Presented Next Day With Severe Flushing, Throbbing Headache, Nausea, And**

**vomiting.**

a) Explain The Possible Reasons For These Symptoms.

Ehanol -------------------------------> Acetaldehyde----------------------------------🡪 Acetic Acid

Alcohol Dehydrogenase Aldehyde Dehydrogenase

Metronidazole Inhibits Aldehyde Dehydrogenase And Prevents The Conversion Of Acetaldehyde To

Acetic Acid .The Concentration Of Acetaldehyde Raises In the Body Giving Raise To

The Above Signs And Symptoms. This Reaction Reinforces Aversion To Alcohol. Hence This Reaction Is

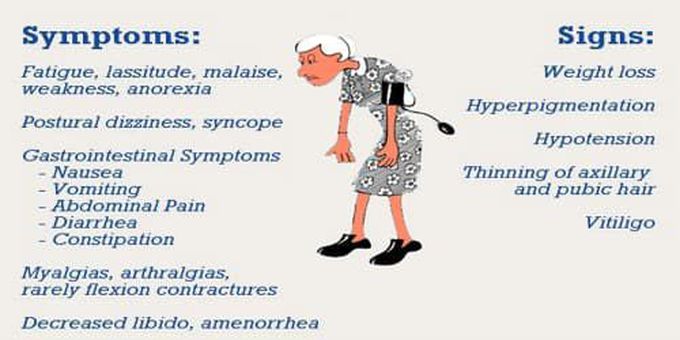
Called Antabuse Reaction.

b) Mention 2 Drugs Which Produce Similar Reaction With Alcohol:

Chlorpropamide, Tolbutamide

Nitrofurantoin

Griseofulvin



**Dehydration, Vascular Collapse,Renal Shut Down,**

**↓ Serum Na+, ↑ Serum K +**

**PH 1.8 DEFINE, IDENTIFY & DESCRIBE THE MANAGEMENT OF ADVERSE DRUG REACTIONS (ADR)**

**CHART –1 ( Spina Bifida)**

1. **Identify & Describe The ADR**:

Spina Bifida.

Type—D ADR . This Is Neural Tube Defect Due To Drug Teratogenecity.

1. **Mention The Drug responsible**

Sodium Valproate

**C) What Is The Line Of Management?**

Avoid Sodium Valproate In Ist Trimester. If Valproate Is To Be Continued In 2nd & 3rd Trimester, Supplement With Folic Acid & Vit K.

**CHART –2 ( Gum Hyperplasia )**

1. **Identify & Describe The ADR:**

Gum Hyperplasia..

Type –A ADR . Undesired Side Effects Occuring With Therapeutic Dose. It Is Due To Over Growth Of Gingival Collagen Fibres Occuring In 20% Of All Patients Receiving Chronic Therapy With Phenytoin.

1. **Mention The Drug Responsible:**

Phenytoin Sodium.

1. **How Do You Treat?**

Good Oral Hygiene With Periodontal Procedures Like Scaling & Root Planning.

Folic Acid Supplementation.

**CHART –3 ( Anaphylaxis )**

1. **Identify & Describe The ADR:**

Anaphylaxis.

Type—B ADR. Bizzare , Unpredictable Type & Not Related To Pharmacological action.

1. **Mention The Drugs Responsible :**

Beta Lactam Antibiotics ---PenicillinG, Cephalosporins

Iodine Containing Agents---Radiocontrast Dye, Povidone Iodine

Sulphur Containing Agents--- Sulphonamides

Fibrinolytics ---Streptokinase.

**C) What Is The Line Of Management?**

* + Inj. Adrenaline – 0.3 To 0.5 ml Of 1in1000 By IM( Or O.5 To 1 ml Of 1 In 10,000) . May Be Repeated Every 10 To 20 min For 3 Doses Until The Patient Improves
  + Inj. Hydrocortisone –100mg IV every 6 hrs
  + Inj. Diphenhydramine –50 To 100mg IM . May Be Repeated Every 4 to 6 hrs.
  + Infuse Normal Saline 1 To 2 L In 30 minutes
  + Nebulise Salbutamol 2.5 To 5mg + Ipratropium Bromide 0.5 mg in 2.5ml of Normal saline. Repeated Every 4 hrs
  + Inj. Aminophylline 5mg/kg IV loading Dose Followed By 1mg/kg/hr Infusion As Maintenance.

**CHART—4 ( Oral Thrush )**

The Picture Is Oral Cavity Of A 60 Year Male Patient , Known Diabetic For 10 years, has Been

Undergoing treatment With Inhalant Ciclesonide For Bronchial Asthma For The Past 2 years.

**CHART—4 ( Oral Thrush )**

1. **Identify & Describe The ADR :**

Oral Thrush.

Type—C ADR. Due To Immunosuppression Due To Prolonged Use Of Inhalant Corticosteroids .

1. **Mention The Drugs Responsible :**

Inhalant Corticosteroids --- Beclomethasone, Ciclesonide, Budesonide etc

Immunosuppressants ----Cyclosporine, Tacrolimus, Methotrexate, Cyclophosphamide.

1. **How Do You Treat ?**

Topical Application Of Clotrimazole, Nystatin

**Precaution** : Gargle/Rinse The Mouth After Using Inhalant Corticosteroids.

Patient’s blood Sugar Should be Monitered Periodically.

**CHART---5 ( Gouty Tophus)**

1. **Identify & Describe The ADR :**

Gouty Tophus.

Type –A ADR. This Is A Undesired Side Effect Occuring Due To Drugs Which cause Hyperuricemia & Precipitates In patients With Gout.

1. **Mention The Drugs Which can Precipitate:**

Thiazides, Furosemide, Pyrazinamide, Ethambutol, Anticancer Drugs Etc.

1. **How Do You Treat?**

Avoid The Drugs Which Cause Hyperuricemia In Gout Patients.

Continue The Other Drugs For Gout.

**CHART—6 ( Yellowish Brown Discolouration Of Teeth)**

1. **Identify & Describe The ADR :**

Yellowish Brown Discolouration Of Teeth.

Type A – ADR. Undesired Side Effect Due To Tetracycline

1. **Explain How Tetracycline Produces The Above ADR?**

Tetracyclines Chelate Calcium From Bone &Teeth In Children Less Than 7 Years ( When Teeth Are Being Calcified). Calcium—Tetracycline Chelate Gets Deposited In Developing Teeth Causing Brown Discolouration, Ill—formed Teeth Which Are More Susceptible To Caries. Given During Late Pregnancy, tetracyclines In Addition To Causing Brownish Discoloration Of Teeth, It Can Cause Temporary Suppression Of Bone Growth In Children.

1. **What Is The Line Of Management?**

Avoid Tetracyclines In Pregnancy & In Children Less Than 7 Years.

**CHART –7 ( Cleft Lip & Cleft Palate)**

1. **Identify & Describe The ADR:**

Cleft Lip & Cleft Palate.

Type—D ADR. This Is Due To Drug Teratogenicity.

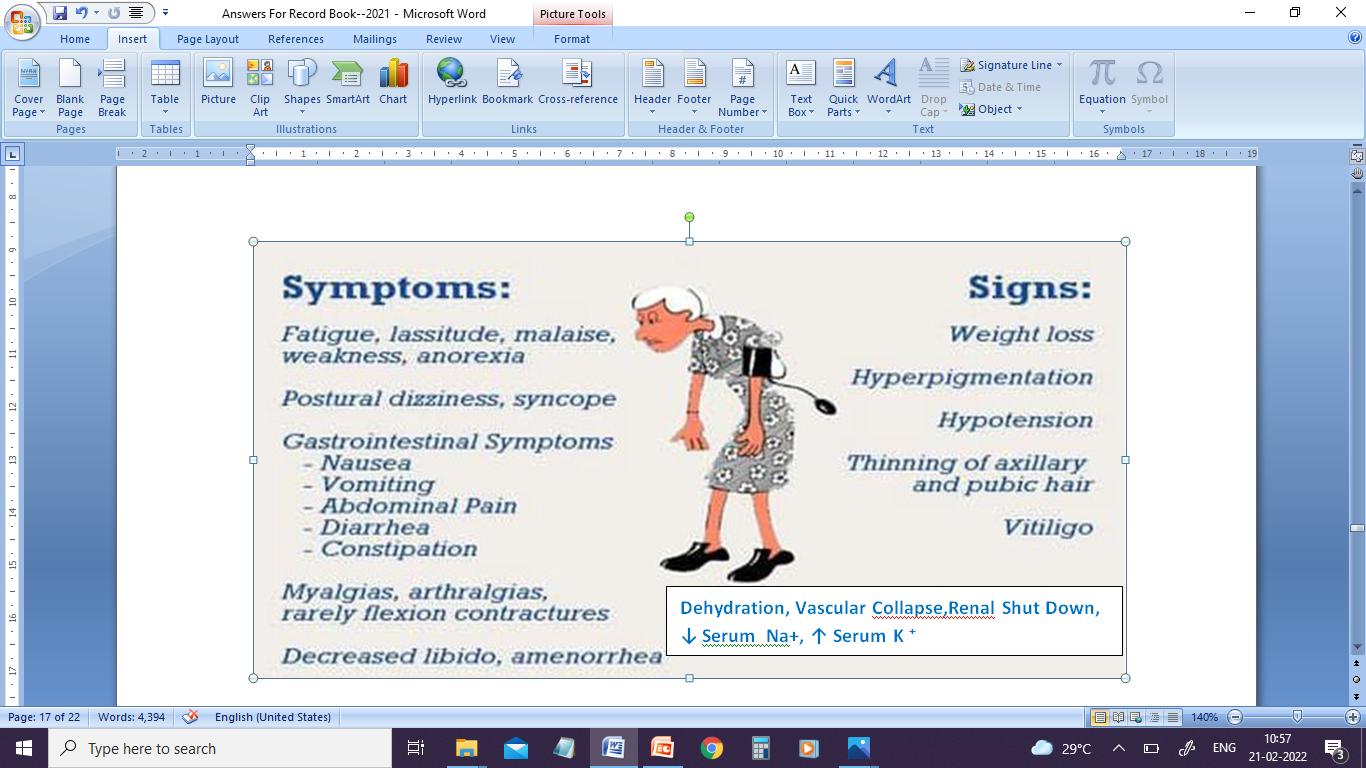
1. **Mention The Drugs Responsible:**

Phenytoin Sodium & Methtrexate.

1. **How Do You Manage?**

Above Drugs Should Be Avoided During Pregnancy.

**CHART—8 ( Acute Adrenal Insufficiency )**

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A 35 Year Old Female Of Inflammatory Bowel Disease Was On Prednisolone 40 mg/Day &

Mesalazine 800mg bd For 4 Weeks. She Stopped taking Prednisolone Abruptly Without Doctor’s

Advice & She Developed Above Signs & Symptoms.

**CHART—8 ( Acute Adrenal Insufficiency)**

1. **Identify & Describe The ADR :**

Acute Adrenal Insufficiency.

Type---E ADR. Due To Abrupt Cessation Of Corticosteroid. Exogenous Steroid For Longer Than

2 To 3 Weeks Suppresses Hypothalamo—Pituitary—Adrenal Axis. Hence Stoppage Of Exogeous

Steroids Precipitates Acute Adrenal Insufficiency.

1. **Mention Other Drugs Which Should Not Be Withdrawn/Stopped Abruptly:**

Beta -- blockers, Clonidine, Anti-epileptic Drugs, Alcohol, Benzodiazepines, Opioids, CNS Stimulants Like Cocaine, Amphetamine, Methamphetamine.

1. **What Is The Line Of Management?**

Acute Adrenal Insufficiency Is Treated By IV Hydrocortisone & IV Isotonic Saline In Glucose

Solution. Any Patient Who Has Received Steroids For > 2 To 3 Weeks Should Be Put On A Scheme Of Gradual Withdrawal.

**PH 4.2 DEMONSTRATE THE EFFECTS OF DRUGS ON BP USING CAL**

**GRAPH NO:3**

**1. Explain the effect of adrenaline and noradrenaline on blood pressure and heart rate?**

Adrenaline is an agonist at **α1 ,α2 , β1 ,β2 ,β3** receptors.

Rapid i.v. pharmacological dose produces biphasic response on BP i.e initial

rise followed by fall in BP. At higher concentrations, adrenaline produces rise in

BP by dominant action of alpha and beta1 receptors (**α**  is predominant & sensitive at higher concentrations).

**β1**--- positive inotropic, positive chronotropic effect which results in increased cardiac output and increased systolic BP.

**α1 ,α2** (post junctional) ---- vasoconstriction of arterioles resulting in increase in peripheral vascular resistance & vasoconstriction of veins resulting increased venous return and increased cardiac output.

As the concentration falls , **α**  action wanes but **β2** action persists and dominates which leads to vasodilatation of blood vessels(Skeletal muscle, abdominal viscera, coronary) and decreased peripheral vascular resistance and decreased diastolic BP. However The mean arterial pressure is not elevated by adrenaline.

Epinephrine increases the heart rate by acting directly on **β1** receptors of myocardium.

Norepinephrine has good agonistic action at **α1 ,α2 , β1 ,β3** receptors with poor **β2** effect. Hence Norepinephrine increases both systolic (**β1**) and diastolic BP(**α)**. So the mean arterial pressure is increased.

But Norepinephrine reduces heart rate. Raised MAP produces compensatory reflex vagal activity, overcoming direct cardiac stimulant activity of norepinephrine.

**2) Explain iso- prenaline effect on BP and heart rate?**

Isoprenaline is an agonist at  **β1 and β2** receptor. Isoprenaline produces fall

in diastolic BP by **β2** mediated vasodilatation. Mean arterial pressure also

falls. Isoprenaline increases heart rate by direct stimulation of **β1** receptors

of myocardium.

**3) Enumerate 2 therapeutically used vasopressors and their indications?**

* Mitodrine and droxidopa used in orthostatic hypotension.
* Norepinephrine used in life threatening hypotension following spinal

anaesthesia,blood transfusion reactions and septic shock.

**4) Name a vasopressor used along with LA. Why it is added?**

Adrenaline is added with Local anaesthetics .

Why ?

* The duration of anaesthesia is prolonged by preventing systemic absorption of local anaesthetic.
* Systemic toxicity of local anaesthetic is also reduced.
* Local bleeding is reduced.

**5) What is the effect of adrenaline ,noradrenaline and isoprenaline on blood**

**pressure & heart rate after giving propranolol. Explain?**

Propranolol is a non selective beta blocker. After giving Propranolol,

* **β2** mediated fall in BP produced by adrenaline is blocked. There is only

rise in BP(**α** action). The heart rate is also reduced due to blockade of

**β1** receptors.

* In case of noradrenaline, there is no change in BP & HR because rise in BP is mediated by **α** receptors.
* Propranolol also blocks the fall in diastolic BP ( **β2**) produced by isoprenaline. So BP remains unchanged. Blockade of  **β1** action of isoprenaline in the heart ,reduces the heart rate

**GRAPH NO 4:**

1. **Explain the effects of Ach, Histamine, Mepyramine on blood pressure of dog**

Ach – agonist at muscarinic & nicotinic receptors.

It reduces both systolic & diastolic pressure by :

**M2** receptor (Gi /Go ) action --Negative chronotropic & inotropic---↓ COP & ↓Systolic BP

**M3** receptor ( Gq ) action On vascular Endothelial cells--->Ca2+ --calmodulin dependent activation of endothelial NO synthase ---> release of NO which diffuses into adjacent vascular smooth muscle causing vasodilatation & ↓diastolic BP.

Histamine----stimulate H1 & H2 receptors(Gq & Gs respectively)on vascular smooth muscles, causing vasodilatation & fall in diastolic BP with compensatory increase in heart rate.

Mepyramine --- Selective H1 antagonist. Does not produce any change In BP . It blocks the effect of Histamine & not Ach & Adr.

**2. Enumerate 4 vasodilators/vasodepressor & their indications**

calcium channel blockers-- Nifedipine, Amlodipine used in hypertension

ACE inhibitors --- Captopril, Enalapril, used in CHF, Hypertension

Alpha blockers--- Pheochromocytoma, BPH

Hydralazine- -- Eclampsia.

**3 .Explain why Ach produces both decrease in BP &HR, But Histamine produces only fall in blood pressure associated with increased HR?**

Ach--- ↓BP & ↓ HR. The reflex baro- receptor mediated increase in heart rate is masked by direct cardiac depressant action on Ach. The vagomimetic action on SA node results in fall in BP & HR.

Histamine--↓ BP& ↑HR. The increase in heart rate is by reflex baro-receptor mediated increase in sympathetic activity ( Masks direct myocardial stimulant action of Histamine)

**4. Explain why Mepyramine blocks the effect of Histamine & not Ach &**

**Adrenaline**

Mepyramine-- It is a Selective H1  antagonist. Hence it can only block the effect of histamine and not Ach/Adrenaline.

**5. What is the interaction between Histamine & Adrenaline**

They have opposite effect on the same physiological function by acting on different receptors. Histamine produces Bronchoconstriction by ↑ H1  receptors & Vasodilatation by acting on both H1 & H2 receptors in blood vessels.

Adrenaline produces bronchodilatation by stimulating ( **β2**) & vasoconstriction by stimulating  **α1 ,α2**  receptors. This is called as Physiological antagonism.

Adrenaline is the physiological antagonist of histamine.

**GRAPH NO 5**

**1. Which drug produces biphasic response on BP?**

Adrenaline produces biphasic response on BP. Mechanism – see previous answer

**2. What is Dale's vasomotor reversal?**

After the administration of a non selective alpha blocker like phentolamine, adrenaline produces only delayed fall in BP **ie β₂** action remains but **α** action is blocked. The biphasic response is converted to monophasic response. This phenomenon is known as Vasomotor reversal of Dale.

**3. Enumerate 4 selective ά₁ blockers and their uses.**

Alfuzosin,Terazosin, Prazosin, Doxazosin and Tamsulosin

They are used in Benign prostatic hyperplasia, Hypertension &Peripheral vascular diseases.

**4. Enumerate 2 non-selective ά blocker and their uses**

Phentolamine is used :

* In hypertensive crisis following abrupt clonidine withdrawal or ingestion of tyramine containing foods during use of non selective MAO inhibitors
* For reversing the duration of local anesthesia
* To prevent dermal necrosis after the inadvertent extravasation of an alpha receptor agonist
* Pseudo obstruction of bowel
* Male sexual impotence (PIPE therapy)

Phenoxybenzamine is used in pheochromocytoma

**5. What is the effect of adrenaline, nor adrenaline and Isoprenaline after giving Phentolamine?**

ADRENALINE: Since the **ά** action is blocked, only **β₂** mediated fall in BP occurs

NOR ADRENALINE: Hypertensive effect mediated by **ά** receptors is blocked.

ISOPRENALINE: Fall in BP is maintained as there is no alpha action with isoprenaline.

**GRAPH 6**

**1. Explain the action of tyramine on BP**

Tyramine increases the Blood pressure of Anaesthetised dog. Tyramine is indirectly acting sympathomimetic drug. It acts by displacing NE from the adrenergic neurons (by facilitated exchange diffusion) which acts at alpha and beta adrenergic receptors of the effector cells & causes rise in BP.

**2.What happens on repeated administration? What is this phenomenon called?**

On repeated administration the effect decreases rapidly ( The initial response of rise in BP is not achieved ) This phenomenon is called tachyphylaxis or acute tolerance. Tachyphylaxis (Tachy-Fast; Phylaxis-Protection) is the rapid development of tolerance, progressive diminution in the response when a drug is repeated at short intervals.

**3. What is the underlying mechanism?**

As Tyramine acts by release of NE from adrenergic neurons, repeated administration within short intervals results in depletion of NE in the stores. Since the rate of synthesis is unable to match the rate of release at short intervals, there is diminution in response.

**4. Enumerate drugs that cause Tachyphylaxis**

Indirectly acting sympathomimetics like Ephedrine, Amphetamine, Nicotine.

**Difference between Tolerance & Tachyphylaxis**

|  |  |
| --- | --- |
| **TACHYPHYLAXIS** | **TOLERANCE** |
| Rapid ↓ response on repeated doses over a short period of time. It is an acute form of acquired tolerance. | Larger dose required to produce the same effect which was originally obtained at lower dose. |
| Develops rapidly within few minutes to few hours. | Develops slowly in days to months. |
| Large dose of the drug may not restore the effect. Effect is rate sensitive i.e withholding the drug for a short period restores the effect. | Effect is restored when large dose is given. |
| Eg:Tyramine,Ephedrine, Amphetamine  Nicotine. | Eg:Benzodiazepines,Barbiturates,Opioids,  Ethanol. |
| Due to depletion of NE in stores due to repeated administration of drug. | **PK or disposition tolerance:**  ↑rate of metabolism, changes in distribution, absorption & excretion on repeated administration.  **PD tolerance:**  Desensitization or down regulation of receptors.↓ efficiency of receptor coupling to signal transduction pathway.  **Learned or behavioral tolerance**:  ↓ in effect due to compensatory mechanisms. |

**GRAPH 7:**

**1.What is the effect of Ach on BP before atropinisation? Explain the MOA.** Before atropinisation Ach produces fall in BP

Ach – agonist at muscarinic & nicotinic receptors. It reduces both systolic & diastolic pressure by :

M2 receptors (Gi /Go ) action -->Negative chronotropic &negative inotropic--->

↓ COP & ↓Systolic BP

M3 receptors ( Gq ) action On vascular Endothelial cells---> Ca2+-calmodulin dependent activation of endothelial NO synthase ---> release of NO which diffuses into adjacent vascular smooth muscle causing vasodilation & ↓diastolic BP.

**2. What is the effect of Atropine on BP?**

No change in BP .

**3. What is the effect of Ach in low & high doses after atropinisation? Explain**

After giving atropine, Ach at low dose of 50microgram does not produce fall in BP because M3 receptors in blood vessels are blocked by atropine.

After atropinisation, Ach at high dose of 5mg produces rise in BP.

At very high dose. Ach directly stimulate the Nn receptor in Autonomic ganglia as well as adrenal medulla, releasing NA & Adr respectively which act upon α & β receptors to increase BP

**4.What are the effects of Ach before and after administration called?**

Before- muscarinic effect

After- nicotinic effect

**5. Enlist 2 therapeutic uses of Atropine**

a) Organophosphorus compound poisoning

b) Heart block