
REFERENCE GUIDE
FOR THE FOREIGN
PHARMACY
LICENSING EXAM
THEORY

(Edition II)

SECOND EDITION 2007-2008

MANAN H. SHROFF

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FOR THE FOREIGN
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Dedicated To
Krishna

PREFACE:

I am very pleased to introduce the “Reference Guide for the Foreign Pharmacy Licensing Exam - Theory, Second Edition.” I have made every attempt to cover as much of the course as possible, which is outlined in the new FPGEE syllabus for 2006-2007. In this second edition, I have added a few new topics as well as some more detailed information regarding existing topics. The new detailed “Organic Chemistry” and “Structure Activity Relationship” chapters will help students to answer chemical structure-based questions on the FPGEE exam. As per the new syllabus, I have also added detailed explanations about microbiology and pathophysiology in this second edition. I would recommend that students read our other publications, including “FPGEE Questions and Answers Second Edition,” “FPGEE Pharmacy Management and Pharmacoeconomic - Theory” and “FPGEE Pharmacy Management and Pharmacoeconomic - Questions and Answers” to achieve competitive scores on the FPGEE exam.

I wish you much success.

Best of luck,

Manan H. Shroff

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**PHARMACEUTICAL SERVICE MANAGEMENT
&
SOCIAL AND BEHAVIORAL SCIENCES**

1-Pharmacy Law

A PURE FOOD AND DRUG ACT OF 1906

- * Congress passed this law in 1906 to protect people from unsanitary and poorly labeled food.

B FOOD, DRUG AND COSMETIC ACT OF 1938

- * This law suggests that no new drug can be marketed until proven safe by the FDA for public use.

C DURHAM HUMPHREY AMENDMENT OF 1951

- * This law is also known as “Prescription Drug Amendment”.
- * It differentiates between prescription and OTC drugs.
- * It also authorizes oral prescriptions and prescription refills.
- * It suggests that each drug should be labeled “Caution: Federal law prohibits dispensing without a prescription.”

D KEFAUVER HARRIS AMENDMENT OF 1962

- * It is also known as the “Drug Efficacy Amendment”.
- * This law indicates that new approved drugs must be safe as well as effective.
- * It also establishes Good Manufacturing Practice requirements.

E MEDICAL DEVICE AMENDMENT OF 1976

- * This law passed in 1976, and includes:

- I The classification of medical devices
- II Safety and efficacy of medical devices

F ORPHAN DRUG ACT OF 1983

- * This law was passed for orphan drugs (drugs for diseases that affect very few people). Congress passed this act to provide tax relief and other incentives for the manufacturers to develop and market orphan drugs.

G DRUG PRICE COMPETITION AND PATENT TERM RESTORATION ACT OF 1984

- * This law is also known as Waxman Hatch Amendment.
- * This law was passed to make generic drugs more readily available to the public.
- * This law also provides more incentive to innovative pharmaceutical companies and encourages them to develop new drugs.

H NATIONAL DRUG CODE NUMBER (NDC)

- * The NDC generally consists of ten to eleven letters.
- I The first four characters indicate the name of the manufacturer or distributor.
II The middle four characters identify the drug name and strength.
III The last two characters identify the package.

H OVER THE COUNTER DRUG

- * The FDA generally classifies drugs into three categories in final monograph.
- I Category I : It includes ingredients generally considered safe, effective and not misbranded.
II Category II : It includes ingredients that are not considered safe, effective and are misbranded.
III Category III : It includes ingredients for which data are insufficient to permit the classification.

I PATIENT PACKAGE INSERT

- * The FDA passed this law in 1970 that states certain drugs require a Patient Package Insert (PPI) indicating the uses, risks and precautions of such drugs. The list of such drugs are :
- * Isotretinoin
- * Oral contraceptives
- * Isoproterenol
- * Ticlopidine
- * Progesterone
- * Estrogen
- * Intrauterine device

J OBRAACT OF 1990

- * It is known as the Omnibus Budget Reconciliation Act of 1990. It requires that pharmacists must offer a patient counseling.

K THE FDA EMPLOYSA TWO LETTER CODING SYSTEM FORTHERAPEUTIC EQUIVALENCE OF DIFFERENT DRUGS

- * AA: Drugs that are available in conventional dosage forms and have no bioequivalence problems.
- * AT : Topical drugs that meet bioequivalence standards.
- * AB: Drugs meeting the necessary bioequivalence requirement.
- * BC : Drugs in extended release dosage form with bioequivalence issues.
- * BT: Topical drugs with bioequivalence issues.
- * BX: Drugs for which adequate information is not available to determine the bioequivalency.

L POISON PREVENTIONACT

- * This law was implemented to prevent the death of children from accidental poisoning. This act was passed in 1973. It indicates that all dispensed drugs must be required to be in a child proof container. Drugs exempt from this law are :
- * Sublingual dosage form of nitroglycerine
- * Sublingual and chewable form of Isosorbide dinitrate (less than 10mg)
- * Cholestyramine powder
- * Methylprednisolone tablets (less than 84 mg)
- * Mebendazole tablets (less than 600 mg of drug)
- * Potassium supplements (unit dose form)
- * Erythromycin ethyl succinate (liquid and granules not more than 8 gm of drug)
- * Colestipol in powder form
- * Erythromycin ethyl succinate (tablets no more than 16 gm of drug)
- * Pancrelipase preparations
- * Prednisone (tablets no more than 105 mg)
- * Oral contraceptives

M CONTROLLED SUBSTANCE ACT

- * CSA = Controlled Substance Act
- * DEA = Drug Enforcement Administration

- * The attorney general of United States has authority to place a drug into one of the five categories of schedule controlled drugs.

- * The controlled drug can be classified into five different classes according to the potential for abuse.

- * The potency of abuse of controlled drugs should be I > II > III > IV > V. Schedule I should be considered the highest potential for abuse and schedule V the lowest potential for abuse.

SCHEDULE II CONTROLLED DRUGS

- * Cannot be refilled in any circumstances.

- * The partial filling of this class of drugs should be done within 72 hours of initial filling.

- * The DEA 222 order form is required to order this class of drug.

Controlled II drugs:

1	Ritalin	=	Methylphenidate
2	Dexedrine	=	Dextroamphetamine
3	Adderall	=	Amphetamine + Dextroamphetamine
4	Ms Contin	=	Morphine sulfate
5	Concerta	=	Methylphenidate
6	Oxycontin	=	Oxycodone
7	Oxy IR	=	Oxycodone
8	MS IR	=	Morphine sulfate
9	Roxanol	=	Morphine sulfate
10	Roxicet	=	Oxycodone + APAP
11	Percocet	=	Oxycodone + APAP
12	Demerol	=	Meperidine
13	Dilaudid	=	Hydromorphone
14	Dolophine	=	Methadone
15	Duragesic	=	Fentanyl
16	RMS unisert	=	Morphine sulfate
17	Percodan	=	Oxycodone + Aspirin
18	Tylox	=	Oxycodone + APAP

DISPENSING OF CIII CIV and CV, DRUGS

- * Cannot be refilled more than five times.
- * Cannot be filled for the prescription older than six months.
- * Do not require any DEA 222 form to fill the order.

Controlled III drugs:

- * Lortab = Hydrocodone + APAP
- * Tylenol # 3 = Acetaminophen + Codeine
- * Fioricet / Codeine = Butalbital + APAP + Caffeine + Codeine
- * Fiorinal / Codeine = Butalbital + Aspirin + Caffeine + Codeine
- * Vicodin = Hydrocodone

Controlled IV drugs:

- * Talwin = Pentazocine
- * Talwin NX = Pentazocine + Naloxone
- * Talacen = Pentazocine + APAP
- * Talwin compound = Pentazocine + Aspirin
- * Darvon = Propoxyphene
- * Darvon compound = Propoxyphene + Aspirin
- * Darvocet = Propoxyphene + APAP
- * Equanil = Meprobamate
- * Librium = Chlordiazepoxide
- * Valium = Diazepam
- * Serax = Oxazepam
- * Tranxene = Clorazepate
- * Dalmane = Flurazepam
- * Klonopin = Clonazepam
- * Ativan = Lorazepam
- * Prosom = Estazolam
- * Restoril = Temazepam
- * Halcion = Triazolam
- * Xanax = Alprazolam
- * Ambien = Zolpidem
- * Cylert = Pemoline

Controlled V drugs:

- * Buprenex = Buprenorphine
- * Lomotil = Diphenoxylate

EMERGENCY DISPENSING OF CII DRUGS REQUIRES CERTAIN CONDITIONS

- * The dispensing quantity of the drug should be limited to cover emergency situations.
- * The prescriptions is immediately reduced to a written prescription by the pharmacist with complete information about the ordering physician's name, address, DEA and telephone number.
- * The prescriber must send a written prescription within seven days from an authorized emergency prescription.

FAXING OF CII DRUGS

- * A pharmacist can fill the CII prescription by using a fax prescription under the condition that before dispensing of the drug one must receive the original prescription. The faxing of CII prescriptions should be considered the original CII prescription only under the following conditions:
 - I When a prescription is faxed by a prescriber that needs to be compounded and administered to a patient via I.V., S.C., I.M. or intraspinal infusion.
 - II When a prescription is faxed by prescriber for a patient living in long-term care institution.
 - III When a prescription is faxed by a prescriber for patient residing in a hospice certified by Medicare.

METHADONE DISPENSING

- * Methadone can be used for pain as well as for treatment of drug detoxification. A pharmacy not registered with the DEA narcotic program cannot dispense Methadone for treatment of drug detoxification.

THE FILING METHOD FOR CONTROLLED SUBSTANCES

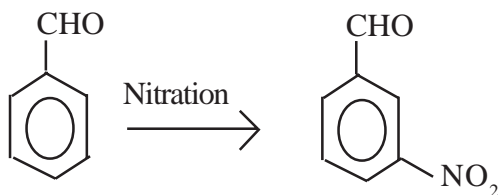
- 1 One file for CII
Second file for CIII, CIV and CV
Third file for non controlled substances
- 2 One file for CII
Second file for CIII, CIV , CV and non-controlled substances
- 3 One file for CII, CIII, CIV and CV with the condition that all III, IV and V should be previously marked "C" with red ink on face of the prescription, so that it can be easily differentiated from CII.
Second file of non-controlled substance.

- * The substituent groups that offer meta isomers are known as meta-director.

Meta-directors:

- | | |
|--|----------------------|
| * -NO ₂ | * -SO ₃ H |
| * -CHO | * -CN |
| * -N(CH ₃) ₃ ⁺ | * -COOH |

Nitration of benzaldehyde:



Benzaldehyde

M-Nitrobenzaldehyde

- * In the above example, nitration of benzaldehyde will yield meta nitro benzaldehyde because the -CHO group present in the ring is a meta director.

Organic Chemistry and Structures

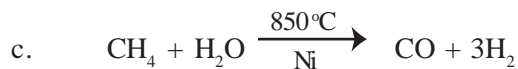
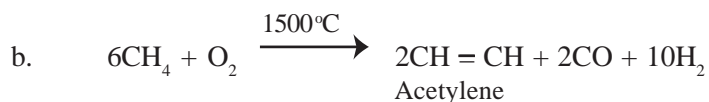
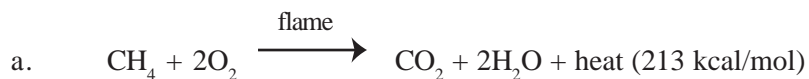
* The largest and most significant is that class of organic compounds known as hydrocarbons; chemical compounds whose molecules are made up of nothing but carbon and hydrogen atoms. There are two basic varieties of hydrocarbons, distinguished by shape: aliphatic and aromatic. The first of these forms straight or branched chains, as well as rings, while the second forms only benzene rings. Within the aliphatic hydrocarbons are three varieties: those that form single bonds (alkanes), double bonds (alkenes), and triple bonds (alkynes.)

1. **Alkanes:** The alkanes are also known as saturated hydrocarbons. The formula for any alkane is C_nH_{2n+2} , where n is the number of carbon atoms.

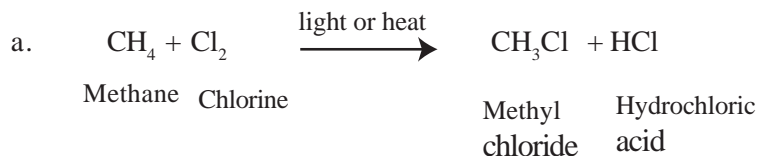
Name	Structures
Methane	CH_4
Ethane	C_2H_6
Propane	C_3H_8
Butane	C_4H_{10}
Pentane	C_5H_{12}
Hexane	C_6H_{14}
Heptane	C_7H_{16}
Octane	C_8H_{18}

Important Reactions of Alkanes:

1. **Oxidation (Heat of combustion):**



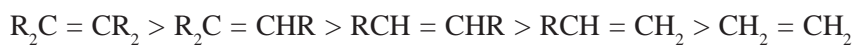
2. **Chlorination:**



2. **Alkenes:** The alkenes are known as unsaturated hydrocarbons. They contain one or more double bond per molecule. The formula for any alkane is C_nH_{2n} , where n is the number of carbon atoms.

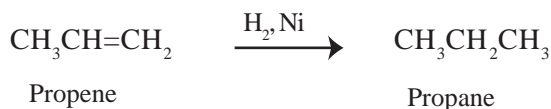
<u>Name</u>	<u>Structures</u>
Ethene	$CH_2 = CH_2$
Propene	$CH_3CH=CH_2$
1-Butene	$CH_3CH_2CH=CH_2$
2-Butene (cis or trans)	$CH_3CH=CHCH_3$
1-Pentene	$CH_3CH_2CH_2CH=CH_2$
2-Pentene	$CH_3CH_2CH = CHCH_3$

Stability of Alkenes:

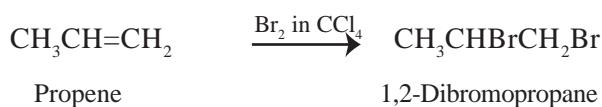


Important Reactions of Alkenes:

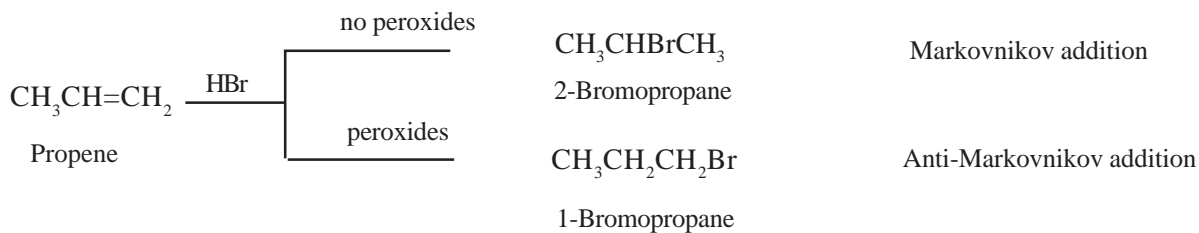
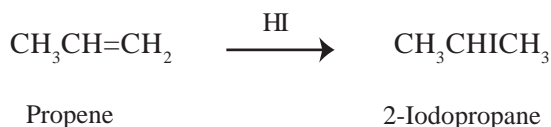
1. **Addition of hydrogen:**



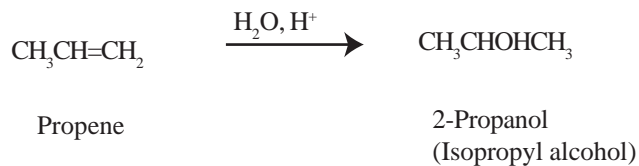
2. **Addition of halogens:**



3. **Addition of hydrogen halide:**



4. **Addition of water:**

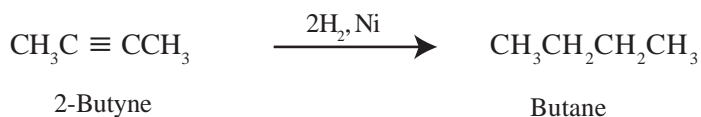


3 **Alkynes:** The alkenes are known as unsaturated hydrocarbons. They contain one or more triple bond per molecule. The formula for any alkane is $\text{C}_n\text{H}_{2n-2}$, where n is the number of carbon atoms.

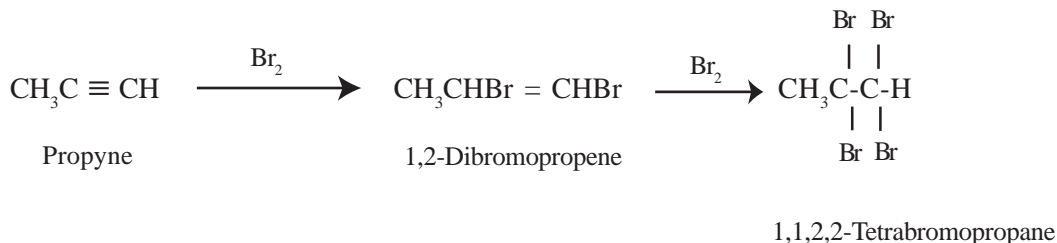
<u>Name</u>	<u>Structures</u>
Acetylene	$\text{CH} \equiv \text{CH}$
Propyne	$\text{CH}_3\text{C} \equiv \text{CH}$
1-Butyne	$\text{CH} \equiv \text{CCH}_2\text{CH}_3$
2-Butyne	$\text{CH}_3\text{C} \equiv \text{CCH}_3$
1-Pentyne	$\text{CH} \equiv \text{C}(\text{CH}_2)_2\text{CH}_3$
2-Pentyne	$\text{CH}_3\text{C} \equiv \text{CCH}_2\text{CH}_3$

Important Reactions of Alkynes:

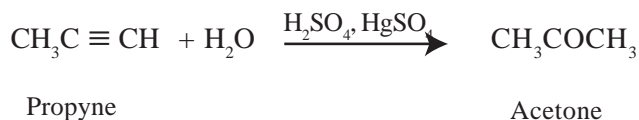
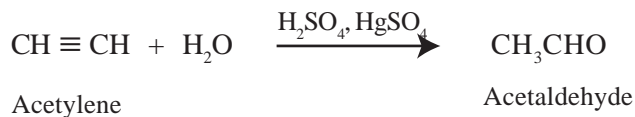
1. **Addition of hydrogen:**



2. **Addition of halogens:**



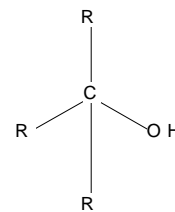
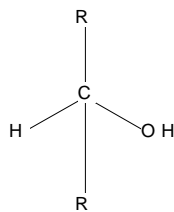
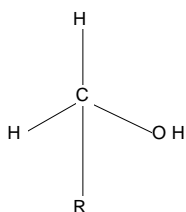
3. **Addition of water:**



4. **Alcohol:** Alcohols are compounds of the general formula ROH, where R is any alkyl or substituted alkyl group.

Classification of Alcohols:

* An alcohol is classified as primary, secondary, or tertiary according to the kind of carbon that bears the -OH group.



Primary (1 degree)

Secondary (2 degree)

Tertiary (3 degree)

Name

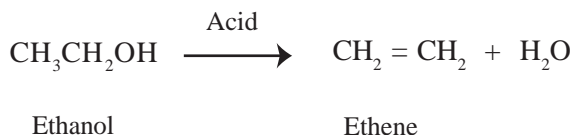
Methanol
Ethanol
1-Propanol
2-Propanol
1-Butanol
2-Butanol
1,2-Ethanediol

Structures

CH_3OH
 $\text{CH}_3\text{CH}_2\text{OH}$
 $\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$
 $\text{CH}_3\text{CHOHCH}_3$
 $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$
 $\text{CH}_3\text{CHOHCH}_2\text{CH}_3$
 $\text{CH}_2\text{OHCH}_2\text{OH}$

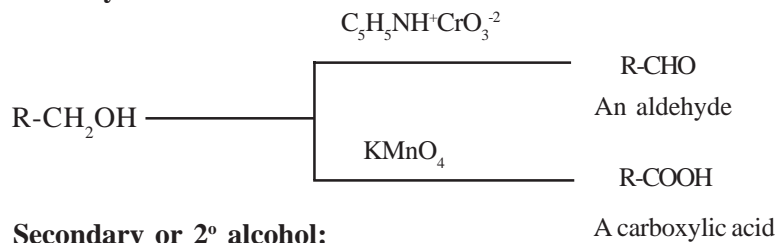
Important Reactions of Alcohols:

1. **Dehydration:**

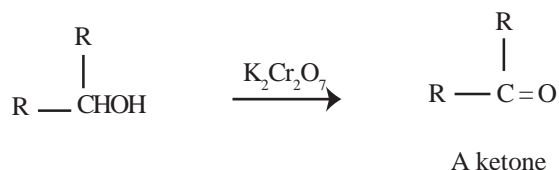


2. **Oxidation:**

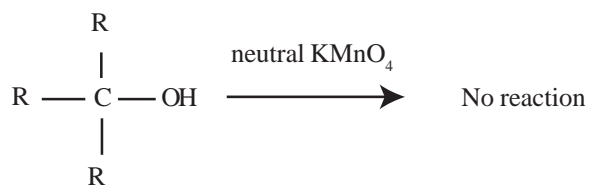
A. **Primary or 1° alcohol:**



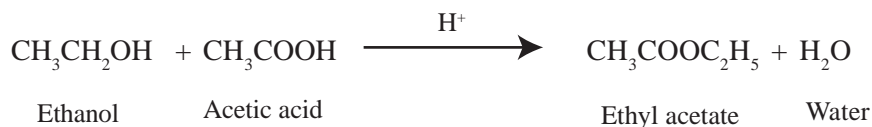
B. **Secondary or 2° alcohol:**



C. **Tertiary or 3° Alcohol:**



3. **Alcohol and Ester formation:**



5. **Ethers:** Ethers are compounds of the general formula R-O-R, Ar-O-R, or Ar-O-Ar. (Ar is phenyl or some other aromatic group).

Name	Structures
Dimethylether	CH ₃ -O-CH ₃
Diethylether	C ₂ H ₅ -O-C ₂ H ₅
Di-n-propyl ether	CH ₃ CH ₂ CH ₂ -O-CH ₂ CH ₂ CH ₃
Di-n-butyl ether	CH ₃ CH ₂ CH ₂ CH ₂ -O-CH ₂ CH ₂ CH ₂ CH ₃

4. **ESRD:** When dialysis becomes necessary to sustain a patient's life, it is defined as ESRD (End Stage Renal Disease).

* **The major causes of ESRD:**

Disease	%
Diabetes	33
Hypertension	28
Glomerulonephritis	12
Cystic kidney disease	3
Interstitial nephritis	3

* **Factors affecting progression of CRF:**

- * The progression of chronic renal disease occurs over months to years. Factors that affect CRF are:

1. Hypertension
2. High-protein diet
3. Dyslipoproteinemias

1. **Hypertension:**

- * Renal injury normally increases single-nephron GFR as one of the adaptive procedures since this mechanism helps the body to maintain hemostasis.

- * However, the increased perfusion of residual nephrons to maintain hemostasis may produce the deleterious effect on the remaining nephrons.

- * Hypertension is directly associated with increased single-nephron glomerular filtration rate and therefore untreated systematic hypertension may lead to CRF.

2. **High-protein diet:**

- * Dietary protein ingestion also increases single-nephron GFR.

- * Restriction of dietary protein and phosphorus may delay the progression of CRF.

3. **Dyslipoproteinemia:**

- * Renal disease or failure normally alters the metabolism of lipoproteins, and this may increase the serum triglyceride concentration in patients.

- * Although reduction of this elevated serum triglyceride by antihyperlipidemic drugs may not help in delaying the progression of CRF, it may prevent cardiovascular diseases such as atherosclerosis and systematic hypertension.

The relationship between other diseases/conditions and CRF:

1. Analgesic nephropathy
2. Lithium nephropathy
3. Sodium/fluid retention
4. Hyperkalemia
5. Metabolic acidosis
6. Calcium and phosphate abnormalities
7. Diabetes
8. Diabetic nephropathy

Analgesic nephropathy:

- * It is characterized by renal papillary necrosis as primary lesion and chronic interstitial nephritis as a secondary lesion.
- * Analgesic nephropathy is a part of the analgesic syndrome.
- * The prolonged use of acetaminophen or NSAIDs may result into analgesic nephropathy.

Management:

- * Avoid use of NSAIDs and acetaminophen
- * High fluid intake

Lithium nephropathy:

- * The prolonged use of lithium may cause a decline in renal ability to concentrate urine and GFR.
- * Nephrotoxic risk is higher with elevated lithium serum concentrations.

Management:

- * Avoid lithium containing medication if possible
- * Monitor serum lithium concentration closely.

Sodium/water retention (edema):

- * Patients with CRF may retain large amounts of sodium and water.
- * This may lead to high blood pressure, weight gain, 2+ pedal edema, and pulmonary congestion.

Management:

- * Restrict sodium and water consumption

4. **Hyperkalemia:**

- * The normal potassium concentration in serum is 3.5 to 5 mEq/L, which is well maintained during chronic renal failure by the adaptive mechanism of body.
- * However, an exogenous potassium load in the form of potassium-containing medications or supplements, an endogenous potassium load in case of hemolysis of RBC or rhabdomyolysis, and metabolic or respiratory acidosis may elevate serum potassium concentrations.

Management:

- * Hyperkalemia may lead to cardiac arrhythmia. This can be prevented by the administration of calcium in the form of I.V. calcium gluconate. Calcium does not have any effect on the serum potassium concentration, however it will protect the myocardium from the dangerous effects of potassium.
- * An I.V. administration of sodium bicarbonate may also help in reducing an elevated potassium concentration. It encourages the movement of extracellular potassium ions back into cells.
- * The I.V. administration of glucose and insulin is another method to shift extracellular potassium into cells.
- * Insulin stimulates potassium uptake by skeletal muscles and hepatic cells. Glucose is given simultaneously to avoid hypoglycemia.
- * The use of calcium gluconate, sodium bicarbonate, glucose and insulin have no effect on reducing the total body load of potassium. They just shift potassium concentrations from extracellular region to the intracellular region. Sodium polystyrene sulfonate is a cation exchange resin which exchanges sodium ions for potassium ions in the intestinal tract, and reduces the total body load of potassium.

Metabolic acidosis:

- * A high blood carbon dioxide content, chloride and potassium concentration is normally observed in patients with CRF. This may lead to metabolic acidosis in individuals suffering from renal diseases.

Management:

- * Patients should receive I.V. sodium bicarbonate to correct metabolic acidosis.

Electrolytes and metabolic disturbances:

- * Hypermagnesemia, hyperphosphatemia and hyperuricemia are reported with CRF patients.
- * Severe hypermagnesemia may cause nausea, vomiting, cardiac function impairment, lethargy and confusion.
- * Hyperphosphatemia and secondary hyperparathyroidism play an important role in the development of osteopathy associated with CRF patients. An elevated serum concentration of phosphate may reduce the serum concentration of ionized calcium, and this may stimulate the release of PTH. Persistent hyperphosphatemia also reduces calcium absorption from the gut. This will lead to severe hypocalcemia in patients suffering from chronic renal failure. To counteract a low serum concentration of calcium, the body stimulates the mobilization of bone calcium to blood, which leads to a softening of bones and osteoporosis.
- * Hyperuricemia is also reported due to diminished urinary excretion of uric acid.

Management:

- * Avoid magnesium, phosphate containing antacids and laxatives.
- * Administer aluminum containing antacids, calcium carbonate, calcium citrate, and calcium acetate to reduce the elevated level of phosphate.

Anemia:

- * Patients with CRF inevitably develop anemia.
- * The principal cause of this anemia is a decreased production of erythropoietin in the kidneys. This may lead to a reduced formation of erythrocytes.
- * The RBC life span is reduced to 30 to 60% under normal levels in CRF patients.
- * Iron, folic acid and vitamin B12 deficiency may also lead to anemia in CRF patients.
- * Blood loss due to impaired hemostasis of uremia also contributes to iron deficiency anemia.
- * Aluminum intoxication due to overingestion of aluminum containing medication may also lead to anemia in CRF patients.

Management:

- * Correct the anemia by administration of vitamin B12, iron and folic acid supplements.
- * By administering recombinant human erythropoietin (Epoen) in CRF patients.
- * By avoiding aluminum containing antacids and related products.
- * By administering hemostatic agents such as cryoprecipitate or DDAVP to prevent uremia induced bleeding.

Diabetes:

- * As CRF progresses, the serum glucose concentration is reduced as well as the insulin requirement.
- * In healthy individuals, six to eight units of insulin are degraded by the kidneys every day. In the case of CRF, less insulin is cleared, and its metabolic half-life is increased.
- * This may provide more insulin to work on available glucose and may lead to severe hypoglycemia.

Management:

- * Monitor the blood glucose concentration.
- * Adjust dose of antidiabetic drugs.

Diabetic nephropathy:

- * It is defined as a urinary albumin excretion rate of 300 mg/24 hours or more in a person with diabetes in the absence of other renal diseases.
- * It accounts for nearly 50% of end stage renal disease.

Management:

- * Monitor and maintain the blood glucose concentration.
- * Avoid high dietary protein intake.
- * Control systematic hypertension.

38-Cystic Fibrosis

Definition: Cystic fibrosis is a genetic disorder generally observed in infants. It is generally associated with dysfunction of the cystic fibrosis transmembrane regulator known as CFTR and disruption of normal transmembrane flow of chloride ion through chloride channel.

The magnitude of disease can be reduced by treating

I **Pulmonary infection**

II **Pancreatic insufficiency**

- * Pulmonary infection is generally caused by *P. aeruginosa*, *S. aureus* and *H. influenza*.
- * Ceftazidime, Tobramycin and Ticarcillin are highly effective against *P. aeruginosa*.
- * Ticarcillin + K clavulanate is highly active against *S. aureus*, *H. influenza* and *P. aeruginosa*.
- * Aerolized Tobramycin (80 mg b.i.d. or tid) with I.V. Carbenicillin is a good choice for treatment of acute upper respiratory tract infection.
- * Prednisone is generally helpful for reducing inflammation during pulmonary infection.
- * Dornase-Alpha should be considered as a drug of choice to reduce viscosity of sputum. The degeneration of nuclei of neutrophils (neutrophil is present due to lung infection) is the principal source of DNA in sputum and contributes significant amount of viscosity to sputum.
- * Dornase-Alpha is an enzyme that helps in breakdown this DNA of nuclei of neutrophils and helps in reducing viscosity of sputum.
- * Deficiency of chloride ions in secretion will lead to desiccation of pancreatic secretion within pancreatic duct. This will promote the accumulation of secretory material within the pancreatic duct which then ultimately leads to obstruction of pancreas. Secretion of digestive enzymes also inhibits which leads to poor digestion of fats, proteins and carbohydrates. The supplement of enzymes from outside may help in solving the above problem to certain extent.
- * Pancreatic enzyme supplement may help patients in following ways:
 - I May help in weight gain.
 - II May minimize the problem of steatorrhea.
 - III May eliminate the problem of abdominal cramping and bloating.

* **List of Pancreatic enzymes supplements:**

Cotazym	Ultrase
Creon	Zymase
Pancrease	Viokase

39-Drugs and Their Specific Side Effects

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Abacavir	Ziagen	Severe hypersensitivity reactions, Life threatening hypotension and death.
*	Acarbose	Precose	Hypoglycemia, abdominal pain, flatulence and diarrhea
*	Abciximab	Reopro	Bleeding, thrombocytopenia
*	Zafirlukast	Accolate	Pulmonary angitis, diarrhea, headache, infection
*	Isotretinoin	Accutane	Contraindicated in pregnancy, depression, psychosis, pseudomotor cerebri, cheilitis, hypertriglyceridemia, hepatotoxicity
*	Acetaminophen	Tylenol	Hepatotoxicity
*	Fentanyl	Duragesic, Actiq	Life threatening hypoventilation
Biphosphonate derivatives			
*	Risedronate	Actonel	Hypocalcemia, infection, back pain, hypertension, nausea, depression, arthralgia
*	Pamidronate	Aredia	
*	Etidronate	Didronel	
*	Alendronate	Fosamax	
*	Tiludronate	Skelid	
*	Raloxifene	Evista	
*	Pioglitazone	Actos	Hypoglycemia
*	Amphetamine + Dextroamphetamine	Adderall	CNS stimulation, insomnia, palpitation restlessness
*	Doxorubicin	Adriamycin	CHF, tissue necrosis, impaired myocardial dysfunction

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Anagrelide	Agrylin	Bleeding
*	Methyldopa	Aldomet	Hemolytic anemia, liver impairment
*	Allopurinol	Zyloprim	Severe rash, renal failure, nausea and vomiting
*	Ace inhibitors		Hyperkalemia, dry cough, angioedema, contraindicated in pregnancy
*	ACE II receptor antagonists		Hyperkalemia, contraindicated in pregnancy
*	Aluminum hydroxide		Constipation, renal failure
*	Oral sulfonylurea agents		Hypoglycemia
	<u>Selective 5HT₁ receptor Agonist</u>		
*	Naratriptan	Amerge	Cardiac ischemia, angina, cerebrovascular syndromes
*	Almotriptan	Axert	
*	Sumatriptan	Imitrex	
*	Rizatriptan	Maxalt	
*	Zolmitriptan	Zomig	
*	Aminoglycosides		Ototoxicity, nephrotoxicity, nephrotoxicity and currarimimetic-effects
*	Clindamycin	Cleocin	Bloody diarrhea
*	Amiodarone	Cordarone	Hypotension, cardiogenic shock, hypothyroidism, hyperthyroidism
*	Tricyclic Antidepressant		Dryness of mouth, constipation, urinary retention, blurred vision
*	Calcium channel blocker		Hypotension, tachycardia

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Penicillin antibiotics		Anaphylactic reactions, pseudomembranous colitis
*	Amphotericin B	Fungizone	Hypokalemia, nausea, vomiting, chills, renal failure, multiple organ failure
*	Amprenavir	Agenerase	Severe and life threatening skin reactions, Steven Johnson syndrome. Contraindicated in infants and children due to presence of propylene glycol excipient.
<u>Serotonin 5HT₃ receptor antagonist</u>			
*	Dolasetron	Anzemet	Hypotension, severe bradycardia, heart block and cardiac abnormality
*	Granisetron	Kytril	
*	Ondansetron	Zofran	
*	Quinolone group of antibiotics		CNS stimulation, seizure, nausea dizziness
*	Leflunomide	Arava	Contraindicated in pregnancy, diarrhea, elevated liver enzymes, alopecia and rash
*	Donepezil	Aricept	Hypertension, chest pain, vasodilation insomnia, nausea and diarrhea
*	Anticholinergic agents		Dryness of mouth, constipation, blurred vision and urinary retention
*	Sulfonamide		Steven Johnson Syndrome, agranulocytosis, hemolytic anemia, toxic epidermal necrolysis and agranulocytosis
*	Bromocriptine	Parlodel	Pulmonary fibrosis, hypotension, dyskinesia

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	<u>Bile acid binding Resin</u>		
*	Cholestyramine	Questran	Constipation, heartburn, nausea, vomiting
*	Colestipol	Colestid	
*	Colesevelam	Welchol	
*	Loop diuretics		Hypokalemia, electrolyte imbalance, ototoxicity, nephrotoxicity
*	Bupropion	Wellbutrin	Seizure, bulimia, anorexia nervosa insomnia
*	Capsfungin	Cancidas	Liver failure, nausea
*	Carbamazepine	Tegretol	Aplastic anemia, agranulocytosis, diplopia, blurred vision, nystagmus, ataxia
*	Phenytoin	Dilantin	Nystagmus, ataxia, dysarthria and lethargy, gingival hyperplasia
*	Ethacrynic acid	Edecrin	Diarrhea, renal failure
	<u>Alpha-1 blocker</u>		
*	Prazosin	Minipress	Syncope, lightheadness, dizziness palpitation
*	Doxazosin	Cardura	
*	Terazosin	Hytrin	
*	NSAIDS		G.I. bleeding, gastric ulcer, renal impairment
*	<u>SSRI (Selective Serotonin Reuptake Inhibitors)</u>		
*	Fluoxetine	Prozac	Insomnia, yawning, dizziness, mania, somnolence, libido decrease,
*	Sertraline	Zoloft	
*	Paroxetine	Paxil	
*	Citalopram	Celexa	

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Cisplatin	Platinol	Nephrotoxicity, severe nausea and vomiting, neurotoxicity, ototoxicity, optic neuritis
*	Clozapine	Clozaril	Agranulocytosis
*	Clopidrogel	Plavix	Bleeding
*	Cilostazole	Pletal	Hypotension, contraindicated in CHF
*	Cidofovir	Vistide	Severe renal failure
*	Entacapone	Comtan	Nephrotoxicity, hypotension, syncope, hallucination and diarrhea
*	Warfarin	Coumadin	Bleeding
*	Ritonavir	Norvir	Nausea and vomiting
*	Indinavir	Crixivan	Hepatic cirrhosis, nephrolithiasis
*	Nelfinavir	Viracept	Diarrhea
*	Didanosine	Videx	Diarrhea, peripheral neuropathy
*	Zalcitabine	Hivid	Pancreatitis, peripheral neuropathy
*	Lamivudine	Epivir	Pancreatitis
*	Zidovudine	Retrovir	Anemia, granulocytopenia, pancreatitis
*	Stavudine	Zerit	Peripheral neuropathy
*	Nevirapine	Viramune	Severe rash
*	Delavirdine	Rescriptor	Rash
*	Lopinavir/Ritonavir	Kaletra	Pancreatitis
*	Cyclosporine	Neoral/Sandimmune	Nephrotoxicity, hypertension

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Metformin	Glucophage	Lactic acidosis, hypoglycemia
*	Enoxaprine	Lovenox	Bleeding
*	Erythromycin estolate	Ilosone	Cholestatic jaundice
*	Pramipexole	Mirapex	Falling asleep during activities
*	Ganciclovir	Cytovene	Anemia, granulocytopenia and thrombocytopenia
*	Dalteparin	Fragmin	Bleeding, neurological impairment
*	Tetracycline		Bone and teeth discoloration, fanconi like syndrome
*	Chloramphenicol	Chloromycetin	Aplastic anemia, gray baby syndrome severe bone marrow suppression
*	Vancomycin	Vancocin	Ototoxicity, nephrotoxicity, Red Neck syndrome
*	Pentamidine	Pentam, Nebupent	Severe hypotension
*	Valproic acid	Depakene	Hepatic failure, bleeding and G.I. irritation
*	Ethosuximide	Zarontin	Blood dyscrasia
*	Gabapentin	Neurontin	Ataxia, nystagmus, somnolence and dizziness
*	Dipyridamole	Persantine	Hypotension, tachycardia, bleeding, warm feeling, flushes and sweating
*	Doxorubicin	Doxil	CHF, flushing, shortness of breath, facial swelling, chills, headache, hypotension and severe myelosuppression
*	Oxybutynin	Ditropan	Dryness of mouth, urinary retention, constipation and blurred vision

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Selegiline	Eldepryl	Severe hypotension and psychomotor agitation
*	Lithium	Lithobid	Ataxia, slurred speech, muscle weakness, tremor
*	Antipsychotic		NMS, tardive dyskinesia, dystonia and drug induced parkinsonism
*	Ethambutol	Myambutol	Optic neuritis, optic neuropathy, color blindness, decreased visual activity
*	Minoxidil	Loniten	Hypertrichosis (excessive hair growth)
*	Misoprostol	Cytotec	Severe diarrhea, contraindicated in pregnancy
*	Finasteride	Proscar	Contraindicated during pregnancy
*	Flecainide	Tambacor	Ventricular tachycardia, CHF, severe negative inotropic effect
*	Foscarnet	Foscavir	Renal impairment, seizure
*	Tiagabine	Gabitril	Dizziness, lightheadness, somnolence, depression, confusion and asthenia
*	Itraconazole	Sporanox	Negative inotropic effect, CHF
*	Griseofulvin	Grifulvin	granulocytopenia, skin rash, urticaria, erythema multiform

HMG COA inhibitors

*	Fluvastatin	Lescol	Myopathy, rhabdomyolysis, myalgia diarrhea
*	Cerivastatin	Baycol	
*	Lovastatin	Mevacor	
*	Pravastatin	Pravachol	
*	Atrovastatin	Lipitor	
*	Simvastatin	Zocor	

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Nicotinic acid	Niacin	Flushing of the skin, pruritus, G.I. distress and liver toxicity
*	Infliximab	Remicade	Serious infections including sepsis and disseminated tuberculosis
*	Isoniazid	INH	Severe hepatitis, peripheral neuropathy
*	Methotrexate	MXT	Severe bonemarrow suppression, hepatotoxicity, nephrotoxicity, ulcerative stomatitis, lung disease, tumor lysis syndrome and diarrhea
*	Ticlopidine	Ticlid	Severe hematological abnormalities including agranulocytosis, neutropenia, aplastic anemia and TTP
*	Tramadol	Ultram	Seizure
*	Levetiracetam	Keppra	Neuropsychiatric adverse events including somnolence, fatigue, coordination difficulties, and behavioral abnormalities
*	Ketorolac tromethamine	Toradol	G.I. ulceration, bleeding, G.I. perforation, renal impairment and anaphylactic reactions
*	Linezolid	Zyvox	Severe myelosuppression including anemia, leukopenia, and thrombocytopenia
*	Mesoridazine	Serentil	Arrhythmia
*	Nateglinide	Starlix	Hypoglycemia
*	Ifosfamide	Ifex	Hemorrhagic cystitis, coma and confusion
*	Cyclophosphamide	Cytosan	Hemorrhagic cystitis, coma and confusion

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Paclitaxel	Taxol	Anaphylaxis and severe hypersensitivity reactions, hypotension, dyspnea and severe bonemarrow suppression specially neutropenia
*	Penicillamine	Cuprimine	Renal function impairment and severe hematological abnormalities
*	Tacrolimus	Prograf	Nephrotoxicity, severe infections and anaphylaxis reactions
*	Plicamycin	Mithracin	Severe thrombocytopenia
*	Pyrazinamide	PZA	Liver function impairment and hyperuricemia
*	Metoclopramide	Reglan	Depression, hypertensive crisis, tardive dyskinesia, extrapyramidal symptoms and Parkinsonian-like symptoms
*	Ropinirole	Requip	Hypotension, syncope, hallucination, falling asleep during activities and drowsiness
*	Propafenone	Rythmol	Hematological abnormalities, conduction disturbances, CHF
*	Carbidopa	Sinemet	Dyskinesia, dystonic reactions and nausea
*	Sucralfate	Carafate	Constipation
*	Hydroxychloroquine	Plaquenil	Retinopathy, ocular toxicities, irritability, nervousness and skeletal muscle myopathy
*	Topiramate	Topamax	Psychomotor slowing, difficulty in concentration and attention, speech or language problems, irritability and depression

	<u>Generic</u>	<u>Brand</u>	<u>Side effects/Contraindication</u>
*	Mycophenolate	Cellcept	Increases susceptibility to infections
*	Valacyclovir	Valtrex	Thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS)
*	Zileuton	Zyflo	Hepatic impairment, elevation of liver enzymes

BIOMEDICAL SCIENCE

40-Accidental Poisoning and Antidotes

- * Accidental poisoning is a problem of great public health significance. It is normally seen in young children due to ingestion of drugs or chemicals in the home.
- * AAPCC is defined as an American Association of Poison Control Center. It was established in 1983. The data collected by this system constitutes the largest body of data about poisoning exposures in the world.
- * The AAPCC has developed standards for region poisoning control centers and provides a process to evaluate a poison center's capabilities and designate centers.
- * According to the AAPCC database, the most frequent substance involved in accidental poisoning in young children is cleaning substances and the most frequent category of toxic substances reported fatalities is antidepressants.
- * **Factor affecting accidental poisoning:**
 1. Age
 2. Accidental proneness
 3. Location
 4. Accessibility
 5. Type of container
- 1. **Age:** Approximately two-thirds of poisonings that occur in children are accidental.
 - * The most critical age period is between 1 and 3 years. During this period, one-half of the poisonings occur.
- 2. **Accidental Proneness:** It is rare. Normally in this type, children treated for poisoning have had a history of having been involved in similar accidents.
 - * This may only occur when accident-prone situations or surroundings are easily accessible to young children.
- 3. **Location:** The majority of childhood accidental poisonings normally occur in the home.
 - * The most common areas for poisoning within the home are the kitchen, bathroom and bedroom.
 - * The most common areas for poisoning outside of the home are the garage and in automobiles.
 - * The highest incidence of accidental poisonings is in the late afternoon and around the dinner hour, or in the early morning hours.

4. **Accessibility:** Accessibility is the principal factor in accidental poisonings in young children. In about 75% of the cases, the materials involved in accidental poisonings have been left within reach of a child.
5. **Type of container:** The type of container also plays an important role in accidental poisoning. For example, a small quantity of gasoline, solvents in a soft drink bottle, cleaning solution, or paint has been transferred from the original container to a drinking glass or dish.

First Aid treatment for poisoning:

- * The first step is to remove the poison from all contact with eyes, skin or mouth.
- * Remove victim from contact with poisonous fumes or gases. Loosen all tight-fitting clothes.
- * Call the poison center immediately.
- * When administering active charcoal and ipecac together, it is advisable to induce vomiting by giving ipecac before administering activated charcoal, since latter may inactivate the ipecac syrup.

ANTIDOTES

- * Activated charcoal is classified as an effective, nonspecific antidote. It absorbs a large number of materials.
- * Below is the list of drugs/poisons and their antidotes.

<u>Drugs</u>	<u>Antidotes</u>
1. Heparin	Protamine
2. Benzodiazepine	Flumazenil
3. Beta blocker	Epinephrine, glucagon
4. Ca-channel blocker	Glucagon, calcium chloride
5. Digoxin	Digoxin-specific Fab antibody
6. Potassium	Calcium chloride, sodium bicarbonate, sodium polystyrene sulfonate, glucose and insulin
7. Acetaminophen	N-Acetylcysteine
8. Anticholinergic	Physostigmine
9. Organophosphorus	Atropine
10. Neostigmine	Atropine
11. Pyridostigmine	Atropine
12. Bromide	Sodium or ammonium chloride
13. Cyanide	Amyl nitrite
14. Fluoride	Calcium gluconate or lactate

Drugs

15. Ethylene glycol
16. Methanol
17. Gold
18. Heavy metals
19. Copper
20. Lead
21. Mercury
22. Iron
23. Isoniazid
24. Phenothiazine
25. Warfarin
26. Tricyclic antidepressant
27. Narcotic analgesic
28. Salicylate
29. Lithium
30. Nitrites
31. Nitrobenzene
32. Chlorates

Antidotes

- Ethanol
- Ethanol
- Dimercaprol
- Dimercaprol
- Penicillamine
- Penicillamine
- Penicillamine
- Deferoxamine
- Pyridoxine
- Diphenhydramine
- Vitamin K (Phytonadione)
- Physostigmine
- Naloxone, Naltrexone
- Alkaline diuresis
- Sodium polystyrene sulfonate
- Methylene blue
- Methylene blue
- Methylene blue

41-Statistic

* Statistic methods are an integral part of the development, education and marketing of drug products. It is a large field with applications in many diverse areas.

* In this chapter, we will briefly discuss the following terms:

1. Average or mean
2. Median or mode
3. Range
4. Standard variation
5. Binomial distribution
6. Confidence limit
7. t-distribution
8. Null hypothesis
9. Chi-square test
10. F-distribution

1. **Average or Mean:** It is defined as a measure of the center of a set of data. It is normally calculated by the following equation:

$$\bar{X} = \frac{x_1 + x_2 + x_3 + x_4 + \dots}{n}$$

Example: Mr. Mike's weekly blood pressure chart is as follows:

Mon	120 mm Hg
Tue	109 mm Hg
Wed	103 mm Hg
Thu	131 mm Hg
Fri	98 mm Hg
Sat	111 mm Hg
Sun	121 mm Hg

* The mean or average of the above data will be:
 $= 120 + 109 + 103 + 131 + 98 + 111 + 121 / 7 = 113.28$

2. **Mode or Median:** It normally divides the data set in half; that is half of the data below the median and half is above. To find out the median or mode of observed data, one must arrange the data in ascending or descending order.

* Example: Referring to Mike's blood pressure data:

98, 103, 109, 111, 120, 121, 131

- * The middle value of the experiment is 111. In the case of even numbers, one should take the average of the middle values.

Example: 98, 103, 109, 111, 120, 121, 131, 135

- * The median or mode would be $= 111 + 120 / 2 = 115.5$

3. **Range:** The difference between the largest and smallest value in a data set is known as range.

Example: Referring to the previous example, the range should be $(135 - 98) = 37$.

Standard Variation: The mean alone is not sufficient to describe a set of data. For example, two set of data may have the same mean or average, but may look very different.

Example:	A	B
	5, 3, 8, 4	1, 7, 10, 2

- * The average of the set of data in group A and group B would be 5 but the variability of the data in both groups is different. In group A, the range is $(8-3 = 5)$, while in group B, the range is $(10-1 = 9)$. Thus both groups have a similar mean but the spreading of data may vary greatly.

- * Therefore it is necessary to calculate the standard deviation of data. The standard deviation is a more common way of expressing the variability of data.

- *
$$S = SD = \sqrt{\sum (X_i - X)^2 / (n-1)}$$

- * The standard deviation of the following numbers would be :

$n = 5, 3, 8, 4$

- * Mean $(X) = 5 + 3 + 8 + 4 = 20 / 4 = 5$

$$\begin{aligned}
 SD &= \sqrt{(5 - 5)^2 + (3-5)^2 + (8-5)^2 + (4-5)^2 / 3} \\
 &= \sqrt{4 + 9 + 1 / 3} \\
 &= \sqrt{14 / 3} \\
 &= 4.66 \qquad \qquad \qquad = \qquad 2.15
 \end{aligned}$$

- * The coefficient of variation or relative variation can be calculated by the following equation:

$$S_x = S / \sqrt{n}$$

where S = standard variation,
n = number of observation
S_x = standard error of mean

- * Example: If the SD of an individual value is 2, the standard error of means of size 4 is

$$S_x = 2 / \sqrt{4} = 2/2 = 1$$

The Binomial and Normal Distribution

- * The Binomial Distribution: It is applicable in data where one of two mutually exclusive and independent outcomes are possible as a result of a single observation or experimental trial. For example, tossing a coin will bring only one outcome at a time, tails or heads.
- * The probability of success in n binomial trials can be calculated by the following equation:

$$P(x) = \binom{n}{x} p^x q^{n-x}$$

$$\binom{n}{x} = n! / (x! (n-x)!)$$

p = probability of success (p + q = 1)
q = probability of failure

- * Example: Calculate the probability of success that 3 or less of 6 patients will be cured if the probability of a cure of an individual patient is 0.8 or 80%.

- *
$$P(3) = \binom{6}{3} (0.8)^3 \times (0.2)^3 \quad (\text{where } p + q = 1)$$
$$= \frac{6 \times 5 \times 4 \times 3 \times 2 \times 1}{(3 \times 2 \times 1) (3 \times 2 \times 1)} \times 0.512 \times 0.008$$
$$= 0.082$$

- * The probability (p) of exactly 3 cures in 6 patients is 0.082.
- * To calculate the mean in binomial distribution, one should use the following formula:

- * Example: What is the probability that a tablet will weigh between 300 and 325 mg, if the average weight of a tablet in normal distribution is 315 mg and there is a standard deviation of 5?

$$[Z(-3) = 0.009 \text{ and } Z(2) = 0.90]$$

$$Z = \frac{x - \mu}{\sigma}$$

$$Z = (300 - 315)/5 = -3.0 = Z(-3) = 0.009$$

$$Z = (325 - 315)/5 = 2.0 = Z(2) = 0.90$$

$Z(-3) = 0.009$ and $Z(2) = 0.90$, therefore the probability of finding a tablet weighing between 300 and 325 mg is $0.90 - 0.009 = 0.891$

95% Confidence Limit

- * The mean of the sample gives no idea about the precision of experiment values.
- * For example, if the average weight of 10 tablets is 50 mg, this will give you no information about how correct or close this value is? You have to compare the value to the desired value in order to find out the closeness of the result.
- * If the desired value for each tablet weight is 45 mg, then we can compare it with the average value (in our example it is 50).
- * Confidence interval or confidence limit gives an interval which may encompass the mean with a known probability. For example, we weigh 100 tablets and the range of tablets weight is from 95 to 105. Now we apply a 95% confidence interval, then one can say that if you give 20 trials to this experiment i.e. you measure 100 tablets and find out the mean each time for 20 trials, there is a chance that 19 times (95%) your true mean falls between the 95-105 mg range.
- * There are a few Z values you should remember:
 1. 68% of the values are within ± 1 standard deviation of the mean value.
 2. 80% of the values are within ± 1.28 standard deviation of the mean value.
 3. 90% of the values are within ± 1.65 standard deviation of the mean value.
 4. 95% of the values are within ± 1.96 standard deviation of the mean value.
 5. 99% of the values are within ± 2.58 standard deviation of the mean value.
- * Example: A drug reduces the average blood pressure 100 mm Hg when tested on 81 patients. The standard deviation is 90 mm Hg. What would be a 95% confidence interval for the mean blood pressure reduction?

It can be calculated by the following equation (for 95% confidence)

$$\bar{X} \pm 1.96 \times \frac{X_i}{\sqrt{n}} \quad \text{where } \bar{X} = 100 \text{ mm Hg}$$

$$X_i = 90 \text{ mm Hg}$$

$$n = 81$$

$$100 \pm 1.96 \times \frac{90}{\sqrt{81}}$$

$$100 \pm 1.96 \times 10$$

$$100 \pm 19.6$$

- * Thus if we give 100 trials to the above experiment with a 95% confidence limit, one can say that 95 times (out of 100 trials) the observed blood pressure values fall between 80.4 mm Hg to 119.6 mm Hg. (100 ± 19.6).
- * Example: A survey of 100 pharmacists showed that 40% have more than 5 years of experience and 60% have less than 5 years experience. A 95% confidence interval on the proportion of pharmacists with more than 5 years experience is:

$$p \pm 1.96 \times \sqrt{pq/n}$$

where $p = 40\% = 0.4$
 $q = 60\% = 0.6$ ($p + q = 1$)
 $n = 100$

$$0.4 \pm 1.96 \sqrt{0.4 \times 0.6 / 100} = 0.4 \pm 0.096 = 40\% \pm 9.6\%$$

- * Thus if we give 100 trials to the above experiment with a 95% confidence limit, one can say that 95 times (out of 100) the observed values fall between 30.4% to 49.6% ($40\% \pm 9.6\%$).
- * In a similar fashion, if we can calculate a 99% confidence limit for the above examples, one can calculate by using the following formulas:

$$\bar{X} \pm 2.58 \times \frac{X_i}{\sqrt{n}} \quad \text{or} \quad p \pm 2.58 \times \sqrt{pq/n}$$

t- distribution

- * When the standard deviation is unknown, but an estimate is available from a relatively small sample, the “t” distribution is used to describe the distribution of mean.
- * It can be expressed by the following formula:

*
$$t = \frac{\bar{X} - \mu}{SD/\sqrt{n}} \quad \text{or} \quad \bar{X} \pm (DF) \times SD \sqrt{\frac{1}{n}}$$

* The degree of freedom in “t” distributions is (n-1). When n is very large, the t distribution approaches the corresponding values from the standard normal curve distribution.

Example: The assay values for 10 (n) randomly picked tablets are as follows:

98.6	97.9
98	99.6
99.3	99.1
100	100.3
98.4	97.5

* The mean value is 98.88 (\bar{X}) and SD is 0.954. Using a 95% confidence interval, where would the true mean of the data with sample size (n) of 10 lie?

[t value for 95% of the area for DF = (10-1) = 9 is 2.262]

$$= 98.88 \pm 2.262 \times 0.954 \sqrt{\frac{1}{10}}$$

$$= 98.88 \pm 0.68$$

$$= 98.20 \text{ to } 99.56$$

* This indicates that the true mean of the data probably lies between 98.20 mg to 99.56 mg.

NULL HYPOTHESIS

* The null hypothesis is a statement which assumes that the parameter is equal to some value. For example, we assume for a population size of 1000 tablets that the average of tablets is a mean of 100 mg. There are three possibilities:

1. The mean would be exactly 100 mg.
2. The mean could be less than 100 mg.
3. The mean could be greater than 100 mg.

* The process of statistical interference will result in one of two possible decisions; either accept or reject the null hypothesis.

α error

* The level of significance is known as alpha-error. The difference is significant at a 5% level. The alpha-error is set in advance. The α error is commonly chosen as 5%, however sometimes it may set up to 1%.

- * This indicates that the difference between the observed value of data and the hypothetical value of data (which we predecided) is real or significant at a 5% difference.
- * For example, the hypothetical mean value for 1000 tablets' weight is 100mg. After real experiment, the observed mean value comes to 94.5 mg. Would it be considered significant at a 5% level?
- * No. The predecided mean value (hypothetical value) is 100mg. The alpha error is significant at a 5% level (predecided). This suggests that if the observed mean value for 1000 tablets falls between 95 mg to 105 mg ($100 \pm 5\% = 95$ to 105), the difference is significant. Any observed mean value which is less than 95 mg or greater than 105 mg would not be considered significant.

β error

- * The beta-error is the probability of declaring no difference between the observed value and the hypothesized value of a parameter, in fact, a difference of size delta exist.
- * For example, the hypothesized mean value for 1000 tablets is 100mg and the observed mean value after real experiment is 99.9999 mg; the beta error should exist.

Two Independent Sample t Tests:

- * It is used to compare two treatments applied to two independent groups.

Example: A drug is used to treat 20 patients and a placebo is used to treat 20 different patients. In this type of example, we will get two averages from two different groups for comparison purposes whereas in a one sample test, the average of a single group is compared to some hypothetical volume.

- * The degree of freedom for a two independent sample t-test would be $(n_1 - 1) + (n_2 - 1)$

Paired t Test:

- * In this type of test, two treatments are applied to a single group of experimental units.

Example: The bioavailability study of a generic drug to its reference standard drug in each of 20 patients. Here two treatments are applied to a single group of experimental unit (20 patients).

- * The paired t test has an advantage over the two independent t-test; since two treatments are applied to a single group, the chances of variability are lower in the paired t-test compared to the two single t-tests.
- * The degree of freedom (DF) in paired t-tests can be calculated by : $(n - 1)$

Chi-Square Test

- * It is used to test differences of two proportions from two independent samples.

Example: Tossing a coin, 50% tails and 50% heads are expected. A coin is tossed 30 times and 20 heads and 10 tails are obtained, where as 15 heads and 15 tails are expected. This type of study can be conducted by Chi-square.

- * It can be calculated by the following formula:

$$\begin{aligned} X^2 &= \sum \frac{(\text{observed frequency} - \text{expected frequency})^2}{\text{expected frequency}} \\ &= \sum \frac{(20-15)^2}{15} + \frac{(10-15)^2}{15} \\ &= 1.66 + 1.66 \\ &= 3.33 \end{aligned}$$

- * The degree of freedom for a Chi-square test can be calculated by : (R-1) x (C-1). The Chi-square is always a positive value.

F distribution

- * t-distribution is useful for comparing two means while F distribution is useful for comparing two variances. Similar to Chi-square, F distribution consists of positive values.
- * F distribution is also used for comparison of more than two means through variances, and is equivalent to a t test if used to compare two means.
- * The degree of freedom (DF) can be calculated by: (n - 2)

42-Immunology

* **Immunology** is a study of a specific mechanism by which living tissues react to foreign biological bodies (including microorganisms) to develop immunity or resistance.

* The immune system can be classified into two major components:

1. Humoral immunity
2. Cellular immunity

Humoral immunity: It is also known as antibody mediated immunity.

* It is carried out by antibodies circulating in the blood.

* When an antigen enters into the body, β lymphocytes initiate the chain of reactions which release antibodies.

Cellular immunity: It is also known as cell mediated immunity.

* It is carried out by T-lymphocytes.

* It occurs at the cellular level, especially when antigens are inside host cells and not accessible by circulating antibodies.

The immune system of humans normally consist of the following cells:

1. Beta-lymphocytes
2. T-lymphocytes
3. Natural killer cells
4. Macrophages

Beta lymphocytes: They develop from lymphoid stem cells in adult bone marrow. They account for up to 15% of the lymphocytes circulating in the blood. Following maturation, they migrate to lymphoid tissues, lymph nodes, spleen, adenoids, and gut associated lymphoid tissues. When foreign antigens invade the body, beta-lymphocytes secrete antibodies.

T lymphocytes: The other lymphoid stem cells migrate from the bone marrow to the thymus, where they turn into T lymphocytes (T cells). They live in the thymus for a prolonged period and do not require constant replacement. They account for 75% of lymphocytes circulating in the blood.

* T cells are divided into two classes:

1. Helper T cells (T_H)
2. Cytotoxic T cells (T_C)

* Helper T cells stimulate other immune cells such as β cells and macrophages while cytotoxic T cells kill cells infected with viruses or other microorganisms.

Natural killer cells (NK):

* They are large lymphocytes. They mature from lymphoid stem cells in the bone marrow.

* They comprise up to 15% of blood lymphocytes. They kill foreign cells, virus-infected cells and tumor cells.

Macrophages:

* Monocytes are derived from myeloid stem cells, while lymphocytes are derived from lymphoid stem cells.

* When these monocytes migrate from the bone marrow into the blood and then from the blood into tissues, they will go through a series of cellular changes and mature into macrophages.

* Macrophages are known as “big eaters” and they destroy microorganisms and larger particles.

They are normally differentiated into two classes:

1. **Fixed macrophages:** They remain stationary in tissues and are given different names depending on tissues.
2. **Wondering macrophages:** They normally circulate in the blood. They move into tissues when microbes and foreign substances are present.

Classes of immunoglobulins:

1. **IgA:** It represents 10% of the total immunoglobulins.

* The main function of IgA is to inhibit microorganisms from binding or adhering to tissues.

* They do not cross the placenta.

* They are normally present in external blood secretions such as tears, colostrum, saliva and urine.

2. **IgD:** It represents less than 1% of total immunoglobulins.
- * The principal function of IgD is to serve as an antigen receptor in the early stages of the immune response.
 - * They are normally found in the serum.
3. **IgE:** It is also known as Reagin.
- * It accounts for less than 1% of total immunoglobulins.
 - * It plays an important role fighting against helminths.
 - * It is elevated in patients suffering from asthma, hay fever or any other allergic diseases.
 - * They are found in body fluids and beneath the skin and mucosa.
4. **IgG:** It is a principal immunoglobulin among all the classes of immunoglobulins.
- * It accounts for as much as 70% of the serum immunoglobulins and 20% of all plasma protein.
 - * It is the only immunoglobulin which can cross the placenta. and provide antibody protection to the developing fetus.
5. **IgM:** It is the first immunoglobulin type produced in response to the immune system.
- * It accounts for 20% of total immunoglobulins in human serum.
 - * It is also the first immunoglobulin produced by a fetus.
 - * It cannot cross the placenta.

Hypersensitivity Reactions:

- * Hypersensitivity reactions can be classified into four different categories:
 - I Type I hypersensitivity (Immediate hypersensitivity, Anaphylaxis reactions)
 - II Type II hypersensitivity (Cytotoxic hypersensitivity)
 - III Type III hypersensitivity (Immune complex hypersensitivity)
 - IV Type IV hypersensitivity (Cell mediated or delayed hypersensitivity)

Type I hypersensitivity reactions: IgE immunoglobulin plays an important role in this type of hypersensitivity. The excessive secretion of IgE in response to specific antigens may cause this type of reaction.

- * Common allergens that may cause this type of hypersensitivity are pollens of trees, grasses, various plants, fungi, soybeans, peanuts, certain dairy products, and drugs that act as haptens such as penicillin, cephalosporin, hormones and certain vaccines.
- * It is characterized by the presence of urticaria, itching, nasal congestion, constriction of bronchioles, tear secretion, runny nose, itchy eyes, diarrhea and vomiting. Atopic dermatitis is a principal symptom associated with Type I hypersensitivity.

Type II hypersensitivity reactions: The immunoglobulins IgM and IgG play an important role in this type of hypersensitivity.

- * They form the immune complexes with specific cell antigens which result in cytotoxicity of cells. It is commonly reported with Rh disease, and with certain drugs and their metabolites act as haptens such as penicillin, cephalosporin, quinidine methyldopa. Drug induced hemolytic anemia is the common form of type II hypersensitivity reactions.
- * It is also reported with certain autoimmune diseases such as myasthenia gravis, Hashimoto's thyroiditis, autoimmune hemolytic anemia and thrombocytopenia.

Type III hypersensitivity reactions: They result due to a high load of antigens or to an underproduction of antibodies.

- * The immune complex between antigens and antibodies remains for a prolonged time in blood or at local tissue sites.
- * It is reported with autoimmune disorders such as glomerulo nephritis, SLE or rheumatoid arthritis. It is also reported with bacterial and protozoal infections. Administration of antisera to achieve passive immunization may also result into such reactions.

Type IV hypersensitivity reactions: They are reported due to a prolonged immune response. T-cells may play an important role in this type of reaction.

- * Acute graf rejection, tuberculin hypersensitivity, contact and exfoliative dermatitis, lupus erythematosus, and bone marrow lesion and infection are caused by *M. tuberculosis*, *M. leprae*, and *listeria monocytogenes* are examples of Type IV hypersensitivity reactions.

Autoimmune Disorders:

- * Normally, when antigens enter a blood stream, the body's protective mechanism produces antibodies against antigens. But sometimes the body produces antibodies against its own cells or organs by identifying the body organ or cell as a foreign subject; this will cause autoimmune disorders. This type of immunity is known as autoimmunity.

Autoimmune disorders: They normally occur when individuals become hypersensitive to specific antigens on cells or tissues of their own bodies. The antigen creates an immune response which produces antibodies against the body's own cells or tissues.

Autoimmunity can be subdivided into:

- I Organ specific autoimmunity
- II Non-organ specific autoimmunity

I **Organ specific autoimmune disorders:** In Organ specific immunities, such as Myasthenia gravies, Graves' disease, Hashimoto's thyroiditis, and Multiple sclerosis, the body produces antibodies particularly against one of its own organ.

- 1 Myasthenia gravies
- 2. Rheumatic fever
- 3. Autoimmune pernicious anemia
- 4. Autoimmune disease of blood cells
- 5. Multiple sclerosis
- 6. Goodpasture syndrome
- 7 Thyroid abnormalities
- 8. Glomerulonephritis
- 9. Junevile diabetes
- 10. Ulcerative colitis

II **Non-organ specific autoimmune disorder:** In non-organ specific autoimmunity, the body produces antibodies against all the tissues, i.e. SLE, sjogren syndrome.

- 1. SLE
- 2. R.arthritis
- 3. Sjogren syndrome

Organ specific autoimmune disorders

1 **Myasthenia gravies:** Autoantibodies formed by the body competitively inhibit the binding of acetylcholine to nicotine receptors. This will cause muscle weakness and fatigue. Neostigmine (anticholinesterase) is a drug of choice since it increases the concentration of acetylcholine at the receptor site.

2 **Rheumatic fever:** In this disease, antibodies formed by the body against streptococci also damage the cardiac muscle fibers. Hydralazine, Procainamide, Quinidine, Methyldopa, Isoniazid, Phenytoin and Chlorpromazine may cause drug induced lupus erythematosus.

- 3 **Autoimmune pernicious anemia:** Intrinsic factors play an important role in absorption of vitamin B₁₂. In certain patients, antibodies formed by the body act as antagonists for intrinsic factors which results in the failure of association of vitamin B₁₂ to intrinsic factors. This will lead to poor absorption of Vitamin B₁₂ and anemia.
- 4 **Autoimmune disease of blood cells:** In this disease, antibodies formed by the body start to destroy the normal cells in blood, i.e. RBC, thrombocytes, neutrophils and lymphocytes.
- 5 **Multiple sclerosis:** T cells and macrophages are part of the body's protective mechanism. Sometimes these cell act as autoantigens and destroy the basic protein of myelin in CNS. This will cause spasticity. When these cells destroy myelin involved with the peripheral nervous system, it results in Guillain Barre syndrome. Baclofen and Dantrolene are drugs of choice.
- 6 **Goodpasture syndrome:** Antibodies formed by autoantigens cause glomerulonephritis and profound deterioration of kidney function. Immunosuppressive agents such as corticosteroids may help to a certain extent.
- 7 **Thyroid abnormalities:** They can be subdivided into three different categories: Myxedema, Graves' disease, and Hashimoto's thyroiditis.
- I **Myxedema:** Antibodies formed by autoantigens may act as antagonists for TSH receptors which will lead to hyposecretion of the thyroid hormone and Myxedema.
- II **Graves' disease:** Antibodies formed by autoantigens may act as agonists for TSH receptors which will lead to hypersecretion of the thyroid hormone.
- III **Hashimoto's thyroiditis:** Antibodies formed by autoantigens may antagonize the thyroid peroxidase effect, and may cause cytotoxicity and inflammation reactions. This will result in hypothyroidism.
8. **Sjogren's syndrome:** Antibodies formed by autoantigens may antagonize salivary glands and endocrine glands of the eyes, respiratory systems and G.I. Dryness of the mouth and eyes, pain and edema are reported.
- * **Monoclonal antibodies:**
- Definition: When a population of Beta cells is exposed to antigens, it produces different antibodies to bind to different epitopes on the antigen. This type of antibodies is known as polyclonal. However, if we develop specific antibodies from a clone of cultured cells which have the unique ability to attach specific epitopes on the antigen, it will be defined as a monoclonal antibody.
- * Normally when an antigen enters into the body, it produces a large number of antibodies. This type of natural antibodies has affinity for both general and specific binding. But monoclonal antibodies have advantages over natural antibodies. They are highly specific and targeted.

- * The normal antibodies are isolated from an animal after it has been periodically exposed to antigens.
- * With the help of genetic engineering techniques, normal antibodies are then fused with myeloid (cancer) cells.
- * The fused cells (hybrid) are allowed to grow in test tubes. Then the tumor cells of hybrid cells will be selectively destroyed with the help of the antitumor drug.
- * The resulting cell is cloned to produce many copies. These cells, when administered into an individual, normally produce highly selective and targeting antibodies.

Immunization: The process of inducing immunity is defined as immunization.

- * Immunization can be classified into two major categories:
 1. Active immunization
 2. Passive immunization
- 1. **Active immunization:** It is generally produced by administering a vaccine that contains live but attenuated (weakened) or dead microorganisms, or by administering toxoids. The toxoid contains inactivated toxins which are not able to create disease but still possess its immunogenic property.
 - * When administered into humans, the immune system of the body recognizes them as foreign and produces antibodies and memory cells.
 - * The immunity produced by active immunization is long-lasting.
 - * Diptheria, tetanus, pertussis, mumps, measles, rubella and hepatitis-B toxoids are classified as active immunization.
- 2. **Passive Immunization:** Passive immunization is used to induce passive immunity. In this type of immunization, the readymade antibodies are administered into patients. It is also known as antisera.
 - * Passive immunization produces immunity quickly, however it is not long lasting.
 - * It is normally used when a patient's exposed to disease and requires immediate immunization.
 - * Hepatitis-B, mumps, rabies, tetanus, and pertussis immunoglobulins are classified as passive immunizations.

<u>Disease</u>	<u>Vaccines</u>	<u>Dosing</u>
Measles	Live virus	Age 15 months and booster at 11 -12 years
Mumps	Live virus	Age 15 months and booster at 11 -12 years
Rubella	Live virus	Age 15 months and booster at 11 -12 years
Diphtheria	Toxoid	Ages 2, 4 and 6 months; 1.5 and 4 to 6 years
Tetanus	Toxoid	Ages 2, 4 and 6 months; 1.5 and 4 to 6 years
Pertussis	Toxoid	Ages 2, 4 and 6 months; 1.5 and 4 to 6 years
Hepatitis-B	Viral antigen fragments	Birth, ages 2 and 6 months
Poliomyelitis	Live virus	Ages 2 and 4 months; 1.5, and 4 to 6 years

43-Microorganisms and Drugs of Choice

<u>Microorganisms</u>	<u>Primary drug</u>	<u>Secondary drug</u>
* S. pyrogen	Penicillin	Erythromycin Cephalosporin
* S. aureus	Nafcillin	Cefazolin Clindamycin SMZ/TMP Vancomycin
* S. epidermis	Nafcillin	Cefazolin Clindamycin SMZ/TMP Vancomycin
* Diptheroids	Penicillin	Cephalosporins
* M. catharrhallis	SMZ/TMP	Amoxicillin + Clavulanic acid Erythromycin Doxycycline
* N. gonorrhoea	Cefixime Quinolone	Ceftriaxone
* N. meningitis	Penicillin	Third generation cephalosporins
* C. fetus	Imipenem	Gentamicin
* Enterobacteria	SMZ/TMP	Quinolone Imipenem Gentamicin
* E.coli	Third generation cephalosporins	Gentamicin
* H.influenza	Third generation cephalosporins	SMZ/TMP
* H.pyroli	Tetracycline + Metronidazole + Bismuth subsalicylate	Amoxicillin + Metronidazole + Bismuth subsalicylate

171. (d) Risedronate (Actonel) is classified as a pyridinyl biphosphonate that inhibits osteoclast-mediated bone resorption and modulates bone metabolism. It is indicated for the treatment of glucocorticoid induced osteoporosis, osteoporosis and Paget's disease of bone. The drug should be taken once per day, at least 30 minutes before the first food or drink of the day other than water. Patients should not lie down 30 minutes after taking the medication. The recommended dose of the drug is 30 mg orally once daily for 2 months. Flu syndrome, chest pain, asthenia and diarrhea are reported side effects of the drug.

172. (b) Methenamine (Urised) is classified as a urinary bactericidal agent. In acidic urine, Methenamine may hydrolyze into formaldehyde. Formaldehyde possesses, bactericidal activities. It is indicated for the relief of discomfort of the lower urinary tract caused by cystitis, urethritis, and trigonitis. The recommended dose of the drug is two tablets by mouth four times daily. Skin rash, flushing, dryness of mouth and dizziness are reported side effects of the drug.

173. (d) Rifabutin (Mycobutin) is classified as an antimycobacterial agent. It is indicated for the prevention of Mycobacterium avium complex (MAC) in immunocompromised patients with HIV. The recommended dose of the drug is 300 mg once daily. Abdominal pain, asthenia, anorexia and nausea are reported side effects of the drug.

174. (b) Pramipexole (Mirapex) is classified as a dopamine receptor agonist. It is indicated for the treatment of idiopathic Parkinsons. Falling asleep during activities of daily living and somnolence are reported side effects of the drug. The recommended dose of the drug is 1.5 to 4.5 mg per day in three divided doses.

175. (c) Ibutilide (Corvert) is classified as a class III antiarrhythmic agent. It is indicated for the rapid conversion of atrial fibrillation or atrial flutter of

recent onset to sinus rhythm. Ventricular arrhythmia in association with QT prolongation is a principal side effect of the drug. The recommended dose of the drug is 2 mg administered as a single I.V. infusion.

176. (b) Almotriptan (Axert) is classified as a selective 5 HT receptor agonist. It is indicated for the treatment of migraine. The recommended dose of the drug is 6.25 mg to 12.5 mg per acute migraine attack. Coronary artery vasospasm, elevation of blood pressure, and hypertensive crisis are reported side effects of the drug.

177. (d) Sertraline (Zoloft) is classified as a Selective Serotonin Uptake Inhibitor (SSRI). It is indicated for the treatment of depression. The recommended dose of the drug is 50 mg to 100 mg at bed time. Agitation, ejaculation failure, dryness of mouth, somnolence and nausea are reported side effects of the drug.

178. (c) Hydroxyzine pamoate (Vistaril) is classified as an antianxiety agent. It is indicated for the symptomatic relief of anxiety and tension. The recommended dose of the drug is 50 to 100 mg per day in divided doses. Dry mouth, drowsiness, dizziness and sedation are reported side effects of the drug.

179. (b) Hydroxyurea (Hydrea) is classified as an antimetabolite. It is indicated for the treatment of myelocytic leukemia, carcinoma of the head and neck, and sickle cell anemia. It increases hemoglobin F levels in RBC, water content of the RBC, and deformability of sickle cell. It reduces neutrophil count. These actions make it useful against sickle cell anemia. The recommended dose of drug is 15 mg once daily. Redness of the face, megaloblastic erythropoiesis and maculopapular rash are reported side effects of the drug.

180. (c) Glyburide (Micronase) is classified as an oral sulfonylurea agent. It stimulates the release of insulin from the functioning beta cells of

the pancreas. It is indicated for the treatment of type II diabetes. Hypoglycemia is the principal side effect of the drug. The recommended therapeutic dose of the drug is 2.5 to 5 mg per day.

181. (a) Trovafloxacin (Trovan) is classified in the quinolone group of antibiotics. Severe hepatic injury leading to liver transplantation is the principal side effect of the drug. It is indicated for the treatment of serious and life threatening infections caused by susceptible strains of gram negative microorganisms.

182. (a) Doxepin (Sinequan) is classified as an antidepressant. It is indicated for the treatment of depression. The recommended dose of the drug is 75 mg to 150 mg per day. Drowsiness, dizziness, dryness of mouth, urinary retention and constipation are reported side effects of the drug.

183. (d) Nifedipine (Procardia) is classified as an antihypertensive agent. It is indicated for the treatment of hypertension. It is a calcium channel blocker. The recommended dose of the drug is 10 to 20 mg (immediate release) three times a day. Severe hypotension, lightheadedness, dizziness, and palpitation are reported side effects of the drug.

184. (b) The principal side effect of Sucralfate (Carafate) is constipation. It is indicated for short-term treatment of duodenal ulcers. It adheres and protects ulcers by forming a barrier. The recommended dose of the drug is 1 gm p.o. q.i.d 1 hour before meals and at bed time. Constipation, nausea, dizziness, dry mouth and flatulence are reported side effects of the drug.

185. (b) Nevirapine (Viramune) is classified as a non-nucleoside reverse transcriptase inhibitor. It is indicated for the treatment of HIV infection. Severe life-threatening hepatotoxicity, cholestatic hepatitis, hepatic necrosis, hepatic failure and skin rash are reported side effects of the drug. The recommended therapeutic dose of the drug is 200

mg by mouth per day for 14 days, followed by 200 mg by mouth twice daily.

186. (c) Prazosin (Minipress) is classified as an alpha-1 blocker. It has a powerful vasodilation property. It is indicated for the treatment of hypertension. The recommended dose of the drug is 1 mg two to three times a day. Severe hypotension including syncope, dizziness, drowsiness and tachycardia are reported side effects of the drug.

187. (b) Donepezil (Aricept) is a reversible inhibitor of enzyme acetylcholinesterase. It is indicated for the treatment of Alzheimer related amnesia. The recommended dose of the drug is 5 mg to 10 mg once a day. Nausea, diarrhea, vomiting, anorexia, insomnia and depression are reported side effects of the drug.

188. (d) Amphotericin B (Fungizone) is classified as an antifungal agent. It is indicated for the treatment of systematic fungal infections. Due to its broad range of side effects, it should be reserved for life threatening fungal infections. Severe hypokalemia, thrombocytopenia, leukopenia, agranulocytosis, acute liver and kidney failure are reported side effects of the drug.

189. (b) Ethosuximide (Zarontin) is classified as an anticonvulsant. It is indicated for the treatment of absence seizure (petit mal). The recommended dose of the drug is 250 mg to 500 mg per day. Nausea, vomiting, anorexia, leukopenia, thrombocytopenia, drowsiness and dizziness are reported side effects of the drug.

190. (b) Bromocriptine (Parlodel) has the longest duration of action (about 50 hours half life) among all the antiParkinson's drugs. It is a dopamine receptor agonist. It is indicated for the treatment of Parkinson's. The recommended dose of the drug is 2.5 mg to 5.0 mg per day; maximum up to 100 mg per day. Hypotension, dizziness, stroke, and acute MI are reported side effects of the drug.

191. (b) Phenytoin (Dilantin) is classified as an antiepileptic agent. It is indicated for the treatment of generalized tonic-clonic (grand mal) and complex partial seizure. The normal therapeutic serum concentration of the drug is 10 to 20 mcg/ml. Ataxia, nystagmus, diplopia, drowsiness and dizziness are reported side effects of the drug. The recommended dose of the drug is 125 mg three times daily.

192. (c) Cilostazole (Pletal) is indicated for the treatment of intermittent claudication. Cilostazole and its metabolites are inhibitors of phosphodiesterase III. This type of enzyme inhibition reduces the survival rate of CHF patients in a controlled trial. Cilostazole is contraindicated to use in patients suffering from CHF. The recommended dose of the drug for treatment of intermittent claudication is 100 mg bid, at least half an hour before or 2 hours after breakfast or dinner.

193. (d) Interleukin is a proinflammatory cytokine involved in etiology and the progression of rheumatoid arthritis.

194. (c) Fluvoxamine (Luvox) is classified as an SSRI. It is indicated for the treatment of Obsessive Compulsive disorder. The recommended dose of the drug is 100 mg to 300 mg per day. Diarrhea, yawning, nausea, depression, phobia and sedation are reported side effects of the drug.

195. (c) Felodipine (Plendil) is classified as a calcium channel blocker. It is indicated for the treatment of hypertension. The recommended dose of the drug is 5 mg to 10 mg per day. Hypotension, dizziness, and peripheral edema are reported side effects of the drug.

196. (b) Tramadol (Ultram) is classified as centrally analgesic. It is indicated for the treatment of moderate to severe pain. Seizure is the principal side effect of the drug. The recommended dose of the drug is 50 mg to 100 mg per day.

197. (b) Finasteride (Proscar) is indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate gland. The recommended dose of drug is 5 mg orally once daily. Impotence, decreased libido, a decrease in volume of ejaculate, and abnormal ejaculation are reported side effects of the drug.

198. (b) Megestrol (Megace) is indicated for the treatment of anorexia associated with weight loss in AIDS patients and advanced carcinoma of the breast and endometrium. The recommended dose for breast cancer is 40 mg q.i.d, and for endometrium carcinoma it is 40 to 320 mg/day. The recommended adult dose for treatment of anorexia associated with weight loss in AIDS patients is 800 mg per day. Diarrhea, impotence, rash, nausea, vomiting and headache are reported side effects of the drug. It is available in oral tablet and suspension form.

199. (b) Mirtazapine (Remeron) is classified as an antidepressant. It is indicated for the treatment of depression. Somnolence, weight gain, dizziness and drowsiness are reported side effects of the drug. The recommended dose of the drug is 15 to 45 mg per day.

200. (d) Mebendazole (Vermox) is classified as a broad spectrum anthelmintic agent. Each chewable tablet contains 100 mg of Mebendazole. Abdominal pain, diarrhea, rash and urticaria are reported side effects of the drug. The recommended dose of the drug is 1 tablet twice a day for 3 days.

Table-1

<u>Name</u>	<u>Causative organism</u>	<u>Recommended dose</u>
Diphtheria	Corynebacterium diphtheria	Adult dose, boost every 10 years.
H.Influenza b	H.influenza	Most children have 3 to 4 doses between age 2 months to 15 months.
Hepatitis A	HAV	3 doses at 1 month, 6 to 12 months old, and for patients age 2 years to 18 years, while 2 doses every 6 months to 1 year apart for patients age more than 18 years.
Hepatitis B	HBV	3 doses at 1 to 2 months old for infants and adults.
Influenza	Influenza	1 dose every year
Measles, Mumps and Rubella	Measles, Mumps and Rubella	2 MMR vaccine at 12-15 months of age, and again at 4 to 6 years of age.
Pertussis	B.Pertusis	It should be given to children ages 6 weeks to 7 months.
Poliomyelitis	Polio virus	It should be given at 2 months, 4 months, 12-18 months, and at 4 to 6 years.
Pneumococcal	S. pneumonia	1 dose
Tetanus	Clostridium tetani	3 to 4 doses plus booster every 10 years.

Table-2

Drugs with a prolonged half-life

- * Chlorpropamide
- * Corgard
- * Piroxicam
- * Amiodarone
- * Bromocriptine
- * Azithromycin
- * Clofazimine

Table-3

DISULFIRAM REACTION PRODUCING DRUGS

- * Metronidazole
- * Chlorpropamide
- * Cefotetan
- * Cefoperazone
- * Moxalactam
- * Cefamandole
- * Tolbutamide
- * Acetohexamide
- * Glyburide
- * Glipizide
- * Disulfiram

DRUGS THAT PRECIPITATE DISULFIRAM-LIKE REACTIONS WITH TABLE-3

- * Alcohol
- * Benadryl Elixir
- * Digoxin Elixir
- * Lanoxicap

PLATELET AGGREGATION INHIBITORS

- * Cefamandole
- * Cefoperazone
- * Moxalactam
- * Cefotetan
- * Plicamycin
- * Ketorolac
- * Aspirin
- * Ticlopidine
- * Clopidrogel

URINE DISCOLORATION PRODUCING DRUGS

- * Phenazopyridine
- * Senna
- * Rifampin
- * Phenolphthalein
- * Levodopa
- * Sulfasalazine

DRUGS THAT REQUIRE A PATIENTS PACKAGE INSERT

- * Isotretinoin
- * Oral contraceptives
- * Isoproterenol
- * Ticlopidine
- * Progesterone
- * Estrogen
- * Intrauterine devices

DRUGS CONTRAINDICATED DURING PREGNANCY

- * Isotretinoin
- * Tetracycline
- * Chloramphenicol
- * Sulfonamide
- * Misoprostol
- * Finasteride
- * Methimazole
- * Warfarine
- * Metronidazole
- * Valproic acid
- * Lithium carbonate
- * Alcohol

DRUGS & THEIR NORMAL BLOOD THERAPEUTIC CONCENTRATIONS

* Digoxin	0.7 to 1.4	ng/ml	Primidone	04 to 12	mcg/ml
* Phenytoin	10 to 20	mcg/ml	Vancomycin	05 to 15	mcg/ml
* Amikacin	10	mcg/ml	Lithium	0.6 to 1.2	mEq/L
* Carbamazepine	10 to 20	mcg/ml	Valproic acid	40 to 100	mcg/ml
* Gentamicin	2	mcg/ml	Haloperidol	05 to 20	ng/ml
* Tobramycin	2	mcg/ml			
* Fosphenytoin	10 to 20	mcg/ml			
* Theophylline	10 to 20	mcg/ml			
* Streptomycin	5	mcg/ml			
* Digitoxin	09 to 25	mcg/ml			
* Quinidine	02 to 06	mcg/ml			
* Carbamazepine	04 to 12	mcg/ml			
* Phenobarbital	10 to 40	mcg/ml			

ANTIDOTE OF DRUGS

Naloxone=Narcan
Nalmefene=Revox
Naltrexon= Revia
Digoxin=Digibind
LeucovorinCa⁺²= Wellcovorin
Mesna = Mesnex
Vitamin K
Protamine sulfate
Deferoxamine mesylate= Desferal
Dimercaptol
Sodium thiosulfate
Flumazenil=Romazicon
Physostigmine=Antilirium
Acetylcysteine= Mucomyst
Dexrazoxane=Zinecard
Pralidoxime = Protopam cl
Glucagon
Edetate disodium
Edetate calcium disodium
Atropine
Hydroxocobalamin

DRUGS

Opioid
Opioid
Opioid
Digoxin, Digitoxin
Methotrexate, Trimethoprim, Pyrimethamine
Cyclophosphamide, Ifosfamide
Coumadin
Heparin
Iron
Arsenic, Gold
Cyanide
Benzodiazepine
Atropine, Anticholinergic
Acetaminophen
Doxorubicin
Organophosphorus compound
Insulin
Digitalis toxicity, hypercalcemia
Lead
Acetylcholine, Cholinergic agent
Cyanide

DRUGS THAT CAUSE PHOTSENSITIVITY REACTION

* Accutane	* Cipro	* Rheumatex
* Micronase	* DiaBeta	* Sulfonamide
* Retin-A	* Doxycycline	* Tetracycline
* Bactrim	* Griseofulvin	* Thiazide diuretic
* Carbamazepine	* Methotrexate	* Tricyclic antidepressant
* Sulfonylureas	* Noroxin	* Glucotrol

ABBREVIATIONS

* aa	of each	* D.A.W	dispense as written
* N and V	nausea and vomiting	* gtt	drop
* a.c.	before meals	* a.m.	morning
* p.c.	after meals	* p.m.	evening
* a.d.	right ear	* h.s	at bed time
* a.s.	left ear	* o.d.	right eye
* a.u.	both ears or each ear	* o.s.	left eye
* q.d	daily	* o.u.	both eyes or each eye
* b.i.d.	twice daily	* o ₂	both eyes
* t.i.d	three times daily	* p.o.	by mouth
* q.i.d	four times daily	* pr	per rectum
* q.o.d	every other day	* q.6h	every 6 hours
* pt.	pint	* prn	as needed

DRUGS THAT CAUSE ENZYME INDUCTION

- * Rifampin
- * Carbamazepine
- * Phenobarbital
- * Troglitazone
- * Phenytoin
- * Nicotine
- * Omeprazole
- * Rifabutin

DRUGS THAT CAUSE ENZYME INHIBITION

- | | |
|-----------------|---------------|
| * Ciprofloxacin | * Clopidogrel |
| * Cimetidine | * Ritonavir |
| * Erythromycin | |
| * Fluvoxamine | |
| * Ketoconazole | |
| * Nelfinavir | |

STOOL DISCOLOR PRODUCING DRUGS

<u>Drug</u>	<u>Color</u>
Rifampin	Red orange
Phenolphthalein	Red
Phenazopyridine	Red
Antacid	White
Kao-pectin	Black
Iron salt	Black brown
Warfarin	Black

DRUGS THAT NEED TO BE STORED IN REFRIGERATOR

Calcimar	Wycillin (Injection)
Xalatan (ophthalmic solution)	Bicillin (Injection)
Viroptic (ophthalmic solution)	Permapen (Injection)
Ophthetic (ophthalmic solution)	Intron-A (Injection)
Fluorocaine (ophthalmic solution)	Epogen (Injection)
Occusert Pilo	Neupogen (Injection)
Phospholine Iodine (ophthalmic solution)	Hyperstat (Injection)
Erythromycin Ethyl Succinate Suspension	Sandostatin (Injection)
Promethazine suppository	Novolin (Injection)
Fosphenytoin (Injection)	Humulin (Injection)
Bicillin-LA (Injection)	Regranex (Cream)
Mose (Injection)	
Harvix-A (Injection)	
Neupogen (Injection)	
Thyrolar	
Mycostatin pastilles	
Fortovase capsules	
Norvir Capsules	
Calcitonin Salmon (Injection, nasal spray)	
Bacid (dietary supplement)	
Lactinex (dietary supplement)	
Sterile Bacitracin powder	
Diltiazem injection	
Pepcid injection	
Urokinase	
Sus-Phrine (injection)	
Dornase-alpha	
Tetanus Toxoid	
Hepatitis-A	
MMR vaccine	

COMMONLY USED UNITS FOR PHARMACEUTICAL CALCULATIONS

*	1 kilogram	=	1000 grams			
*	1 gram	=	1000 milligrams			
*	1 milligram	=	1000 micrograms			
*	1 microgram	=	0.001 milligrams			
*	1 microgram	=	10^{-6} grams			
*	1 nanogram	=	10^{-9} grams			
*	1 grain	=	65 milligrams			
*	1 liter	=	1000 cc			
*	1 ounce (oz)	=	30 cc			
*	16 ounce (oz)	=	480 cc	=	1 pint	
*	1 pint	=	480 cc			
*	1 quart	=	960 cc	=	2 pints	
*	1 gallon	=	3840 cc	=	8 pints	= 4 quarts
*	1 kg	=	2.2 lbs			
*	1 lb	=	454 grams			
*	1 teaspoonful	=	5 cc			
*	1 tablespoonful	=	15 cc			
*	1 teacupful	=	120 cc			
*	Density	=	weight/volume			
*	Proof gallon	=	$(\text{gal} \times \% \text{ v/v strength}) / 50\% \text{ v/v}$			
*	% strength	=	proof spirit / 2			
*	Proof gal	=	$(\text{gal} \times \text{proof spirit}) / 100$			
*	PV	=	nRT			
*	PV	=	W/M x R x T			
*	Equivalent wt	=	molecular weight / number of valence			
*	mEq	=	equivalent weight in mg / 1000			
*	mOsmol/L	=	$(\text{weight of substance [g/L]} \times \text{no of species} \times 1000) / \text{mol wt}$			
*	pH	=	$\text{pKa} + \log (\text{salt/acid})$			
*	Young (child)	=	$(\text{age in years} / \text{age} + 12) \times \text{adult dose}$			
*	Clark's	=	$(\text{weight in lbs} / 150) \times \text{adult dose}$			
*	Child's dose	=	$(\text{body surface area of child} / 173 \text{ mm}^2) \times \text{adult dose}$			
*	Fried's rule	=	$(\text{age in months} / 150) \times \text{adult dose}$			
*	FP of blood	=	-0.52°C			
*	Each gm of hydrous dextrose provides	=	3.4 calories / kcal			
*	Each gm of anhydrous dextrose provides	=	4 calories / kcal			
*	Each gm of fat provides	=	9 calories / kcal			
*	Each gm of protein/aminoacid provides	=	4 calories / kcal			
*	Each gm of medium chain triglyceride (mct)	=	8.3 calories / kcal			
*	Each gm of glycerol provides	=	4.3 calories / kcal			
*	Each cc of alcohol provides	=	5.6 calories / kcal			
*	1 cc of 10% fat emulsion provides	=	1.1 calories / kcal			
*	1 cc of 20% fat emulsion provides	=	2.0 calories / kcal			