Sri Lakshmi Narayana Institute of Medical Sciences

Date: 14.10.2019

From

Dr.G.Somasundram
Principal of Allied Health Sciences,
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

To

The Dean,
Sri Lakshmi Narayana Institute of Medical College
Bharath Institute of Higher Education and Research,
Chennai.

Sub: Permission to conduct value-added course: "CLINICAL PAHARMACOLOGY"

Dear Sir,

With reference to the subject mentioned above, the department proposes to conduct a value-added course titled: **"CLINICAL PAHARMACOLOGY"** from. We solicit your kind permission for the same.

Kind Regards

Dr.G.Somasundram

FOR THE USE OF DEANS OFFICE

Names of Committee members for evaluating the course:

The Dean: **Dr. Balagurunathan. K**

The HOD: **Dr. Somasundram. G**

The Expert: **Dr. Sumitra**

The committee has discussed about the course and is approved.

Dean	Subject Expert	HOD
(Sign & Seal)	(Sign & Seal)	(Sign & Seal)

DEAN
Prof.K.BALAGURUNATHAN,M.S
(General surgeon)
SRI LAKSHMI NARAYANA
INSTITUTE OF MEDICAL SCIENCES
OSUDU PONDICHERRY

PRINCIPAL
Allied Health Sciences
Sri Lakshmi Narayana Institute of Allied Health Sciences
Osudu, Agaram Post, Puducherry - 605 502.

OFFICE OF THE DEAN

Sri Lakshmi Narayana Institute of Medical Sciences

OSUDU, AGARAM VILLAGE, VILLIANUR COMMUNE, KUDAPAKKAM POST,
PUDUCHERRY - 605 502.
[Recognised by Medical Council of India, Ministry of Health letter No. U/12012/249/2005-ME (P -II) dt. 11/07/2011]
[Affliated to Bharath University, Chennai - TN]

Circular

04.11.2019

Sub: Organizing Value-added Course: "CLINICAL PAHARMACOLOGY".**reg**

With reference to the above mentioned subject, it is to bring to your notice that Sri Lakshmi Narayana Institute of Medical Sciences, **Bharath Institute of Higher Education and Research** is organizing **"CLINICAL PAHARMACOLOGY"**. The course content and registration form is enclosed below."

The application must reach the institution along with all the necessary documents as mentioned. The hard copy of the application should be sent to the institution by registered/ speed post only so as to reach on or before November to December 2019. Applications received after the mentioned date shall not be entertained under any circumstances.

Dean

DEAN
Prof.K.BALAGURUNATHAN,M.S
(General surgeon)
SRI LAKSHMI NARAYANA
INSTITUTE OF MEDICAL SCIENCES
OSUDU PONDICHERRY

Encl: Copy of Course content

VALUE ADDED COURSE

1. Name of the programme & Code

"CLINICAL PAHARMACOLOGY" & VAC04/AHS/2019-18/11

2. Duration & Period

30 hrs. & November to December 2019

3. Information Brochure and Course Content of Value-Added Courses

Enclosed as Annexure- I

4. List of students enrolled

Enclosed as Annexure- II

5. Assessment procedures:

Assessment - *Enclosed as Annexure- III*

6. Certificate model

Enclosed as Annexure- IV

7. No. of times offered during the same year:

1-time November to December 2019

8. Year of discontinuation: 2020

9. Summary report of each program year-wise

Value Added Course- November to December 2019					
Sl. No	**Course Code**	**Course Name**	**Resource Persons**	**Target Students**	**Strength & Year**
1	VAC04/AHS/2019-18/11	**"CLINICAL PAHARMACOLOGY"**	**Dr. Sumitra**	AHS	30 students October to December 2019

10. Course Feed Back

Enclosed as Annexure- V

RESOURCE PERSON

COORDINATOR
Dr. G Somasundaram

PRINCIPAL
Allied Health Sciences
Sri Lakshmi Narayana Institute of Allied Health Sciences
Osudu, Agaram Post, Puducherry - 605 502.

Course Proposal

Course Title: "**CLINICAL PHARMCOLOGY"**

Course Objective:

1. To enhance the performance skill in Clinical Pharmacology.
2. To assess the objectives and protocols in Clinical Pharmacology.
3. To assess the reaction of target allied Health students towards the Clinical Pharmacology by getting their feedback.

Course Outcome: Improvement in the "CLINICAL PHARMCOLOGY"
Course Audience: Students of AHS Batch 2019
Course Coordinator: Dr. G. Somasundaram
Course Faculties with Qualification and Designation:
1.Dr. Sumitra
Course Curriculum/Topics with schedule (Min of 30 hours)

SlNo	Date	Topic	Time	Hours
1.	18.11.2019	Introduction to Clinical pharmacology	4-5p.m	1
2.	19.11.2019	Principles Clinical pharmacology	2-3p.m	1
3.	20.11.2019	Pharmacodynamics	4-5p.m	1
4.	21.11.2019	Pharmacokinetics	4-5p.m	1
5.	22.11.2019	Routes of drug administration	4-5p.m	1
6.	23.11.2019	Advantages of oral route and Disadvantages of oral route	4-5p.m	1
7.	25.11.2019	Bioavailability	4-5P.M	1
8.	26.11.2019	Factors affecting drug absorption and bioavailability	4-5p.m	1
9.	27.11.2019	Distribution of drugs and Factors determining the rate of distribution of drugs	4-5p.m	1
10.	28.11.2019	Plasma concentration of drug (PC)	4-5p.m	1
11.	29.11.2019	metabolism of drugs and Enzymes responsible for metabolism of drugs	4-5p.m	2
12.	30.11.2019	Excretion of drugs and Different routes of drug excretion	4-5p.m	1
13.	02.12.2019	Drug safety and effectiveness	2-3p.m	1
14.	03.12.2019	Factors modifying the dosage and action of drugs	4-5p.m	1
15.	04.12.2019	Acetylation and hydroxylation of drugs	4-5p.m	1
16.	05.12.2019	Pharmaceutical drug interactions and	3-5p.m	2

		Pharmacokinetic drug interactions		
17.	06.12.2019	Interactions during biotransformation	3-5p.m	2
18.	07.12.2019	Enzyme inhibitors: Disulfiram, isoniazid, allopurinol, cimetidine, etc.	4-5p.m	1
19.	09.12.2019	Drug tolerance, Emotional factors, Adverse drug reactions	4-5p.m	1
20.	10.12.2019	Side effects are intact pharmacological effects	3-5p.m	2
21.	11.12.2019	Untoward effects and Allergic reactions	4-5p.m	1
22.	12.12.2019	Development and evaluation of new drugs	4-5p.m	1
23.	13.12.2019	Assessment procedure and giving feedback in weaker areas	1-5p.m	4
		Total		30hrs

REFERENCE BOOKS:

1. Aronson JK. A manifesto for clinical pharmacology from principles to practice. Br J Clin Pharmacol 2010; 70: 3–13.
2. Martin, Jennifer H., David Henry, Jean Gray, Richard Day, Felix Bochner, Albert Ferro, Munir Pirmohamed, Klaus Mörike, and Matthias Schwab. "Achieving the World Health Organization's vision for clinical pharmacology." British journal of clinical pharmacology 81, no. 2 (2016): 223-227.
3. https://ascpt.onlinelibrary.wiley.com/hub/journal/15326535/aims-and-scope/read-full-aims-and-scope
4. *Atkinson, Arthur (2012). Principles of clinical pharmacology. London: Elsevier Academic Press. ISBN 978-0123854711.*
5. *Ambrose, Paul G (January 2007). Pharmacokinetics-Pharmacodynamics of Antimicrobial Therapy, Clinical Infectious Diseases, Volume 44, Issue 1.*

"CLINICAL PHARMACOLOGY"

What is Clinical Pharmacology?

Clinical pharmacology is the study of drugs in humans.

It is underpinned by the basic science of pharmacology, with added focus on the application of pharmacological principles and methods in the real world. It has a broad scope, from the discovery of new target molecules, to the effects of drug usage in whole populations.

Clinical pharmacologists are physicians, pharmacists, and scientists whose focus is developing and understanding new drug therapies. Clinical pharmacologists work in a variety of settings in academia, industry and government. In the laboratory setting they study biomarkers, pharmacokinetics, drug metabolism and genetics. In the office setting they design and evaluate clinical trials, create and implement regulation guidelines for drug use, and look at drug utilization on local and global scales. In the clinical setting they work directly with patients, participate in experimental studies, and investigate adverse reactions and interactions.

Clinical Pharmacology, in theory, has been practiced for centuries through observing the effects of herbal remedies and early drugs on humans. Most of this work was done through trial and error. In the early 1900s, scientific advances allowed scientists to combine the study of physiological effects with biological effects. This led to the first major breakthrough when scientists used clinical pharmacology to discover insulin. Since that discovery clinical pharmacology has expanded to be a multidisciplinary field and has contributed to the understanding of drug interaction, therapeutic efficacy and safety in humans. Over time clinical pharmacologists have been able to make more exact measurements and personalize drug therapies.

Part 2 Aspects of therapeutics

Introduction to Pharmacology

A. Definitions:

1. **Pharmacology**: Pharmacology is the study of interaction of drugs with living organisms. It also includes history, source, physicochemical properties, dosage forms, and methods of Administration, absorption, distribution mechanism of action, biotransformation, Excretion, clinical uses and adverse effects of drugs.
2. **Clinical Pharmacology**: It evaluate the pharmacological action of drug preferred route of administration and safe dosage range in human by clinical trails.
3. **Drugs:** Drugs are chemicals that alter functions of living organisms. Drugs are generally given for the diagnosis, prevention, control or cure of disease.
4. **Pharmacy:** It is the science of identification, selection, preservation, standardization, Compounding and dispensing of medical substances.
5. **Pharmacodynamics:** The study of the biological and therapeutic effects of drugs (i.e, "what the drug does to the body").
6. **Pharmacokinetics:** Study of the absorption, distribution metabolism and excretion (ADME) of drugs ("i.e what the body does to the drug").
7. **Pharmacotherapeutics**: It deals with the proper selection and use of drugs for the Prevention and treatment of disease.
8. **Toxicology:** It's the science of poisons. Many drugs in larger doses may act as poisons. Poisons are substances that cause harmful, dangerous or fatal symptoms in living Substances.

9. **Chemotherapy:** It's the effect of drugs upon microorganisms, parasites and neoplastic Cells living and multiplying in living organisms.
10. **Pharmacopoeia**: An official code containing a selected list of the established drugs and Medical preparations with descriptions of their physical properties and tests for their Identity, purity and potency e.g. Indian Pharmacopoeia (I.P), British Pharmacopoeia (B.P).

B. Drugs are obtained from:

1. Minerals: Liquid paraffin, magnesium sulfate, magnesium trisilicate, kaolin, etc.
2. Animals: Insulin, thyroid extract, heparin and antitoxin sera, etc.
3. Plants: Morphine, digoxin, atropine, castor oil, etc.
4. Synthetic source: Aspirin, sulphonamides, paracetamol, zidovudine, etc.
5. Micro organisms: Penicillin, streptomycin and many other antibiotics.
6. Genetic engineering: Human insulin, human growth hormone etc.

Out of all the above sources, majority of the drugs currently used in therapeutics are from Synthetic source.

Principles of clinical Pharmacology

1. Pharmacodynamics and pharmacokinetics

2 Clinical trials and drug developments

Pharmacodynamics

Involves how the drugs act on target cells to alter cellular function.

A. Receptor and non-receptor mechanisms: Most of the drugs act by interacting with a

Cellular component called receptor. Some drugs act through simple physical or chemical

Reactions without interacting with any receptor.

• Receptors are protein molecules present either on the cell surface or with in the cell

E.g. adrenergic receptors, cholinoceptors, insulin receptors, etc.

• The endogenous neurotransmitters, hormones, autacoids and most of the drugs

Produce their effects by binding with their specific receptors.

• Aluminium hydroxide and magnesium trisilicate, which are used in the treatment of

Peptic ulcer disease act by non-receptor mechanism by neutralizing the gastric acid.

Many drugs are similar to or have similar chemical groups to the naturally occurring chemical

And have the ability to bind onto a receptor where one of two things can happen- either the

Receptor will respond or it will be blocked.

A drug, which is able to fit onto a receptor, is said to have affinity for that receptor. Efficacy is

The ability of a drug to produce an effect at a receptor. An agonist has both an affinity and

Efficacy whereas antagonist has affinity but not efficacy or intrinsic activity.

When a drug is able to stimulate a receptor, it is known as an agonist and therefore mimics the

Endogenous transmitter.

When the drug blocks a receptor, it is known as antagonist and therefore blocks the action of

The endogenous transmitter (i.e. it will prevent the natural chemical from acting on the receptor).

However, as most drug binding is reversible, there will be competition between the drug and the

Natural stimulus to the receptor.

The forces that attract the drug to its receptor are termed chemical bonds and they are (a)

Hydrogen bond (b) ionic bond (c) covalent bond (d) Vander walls force. Covalent bond is the

Strongest bond and the drug-receptor complex is usually irreversible.

K1 K3

DR Biological effect

D+R K2

Where D = Drug, R= receptor DR= Drug receptor complex (affinity)

K1 = association constant

K2 = dissociation constant

K3 = intrinsic activity

When first messengers like neurotransmitters, hormones, autacoids and most of drugs bind with

Their specific receptors, the drug receptor complex is formed which subsequently causes the synthesis and release of another intracellular regulatory molecule termed as second messengers e.g. cyclic AMP, calcium, cyclic GMP, inositol triphosphate (IP3), diacylglycerol and calmodulin which in turn produce subcellular or molecular mechanism of drug action.

B. Site of drug action:

- A drug may act:

(I) intracellular e.g.: osmotic diuretics, plasma expanders.

(ii) On the cell surface e.g.: digitalis, penicillin, catecholamines

(iii) Inside the cell e.g.: anti-cancer drugs, steroid hormones.

C. Dose Response relationship

The exact relationship between the dose and the response depends on the biological object under observation and the drug employed.

When a logarithm of dose as abscissa and responses as ordinate are constructed graphically, the “S” shaped or sigmoid type curve is obtained.

The lowest concentration of a drug that elicits a response is minimal dose, and the largest concentration after which further increase in concentration will not change the response is the maximal dose.

1. **Graded dose effect:**
   As the dose administered to a single subject or tissue increases, the Pharmacological response also increases in graded fashion up to ceiling effect.
   - It is used for characterization of the action of drugs. The concentration that is required to Produce 50 % of the maximum effect is termed as EC50 or ED50.
2. **Quantal dose effect:**
   - It is all or none response, the sensitive objects give response to small Doses of a drug while some will be resistant and need very large doses. The quantal doseeffect curve is often characterized by stating the median effective dose and the median lethal dose.

Median lethal dose or LD50:

This is the dose (mg/kg), which would be expected to kill one Half of a population of the same species and strain.

Median effective dose or ED50:

This is the dose (mg/kg), which produces a desired Response in 50 per cent of test population.

Therapeutic index:

It is an approximate assessment of the safety of the drug. It is the ratio of the median lethal dose and the median effective dose. Also called as therapeutic window

Or safety.

The larger the therapeutic index, the safer is the drug. Penicillin has a very high therapeutic Index, while it is much smaller for the digitalis preparation.

D. Structural activity relationship

The activity of a drug is intimately related to its chemical structure. Knowledge about the Chemical structure of a drug is useful for:

(i) Synthesis of new compounds with more specific actions and fewer adverse Reactions

(ii) Synthesis of competitive antagonist and

(iii) Understanding the mechanism of drug action.

Slight modification of structure of the compound can change the effect completely.

PHARMACOKINETICS

Pharmacokinetics deals with the absorption, distribution, metabolism and excretion drugs in the body.

A. **Biotransport of drug:** It is translocation of a solute from one side of the biological barrier to the other.

1. Structure of biological membrane:

The outer surface of the cell covered by a very thin structure known as plasma membrane. It is composmembrane proteins have many functions like (a) contributing structure to the membrane (b) acting as enzyme (c) acting as carrier for transport of substances (d) acting as receptors. The

plasma membrane is a semipermeable membrane allowing certain chemical substances to pass freely e.g. it allows water, glucose, etc. but it won't allow sucrose until it is converted into glucose and fructoseis converted into glucose and fructose.

2. Passage of drug across membrane:

(a) Passive transfer

I) Simple diffusion

ii) Filtration

(b) Specialized transport

I) Facilitated diffusion

ii) Active transport

iii) Endocytosis.

(a) I) Simple diffusion:

Movement of a solute through a biological barrier from the phase of higher concentration to phase of lower concentration. No need of energy e.g. highly Lipid soluble drugs

ii) Filtration:

Is the process by which water soluble drug of relatively low molecular weight crosses the plasma membrane through pores as a result of hydrodynamic pressure gradient across the membrane e.g. urea and ethylene glycol.

(b) I) Facilitated diffusion:

It means the passage of drug across the biological membrane along the concentration gradient by the protein carrier mediated system also called as carrier mediated diffusion. It depends on number of carrier e.g. tetracycline, pyrimidine

ii) Active transport:

The process by which drugs pass across the biological membrane most often against their gradient with the help of carriers along with the expenditure of energy e.g. alpha methyl dopa, levodopa, 5-fluoro-uracil, 5 bromouracil.

iii) Endocytosis:

It is the process by which the large molecules are engulfed by the cell
Membrane and releases them intracellularly e.g. protein, toxins (botulinum, diphtheria)

Characteristics	**Simple diffusion**	**Facilitated**	**Active transport**
Incidence	Commonest	Less common	Least common

Process	Slow	Quick	Very quick
Movement	Along concentration gradient	Along concentration gradient	Against concentration gradient
Carrier	Not needed	Needed	Needed
Energy	Not needed	Not required	Required

B. **Drug absorption**:

Absorption is the process by which the drug enters in to the systemic Circulation from the site of administration through biological barrier. In case of intravenous or Intra-arterial administration the drug bypasses absorption processes and it enters into the Circulation directly.

1. **Routes of drug administration**:

a) From the alimentary tract:
   (i) Buccal cavity: e.g. nitrates
   (ii) Stomach: e.g. aspirin, alcohol
   (iii) Intestine: e.g. most of non ionized and ionized drugs.
   (iv) Rectum: e.g. rectal suppositories, bisacodyl laxatives.

Advantages of oral route: This route is safe, convenient and economical.
Disadvantages of oral route: Onset of drug action is slow, irritant drugs cannot be Administered and it is not useful in vomiting and severe diarrhea, gastric acid and digestive Enzymes may destroy some drugs, and water soluble drugs are absorbed poorly.

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b) **From the parenteral route**:

   (i) **Intradermal**: This is given into the layers of the skin e.g. B.C.G. vaccine
   (ii) **Subcutaneous:** Non-irritant substances are given into subcutaneous tissue e.g. insulin
   (iii) **Intramuscular:** Soluble substances, mild irritants, suspensions and colloids can be injected by this route. These injections can be given to deltoid or gluteal muscle. This Route is one of the more common routes e.g. multivitamins, streptomycin, etc.

Advantages:

Rate of absorption is uniform, onset of action is faster than oral and It can be given in diarrhoea or vomiting.

Disadvantages:

Pain at local site of injection, the volume of injection should not Exceed 10 ml.

(iv) Intravenous: Drugs directly given into a vein, produce rapid action, no need of Absorption as they enter directly into blood, can be given as bolus e.g. furosemide, Morphine, dopamine or as continous infusion e.g. fluids during shock or Dehydration.

Advantages: It can be given in large volumes, production of desired blood Concentration can be obtained with a well designed dose.

Disadvantages: Drug effect cannot be halted if once the drug is injected, Expertise is needed to give injection.

(v)Intrathecal: Injected into subarachnoid space of spinal cord e.g. spinal anesthetics.

(vi) Intraperitoneal: Injections given into the abdominal cavity e.g. infant saline, glucose.

(vii) Intra-articular: Injected directly into a joint e.g. hydrocortisone.

C) Transcutaneous route:

I) Iontophoresis: Galvanic current is used for bringing about the penetration of drugs into the deeper tissue e.g. salicylates.

Ii) Inunctions: Absorbed when rubbed in to the skin e.g. nitroglycerin ointment in angina Pectoris.

Iii) Jet injection: With help of high velocity jet produced through a micro fine orifice; No Need of needle and therefore painless. E.g. mass inoculation programes.

Iv) Adhesive units: A transdermal therapeutic system produce prolonged effect e.g. scopolamine for motion sickness.

D) Topical/ local route:

The absorption through skin is a passive process. The absorption occurs more easily through the cell lining e.g. dusting powder, paste, lotion, drops, ointment, suppository for vagina and rectum.

E) Inhalation:

Drugs may be administered as dry powders, and nebulized particles when sprayed as fine Droplets get deposited over the mucous membrane producing local effects and may be absorbed for systemic effects e.g. salbutamol spray used in bronchial asthma and volatile General anesthetics.

2. **Bioavailability**:

It is the rate and amount of drug that is absorbed from a given dosage form and reaches the Systemic circulation following non-vascular administration. When the drug is given IV, the Bioavailability is 100%. It is important to know the manner in which a drug is absorbed. The Route of administration largely determines the latent period between administration and onset of Action.

Drugs given by mouth may be inactive for the following reasons:

a) Enzymatic degradation of polypeptides within the lumen of the gastrointestinal tract e.g. Insulin, ACTH.
b) Poor absorption through gastrointestinal tract e.g. aminoglycoside antibiotic.
c) Inactivation by liver e.g. testosterone during first passage through the liver before it reaches Systemic circulation.

3. Factors affecting drug absorption and bioavailability:

a) Physico-chemical properties of drug

b) Nature of the dosage form

c) Physiological factors

d) Pharmacogenetic factors

e) Disease states.

a) Physico-chemical properties of drug:

Physical state: Liquids are absorbed better than solids and crystalloids absorbed better Than colloids.

ii) Lipid or water solubility: Drugs in aqueous solution mix more readily than those in oily Solution. However at the cell surface, the lipid soluble drugs penetrate into the cell more Rapidly than the water soluble drugs.

iii) Ionization: Most of the drugs are organic compounds. Unlike inorganic compounds, the Organic drugs are not completely ionized in the fluid. Unionized component is Predominantly lipid soluble and is absorbed rapidly and an ionized is often water soluble Component which is absorbed poorly. Most of the drugs are weak acids or weak bases. It may be assumed for all practical purposes that the mucosal lining of the G.I.T is Impermeable to the ionized form of a weak organic acid or a weak organic base. These Drugs exist in two forms.

Acidic drugs:

Rapidly absorbed from the stomach e.g. salicylates and barbiturates.

Basic drugs:

Not absorbed until they reach to the alkaline environment i.e. small Intestine when administered orally e.g. pethidine and ephedrine.

Dosage forms:

Particle size: Small particle size is important for drug absorption.

Drugs given in a dispersed or emulsified state are absorbed better e.g. vitamin D and vitamin A.

Disintegration time and dissolution rate.

Disintegration time: The rate of break up of the tablet or capsule into the drug granules.

Dissolution rate: The rate at which the drug goes into solution.

Formulation: Usually substances like lactose, sucrose, starch and calcium phosphate

Are used as inert diluents in formulating powders or tablets. Fillers may not be totally

Inert but may affect the absorption as well as stability of the medicament. Thus a faulty

Formulation can render a useful drug totally useless therapeutically.

Physiological factors:

Gastrointestinal transit time: Rapid absorption occurs when the drug is given on empty stomach. However certain irritant drugs like salicylates and iron preparations are deliberately administred after food to minimize the gastrointestinal irritation. But some times the presence of food in the G.I tract aids the absorption of certain drugs e.g. griseofulvin, propranolol and riboflavin.

ii) Presence of other agents: Vitamin C enhances the absorption of iron from the G.I.T. Calcium present in milk and in antacids forms insoluble complexes with the tetracycline antibiotics and reduces their absorption.

Area of the absorbing surface and local circulation: Drugs can be absorbed better from the small intestine than from the stomach because of the larger surface area of the former. Increased vascular supply can increase the absorption.

Enterohepatic cycling: Some drugs move in between intestines and liver before they reach the site of action. This increases the bioavailability e.g. phenolphthalein.

Metabolism of drug/first pass effect: Rapid degradation of a drug by the liver during the first pass (propranolol) or by the gut wall (Isoprinosine) also affects the bioavailability. Thus a drug though absorbed well when given orally may not be effective because of its extensive first pass metabolism.

Pharmacogenetic factors:

Individual variations occur due to the genetically mediated reason in drug absorption and response.

Disease states:

Absorption and first pass metabolism may be affected in conditions like malabsorption, thyrotoxicosis, achlorhydria and liver cirrhosis.

Bioavailability curves

Single dose bioavailability test involves an analysis of plasma or serum concentration of the drug at various time intervals after its oral administration and plotting a serum concentration time crave.

C) Distribution of drugs

Definition: Penetration of a drug to the sites of action through the walls of blood vessels from the administered site after absorption is called drug distribution. Drugs distribute through various body fluid compartments such as

Plasma

Interstitial fluid compartment

Trans-cellular compartment.

Apparent Volume of distribution (VD): The volume into which the total amount of a drug in the body would have to be uniformly distributed to provide the concentration of the drug actually measured in the plasma. It is an apparent rather than real volume.

Factors determining the rate of distribution of drugs:

1. Protein binding of drug: A variable and other significant portion of absorbed drug may become reversibly bound to plasma proteins. The active concentration of the drug is that Part which is not bound, because it is only this fraction which is free to leave the plasma and Site of action.
   (a) Free drug leave plasma to site of action
   (b) Binding of drugs to plasma Proteins assists absorption
   (c) Protein binding acts as a temporary store of a drug and tendsTo prevent large fluctuations in concentration of unbound drug in the body fluids
   (d) Protein Binding reduces diffusion of drug into the cell and there by delays its metabolic degradation

E.g. high protein bound drug like phenylbutazone is long acting.

Low protein bound drug like thiopental sodium is short acting.

2. **Plasma concentration of drug (PC):** It represents the drug that is bound to the plasma Proteins (albumins and globulins) and the drug in free form. It is the free form of drug that is distributed to the tissues and fluids and takes part in producing pharmacological effects.

The concentration of free drug in plasma does not always remain in the same level e.g.

i) After I.V. administration plasma concentration falls sharply

ii) After oral administration plasma concentration rises and falls gradually.

iii) After sublingual administration plasma concentration rise sharply and falls gradually.

3. Clearance: Volume of plasma cleared off the drug by metabolism and excretion per unit time.

Protein binding reduces the amount of drug available for filtration at the glomeruli and hence

Delays the excretion, thus the protein binding reduces the clearance.

4. Physiological barriers to distribution: There are some specialized barriers in the body due

To which the drug will not be distributed uniformly in all the tissues.

These barriers are:

a) Blood brain barrier (BBB) through which thiopental sodium is easily crossed but not

Dopamine.

b) Placental barrier: which allows non-ionized drugs with high lipid/water partition

Coefficient by a process of simple diffusion to the foetus e.g. alcohol, morphine.

5. Affinity of drugs to certain organs: The concentration of a drug in certain tissues after a Single dose may persist even when its plasma concentration is reduced to low. Thus the Hepatic concentration of mepacrine is more than 200 times that of plasma level. Their Concentration may reach a very high level on chronic administration. Iodine is similarly concentrated in the thyroid tissue.

D. metabolism of drugs: Drugs are chemical substances, which interact with living organisms and produce some Pharmacological effects and then, they should be eliminated from the body unchanged or by Changing to some easily excretable molecules. The process by which the body brings about Changes in drug molecule is referred as drug metabolism or biotransformation.

Enzymes responsible for metabolism of drugs:

a) Microsomal enzymes: Present in the smooth endoplasmic reticulum of the liver, kidney And GIT e.g. glucuronyl transferase, dehydrogenase, hydroxylase and cytochrome P450.

b) Non-microsomal enzymes: Present in the cytoplasm, mitochondria of different organs. E.g. esterases, amidase, hydrolase.

Types of biotransformation: The chemical reactions involved in biotransformation are classified as phase-I and phase – II (conjugation) reactions. In phase-I reaction the drug is Converted to more polar metabolite. If this metabolite is sufficiently polar, then it will be excreted in urine. Some metabolites may not be excreted and further metabolised by phase –II reactions.

Phase-I: Oxidation, reduction and hydrolysis.

Phase-II: Glucuronidation, sulfate conjugation, acetylation, glycine conjugation and Methylation reactions.

PHASE – I REACTIONS

a) **Oxidation:** Microsomal oxidation involves the introduction of an oxygen and/or the removal of A hydrogen atom or hydroxylation, dealkylation or demethylation of drug molecule e.g. Conversion of salicylic acid into gentisic acid.

b) **Reduction:** The reduction reaction will take place by the enzyme reeducates which catalyze the reduction of ado (-N=N-) and nitro (-NO2) compounds e.g. prontosil converted to Sulfonamide.

c) **Hydrolysis**: Drug metabolism by hydrolysis is restricted to esters and amines (by esterase's and amides) are found in plasma and other tissues like liver. It means splitting of drug Molecule after adding water e.g. pethidine undergoes hydrolysis to form pethidinic acid. Other drugs which undergo hydrolysis are atropine and acetylcholine.

Phase – II reactions (conjugation reactions):

This is synthetic process by which a drug or its metabolite is combined with an endogenous Substance resulting in various conjugates such as glucoronide, ethereal sulfate, methylated Compound and amino acid conjugates.

Glucuronide conjugation: It is the most common and most important conjugation reaction of Drugs. Drugs which contain

a) Hydroxyl, amino or carboxyl group undergo this process e.g. phenobarbitone.
b) Sulfate conjugation: Sulfotransferase present in liver, intestinal mucosa and kid
c) Acetyl conjugation: The enzyme acetyl transferase, which is responsible for acetylation, is present in the kupffer cells of liver. Acetic acid is conjugated to drugs via its activation By CoA to form acetyl CoA. This acetyl group is then transferred to-NH2 group of drug e.g. dapsone, isoniazid.
d) Glycine conjugation: Glycine conjugation is characteristic for certain aromatic acids

E.g. salicylic acid, isonicotinic acid, p-amino salicylic acid. These drugs are also metabolized by other path ways.

e) Methylation: Adrenaline is methylated to metanephrine by catechol-o-methyl transferase.

Here the source of methyl group is s – adenosyl methionine.

E. Excretion of drugs

Excretion of drugs means the transportation of unaltered or altered form of drug out of theBody. The major processes of excretion include renal excretion, hepatobiliary excretion and pulmonary excretion. The minor routes of excretion are saliva, sweat, tears, breast milk, vaginal Fluid, nails and hair. The rate of excretion influences the duration of action of drug. The drug that is excreted slowly, the concentration of drug in the body is maintained and the effects of the drug will continue for longer period.

Different routes of drug excretion

a) **Renal excretion**: A major part of excretion of chemicals is metabolically unchanged or changed. The excretion of drug by the kidney involves.

i) Glomerular filtration

ii) Active tubular secretion

iii) Passive tubular reabsorption.

The function of glomerular filtration and active tubular secretion is to remove drug out of theBody, while tubular reabsorption tends to retain the drug.

i) **Glomerular filtration:** It is a process, which depends on
(1) The concentration of drug in the Plasma
(2) Molecular size, shape and charge of drug
(3) Glomerular filtration rate.

Only the Drug which is not bound with the plasma proteins can pass through glomerulus. All the drugs which have low molecular weight can pass through glomerulus e.g. digoxin, ethambutol, etc. In congestive cardiac failure, the glomerular filtration rate is reduced due to decrease in renal Blood flow.

ii) Active tubular secretion:

The cells of the proximal convoluted tubule actively transport drugs from the plasma into the lumen of the tubule e.g. acetazolamide, benzyl penicillin, dopamine, pethidine, thiazides, histamine.

iii) Tubular reabsorption:

The reabsorption of drug from the lumen of the distal convoluted tubules into plasma occurs either by simple diffusion or by active transport. When the urine is acidic, the degree of ionization of basic drug increase and their reabsorption decreases. Conversely, when the urine is more alkaline, the degree of ionization of acidic drug increases and the reabsorption decreases.

b) **Hepatobiliary excretion**: the conjugated drugs are excreted by hepatocytes in the bile. Molecular weight more than 300 Daltons and polar drugs are excreted in the bile. Excretion Of drugs through bile provides a back up pathway when renal function is impaired. After Excretion of drug through bile into intestine, certain amount of drug is reabsorbed into portal Vein leading to an enterohepatic cycling which can prolong the action of drug e.g. Chloramphenicol, oral estrogen are secreted into bile and largely reabsorbed and have long Duration of action. Tetracycline's which are excreted by biliary tract can be used for treatment of biliary tract infection.
c) **Gastrointestinal excretion:** When a drug is administered orally, a part of the drug is not Absorbed and excreted in the faeces. The drugs which do not undergo enterohepatic cycle After excretion into the bile are subsequently passed with stool e.g. aluminium hydroxide Changes the stool into white colour, ferrous sulfate changes the stool into black and Rifampicin into orange red.
d) **Pulmonary excretion:** Drugs that are readily vaporized, such as many inhalation Anesthetics and alcohols are excreted through lungs. The rate of drug excretion through Lung depends on the volume of air exchange, depth of respiration, rate of pulmonary blood Flow and the drug concentration gradient.
e) **Sweat**: A number of drugs are excreted into the sweat either by simple diffusion or active Secretion e.g. rifampicin, metalloids like arsenic and other heavy metals.
f) **Mammary excretion**:
Many drugs mostly weak basic drugs are accumulated into the milk. Therefore lactating mothers should be cautious about the intake of these drugs because they may enter into baby through breast milk and produce harmful effects in the baby e.g. Ampicillin, aspirin, chlordiazepoxide, coffee, diazepam, furosemide, morphine, streptomycin Etc.

Clearance of a drug: It is the volume of plasma cleared of the drug by metabolism (hepatic) and excretion (renal) and other organs.

Total clearance will be calculated by Ct = Ch + Cr + C others

Ct = total clearance

Ch = hepatic clearance

R = Renal clearance

IV. Theoretical Pharmacokinetics

Information about the time course of drug absorption, distribution and elimination (pharmacokinetics) can be expressed in mathematical terms and has contributed to our Understanding and planning of drug regimens. Pharmacokinetic principles aid in the selection and adjustment of drug-dose schedules.

Half life:

Half life (t1/2) of a drug is the time taken for the concentration of drug in the blood or plasma to Decline to half of original value or the amount of drug in the body to be reduced by 50%. It has two phases' i.e. half-life of distribution and half-life of elimination. A half-life value can be readily determined for most drugs by administering a dose of the drug to A subject, taking blood samples at various time intervals and then assaying the samples., For Example if a blood level of drug A is 8.6 mg/ml at 10 minutes and 4.3 mg/ml at 60 minutes, so

The half – life of that drug is 50 minutes.

In most of the cases the rate of disappearance of a drug from the body is reflected in the rate of Lowering of its plasma concentration following a single intravenous dose, the plasma Concentration of the drug is focused to fall exponentially. With drugs whose elimination is Exponential, the biological half – life is independent of the dose, the route of administration and the plasma concentration. It depends on VD as well as on the metabolism and renal excretion of the drug.

Order of kinetics

Drugs are used for the treatment of diseases but the modes of administration of drugs are different. For example atenolol is administered once daily where as paracetamol needs 3-4times administration daily. Morphine is more effective in intramuscular route, and insulin is in subcutaneous route. The mode of administration is designed on the basis of absorption, distribution, metabolism and excretion (ADME) of drugs. Drugs usually follow two processes for their pharmacokinetic behavior in the body. These are first order and zero order process.

First order:

This is the most common process for many drugs. The rate at which absorption, distribution, metabolism and excretion occur are proportional to the concentration of drugs i.e. constant fraction of this drug in the body disappears in each equal interval of time.

Zero order kinetic:

It is independent of the amount of drug present at the particular sites of drug absorption or elimination. Few drugs follow this process e.g. ethanol, phenytoin. Here constant amount of the drug is eliminated in each equal interval of time. On repeated administration of drug after certain stage it goes on accumulating in the body and leads to toxic reactions.

Steady state plasma concentration:

When a drug dose is given repeatedly over a given period, a steady state is eventually reached, at which point the amount of drug absorbed is in equilibrium with that eliminated from the body. Steady

state is achieved after 4 to 5 half –lives for most of the drugs which follow first order kinetics. For example a drug with half life of 6 hours will be expected to be at steady state after more than 24 hours of administration. The pattern of drug accumulation during repeated administration of drug at intervals equal to its elimination half-life. For some drugs, the effects are difficult to measure, toxicity and lack of efficacy are both Potential dangers, and/or the therapeutic window is narrow. In these circumstances doses must be adjusted carefully to a desired steady- state concentration by giving loading and Maintenance doses.

Loading dose: The loading dose is one or a series of doses that may be given at the onset of Therapy with the aim of achieving the target concentration rapidly.

Maintenance dose: To maintain the chosen steady-state or target concentration, the rate of drug Administration is adjusted such that the rate of input equals to rate of loss.

V. Drug safety and effectiveness

A. Factors modifying the dosage and action of drugs :

Individuals differ both in the degree and the character of the response that a drug may elicit and therefore the optimum dose of a drug which produces the desired therapeutic effect varies from Person to person. The important factors which influence the effect of a drug are:

1. **Drug intolerance:** It is a quantitative deviation from the anticipated response to a given dose of a drug. Thus drug intolerance is inability of the individual to tolerate a drug. It is also called as hyper susceptibility.
2. **Sex difference**: Special care should be exercised when drugs are administrated during Menstruation, pregnancy and lactation.
    a) **Menstruation**: Drugs producing pelvic congestion should be avoided during menstruation e.g. drastic purgatives.
    b) **Pregnancy**: During pregnancy, the use of all drugs except those essential to maintain Pregnancy should be used with caution. Drugs which may stimulate the uterine smooth Muscle, are contraindicated during pregnancy. Further, many drugs administered to Mother are capable of crossing the placenta and affecting the foetus. Most of drugs can produce teratogenicity when they are used in pregnancy. Teratogenicity means Congenital malformation
        i) Drugs known to produce teratogenicity e.g thalidomide, Cyclophosphamide, methotrexate, tetracycline, phenytoin, carbamazepine and Progestogens.
        ii) Ii) Drugs may be teratogenicity e.g Warfarin, lithium, quinine, primaquine, Trimethoprim, rifampicin, anesthetic agents.
    c) **Breast feeding:** Nearly all agents received by mother are likely to be found in her milk and could theoretically harm the infant. Most of the lipid soluble drugs get into breast Milk. Therefore the drugs, which are excreted in the milk and harm the infant health should be, avoided by breast-feeding mothers e.g. sulphonamides, tetracycline's, Nalidixic acid, isoniazid, diazepam, lithium, Indomethacin, aspirin, etc.

3. **Body Weight:** The average dose is mentioned either in terms of mg per kg body weight or as the total single dose for an adult weighing between 50-100kg. However, dose expressed in this fashion may not apply in cases of excessively obese individuals or those suffering from Edema, or dehydration nutritional factors can sometimes alter drug metabolizing capacity and this should be kept in mind in malnourished patients.
4. **Age**: The pharmacokinetics of many drugs changes with age. Thus gastric emptying is Prolonged and the gastric pH fluctuates in neonates and infant, further the liver capacity to Metabolize drugs is low, renal function is less developed and the proportion of body water is Higher in the newborn and the neonates. Hence children may not react to all drugs in the same fashion as young adults. With a few exceptions, drugs are more active and more toxic in the new born than the adults. The pediatric doses are expressed in terms of body weight (mg/kg per dose or day) or in terms Of body surface area (mg/m2Per day). The body surface area can be calculated from the height and weight of the child. Like children, old people also present problems in dosage adjustment and this may vary widely with different people. The metabolism of drugs may diminish in the elderly and the renal function Declines with age. Elderly are sensitive to the drugs like hypnotics, tranquilizers, Phenylbutazone, diazepam, pethidine, etc.

5. Disease state: Some antimicrobial agents penetrate the cerebrospinal fluid well across the meninges while other antimicrobials penetrate well only when the meninges are inflamed (meningitis) e.g. sulphonamides, metronidazole, chloramphenicol, isoniazid and rifampicin penetrate well through the normal meninges and other antimicrobial agents like benzyl penicillin, ampicillin, tetracycline, streptomycin, gentamicin and cephalosporin penetrate only when the meninges are inflamed. Acute or chronic liver diseases markedly modify the rate and extent of biotransformation of drugs. The t1/2 of chlordiazepoxide and diazepam in patients with liver cirrhosis is greatly increased with corresponding prolongation of their effects. Cardiac disease by limiting blood flow to the liver may impair disposition of those drugs whose biotransformation is flow limited e.g. imipramine, isoniazid, lignocaine, morphine and propranolol. Similarly renal and pulmonary diseases may modify the biotransformation of drugs like insulin or Isoprinosine. Excretion of drug is impaired in chronic renal disease.

6. **Pharmacogenetic**: The science Pharmacogenetic is concerned with the genetically mediated variations in drug responses. Some examples of genetically mediated variations are:

Acetylation and hydroxylation of drugs: The rate of acetylation of INH, dapsone, hydralazine procainamide and some sulfonamides is controlled by an autosomal recessive gene and the dosage of these drugs depends up on the acetylator status of individuals.

7) Drug interactions:

It is usual for patients to receive a number of drugs at the same time. It is a phenomenon which occurs when the effects of one drug are modified by the prior or concurrent administration of another drug(s). A drug interaction may result in beneficial or harmful effects and may be classified into:

a) Pharmaceutical drug interactions:

Serious loss of potency can occur from incompatibility between an infusion fluid and a drug that is added to it.

For example diazepam if added to infusion fluid there will be a precipitate formation → loss of therapeutic effect.

b) Pharmacokinetic drug interactions:

1) Interaction during absorption: Drugs may interact in the gastrointestinal tract resulting in either decreased or increased absorption.

E.g. Tetracycline + Calcium → Decreased absorption of tetracycline.

2) Interaction during distribution: A drug which is extensively bound to plasma protein can be displaced from its binding sites by another drug or displacement from other tissue binding sites.

e.g. (I) Sulfonamide can be displaced by salicylates from plasma proteins and it leads to sulfonamide toxicity.

(ii) Quinidine displaces digoxin from binding sites in tissues and plasma and leads to digoxin toxicity.

3) Interactions during biotransformation: This can be explained by two mechanisms:

(i) Enzyme induction.
(ii) Enzyme inhibition.

(i) **Enzyme induction:** By this the biotransformation of drugs is accelerated and is a cause of Therapeutic failure. If the drug A is metabolized by the microsomal enzymes, then concurrent Administration with a microsomal inducer (drug B) will result in enhanced metabolism of drug
A.

E.g. Warfarin (anticoagulant) + Barbiturate (enzyme inducer) → decreased anticoagulation.

Enzyme inducers: Rifampicine, phenytoin, sulfonamides, etc.

(iii) **Enzyme inhibition:** By this the biotransformation of drugs is delayed and is a cause of increased intensity, duration of action and some times toxicity.

E.g. Warfarin + Metronidazole (enzyme inhibitor) → Haemorrhage.

Enzyme inhibitors: Disulfiram, isoniazid, allopurinol, cimetidine, etc.

f) Interactions during excretion: Some drugs interacts with others at the site of excretion i.e. in kidneys.

E.g. Penicillin (antibiotic) + Probenecid (antigout drug) → Increases the duration of action of

Penicillin (Both drugs excreted through tubular secretion).

B. Pharmacodynamic interactions:

(i) Drug Synergism: When the therapeutic effect of two drugs are greater than the effect of Individual drugs, it is said to be drug synergism.It is of two types.

(a) Additive effect: When the total pharmacological action of two or more drugs administered

Together is equivalent to the summation of their individual pharmacological actions is called

Additive effect.

I.e. A + B = AB

E.g. Combination of ephedrine and aminophyllin in the treatment of bronchial asthma.

(b) Potentiation effect: When the net effect of two drugs used together is greater than the sum of

d) Check liver and kidney function before and during drug administration, as even an otherwise non-cumulative drug would produce cumulation in the presence of hepatic and renal damage.

9) Drug tolerance:

When an unusually large dose of a drug is required to elicit an effect ordinarily produced by the normal therapeutic dose of the drug, the phenomenon is termed as drug tolerance.

Tachyphylaxis: Rapid development of tolerance on repeated administration is called tachyphylaxis e.g. Ephedrine, amphetamine and nitroglycerine which produce tachyphylaxis on repeated administration.

10) Emotional factors.

E.g. Placebo response.

Placebo: It is a Latin word meaning" I shall please" and it is a tablet looking exactly like the active treatment but containing no active component. It refers originally to substances merely to please the patient when no specific treatment was available.

B. Adverse drug reactions:

The drugs that produce useful therapeutic effect may also produce unwanted or toxic effects. It been estimated that about 0.5% of patients who die in hospitals do so as a result of their treatment rather than the condition for which they were treated. Serious systemic drug toxicity may result from overdoses. If is always an exaggeration of its pharmacological actions and some times it is predictable. E.g. Hypotension following antihypertensive drugs. Hypoglycaemia following insulin. An adverse drug reaction is defined as any response to a drug that is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy (WHO).

The adverse effects are

1) Side effects

2) Untoward effects

3) Allergic reactions

4) Idiosyncratic reactions and

5) Teratogenicity effects.

C. **1) Side effects:** Side effects are infact pharmacological effects produced with therapeutic dose
D. Of the drug.
E. e.g: Dryness of mouth with atropine which is troublesome in peptic ulcer patients and useful
F. When used as a preanaesthetic medication.

2) Untoward effects: Untoward effects develop with therapeutic dose of a drug. They are Undesirable and if very severe, may necessitate the cessation of treatment.

e.g: Diarrhoea with ampicillin and potassium loss with diuretics.

3) Allergic reactions: Most of the drugs and sera used in therapeutics are capable of causing Allergic or hypersensitive reactions. These reactions may be mild or very severe like. When an individual has been sensitized to an antigen (allergen) further contact with that antigen can some times lead to tissue damaging reactions. These allergic reactions

Are 4 types.

- Type-I reactions or anaphylactic reactions (Immediate hypersensitive reaction).
- Type-II reactions or cytotoxic reactions.
- Type-III reactions or immune complex mediated reactions.
- Type-IV reactions or cell mediated reactions (Delayed hypersensitive reactions).

4) Idiosyncratic reactions: The term idiosyncrasy means one's peculiar response to drugs. With the increasing knowledge of Pharmacogenetic, many idiosyncratic reactions have been found to be genetically determined.

e.g: Drugs like primaquine, sulfonamides and dapsone may cause hemolysis in patients with glucose - 6 phosphate dehydrogenase deficiency.

5) Teratogenic effect: Some drugs given in the first three months of pregnancy may cause congenital abnormalities and are said to be teratogenic. The best known example is Thalidomide which results in early easily recognizable abnormalities such as absent or grossly abnormal limbs.

Other drugs with teratogenic potential are androgens, steroids, anti consultants, anti neoplastic Drugs, cortisone, lithium, pencillamine, tricyclic antidepressants and warfarin.

V) Development and evaluation of new drugs:

The ultimate aim of pharmacological studies in animals is to find out a therapeutic agent suitable for clinical evaluation in man. No doubt, animal studies provide analogies and serve as useful Models. The administration of biologically active agent to human beings is associated with an Element of risk, which cannot be predicted by even the most careful and exhaustive animal Experiments.

Scientists all over the world are in a continuous effort to develop new drugs although drug Development is an extremely technical and enormously expensive operation. Among the contributors to new drug development, pharmacologists are more concerned in evaluating "new

Chemical entities" (NCE). Synthesis and evaluation of thousands of NCEs are usually necessary for new drugs to be introduced in the market. Research and development of new drugs have been done under strict government regulations which have greatly increased over the past couple of decades.

Drug development comprises of two steps.

a) Preclinical development and

b) Clinical development

A) Preclinical development: Synthesis of new chemical entities is done as per research policy decision which is based on:

(I) Random synthesis

(ii) Structure activity relationship (SAR)

(iii) Biochemical and pharmacological insight and

(iv) Chance finding.

The aim of the preclinical development phase for a potential new medicine is to explore the drug's efficacy and safety before it is administrated to patients. In this preclinical phase, varying drug doses are tested on animals and/or in vitro systems.

If active compounds are found, then studies on animals are done which include pharmacodynamics, pharmacokinetics, toxicology and special toxicological studies (mutagenicity and carcinogenicity) have to be done. In this study single dose is used for acute toxicity and repeated doses for sub chronic and chronic toxicity studies. Most of the preclinical tests have to be conducted in accordance with the standards prescribed.

B) Clinical development: About one in 1000 NCEs reach this stage. The steps to be studied in

This stage include:

a) Pharmaceutical study

b) Pharmacological study

c) Clinical trial.

a) Pharmaceutical study covers stability of formulation and compatibility of the NCEs with other tablet or infusion ingredients.

b) Pharmacological study includes further chronic toxicological study in animal, initially animal Metabolic and pharmacokinetic study. When studies in animals predict that a NCE may be Useful medicine i.e. effective and safe in relation to its benefits, then the time has come to put it to the test in man i.e. clinical trial.

c) Studies on human or Clinical Trial: Clinical trial is a means by which the efficacy of drug is tested on human being. It may also give some idea about the risk involved. It is divided into 4 phases. With each phase, the safety and Efficacy of the compound are tested progressively.

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SRI LAKSHMI NARAYANA INSTITUTE OF ALLIED HEALTH SCIENCE

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5	ELANGO N	UAH1801142	
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7	KEERTHANA.R	UAH1801144	
8	METHINE.G	UAH1801145	
9	NEELAMBARI S	UAH1801146	
10	PAVITHRA K	UAH1801147	
11	SANDHIYA K	UAH1801148	
12	VASANTHAN S	UAH1801149	
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18	AJAY A	UAH1901101	
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22	BARATH G	UAH1901105	
23	BEN SONA NELSON	UAH1901106	
24	BHARATHI P	UAH1901107	
25	DEVA M	UAH1901108	
26	ENIYAN VASANTHA KUMAR S	UAH1901109	
27	GAYATHRI M	UAH1901110	
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Annexure - III

Assessment Form

Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry.

Course code: VAC04/AHS/2019-18/11

Multiple Choice Question 12x2=24

1. Type I ADR reactions is_____

A) Caused when T-cells bind to a specific antigen
b) Caused by tissue injury
c) IgE mediated
d) Caused by cytotoxic antibodies

2. Average time period for phase II clinical trials study is _____

a) Up to 4 year
b) Up to few month
c) Up to Two year
d) Up to several year

3. _____ drug can cause lactic acidosis.

a) Metformin
b) Pioglitazone
c) Repaginate
d) Glibenclamide

4. The incidence ADR is highest in _____.

a) Children
b) Elderly
c) Women
d) Men

5. _____ antihypertensive therapy should be avoided in type-1 diabetes mellitus

a) ACE inhibitors
b) High dose diuretics
c) Centrally acting
d) Calcium channel blockers

6. _____ is an example of Category X drugs

a) Diclofenac
b) Ranitidine
c) Lorazepam
d) Paracetamol

7. _____ is indicated in agitation and restlessness in the elderly, despite the high incidence Of extrapyramidal side-effects.

a) Prochlorperazine
b) Clozapine
c) Haloperidol
d) Flupentixol

8. _____ is contraindicated during pregnancy due to its Teratogenicity.

a) Folic acid
b) Calcium
c) Retinol
d) Iron

9. _____ commonly reported ADR of diuretic class of drugs.

a) Hypokalaemia
b) Alopecia
c) Skin disorder
d) Rhinitis

10. Which of the following responsibility of the clinical pharmacist is in direct patient care area?

a) Supervision of drug administration techniques.
b) Providing drug information to physicians and nurses.
c) Identify drugs brought into the hospital by patients.
d) Reviewing of each patient's drug administration forms periodically to ensure all doses have been administered.

11. Which of the following responsibility of community pharmacist is in dispensing area?

a) Reviews all doses missed, reschedule the doses as necessary & signs all drugs not given notices.
b) Supervision of drug administration.
c) Ensures that establishes policies & procedures are followed.
d) Reviewing of each patient's drug administration forms periodically to ensure all doses have been administered.

12. The most specific & sensitive method for assessment of compliance can be used to Detect potent therapeutic agent in body fluids is

a) Drug analysis.
b) Interrogation.
c) Urine marker.
d) Residual Tablet counting.

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Annexure - III

Assessment Form

Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry.

Course code: VAC04/AHS/2019-18/11

Multiple Choice Question 12x2=24

1. Type I ADR reactions is_____

A) Caused when T-cells bind to a specific antigen
b) Caused by tissue injury
c) IgE mediated
d) Caused by cytotoxic antibodies

2. Average time period for phase II clinical trials study is _____

a) Up to 4 year
b) Up to few month
c) Up to Two year
d) Up to several year

3. _____ drug can cause lactic acidosis.

a) Metformin
b) Pioglitazone
c) Repaginate
d) Glibenclamide

4. The incidence ADR is highest in _____.

a) Children
b) Elderly
c) Women
d) Men

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5. _____ antihypertensive therapy should be avoided in type-1 diabetes mellitus

a) ACE inhibitors
b) High dose diuretics
c) Centrally acting
d) Calcium channel blockers

6. _____ is an example of Category X drugs

a) Diclofenac
b) Ranitidine
c) Lorazepam
d) Paracetamol

7. _____ is indicated in agitation and restlessness in the elderly, despite the high incidence Of extrapyramidal side-effects.

a) Prochlorperazine
b) Clozapine
c) Haloperidol
d) Flupentixol

8. _____ is contraindicated during pregnancy due to its Teratogenicity.

a) Folic acid
b) Calcium
c) Retinol
d) Iron

9. _____ commonly reported ADR of diuretic class of drugs.

a) Hypokalaemia
b) Alopecia
c) Skin disorder
d) Rhinitis

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10. Which of the following responsibility of the clinical pharmacist is in direct patient care area?

a) Supervision of drug administration techniques.
b) Providing drug information to physicians and nurses.
c) Identify drugs brought into the hospital by patients.
d) Reviewing of each patient's drug administration forms periodically to ensure all doses have been administered.

11. Which of the following responsibility of community pharmacist is in dispensing area?

a) Reviews all doses missed, reschedule the doses as necessary & signs all drugs not given notices.
b) Supervision of drug administration.
c) Ensures that establishes policies & procedures are followed.
d) Reviewing of each patient's drug administration forms periodically to ensure all doses have been administered.

12. The most specific & sensitive method for assessment of compliance can be used to Detect potent therapeutic agent in body fluids is

a) Drug analysis.
b) Interrogation.
c) Urine marker.
d) Residual Tablet counting.

Annexure- V

Student Feedback Form

Course Name: "CLINICAL PHARMACOLOGY"

Subject Code: VAC04/AHS/2019-18/11

Name of Student: _____ Roll No.: _____

We are constantly looking to improve our classes and deliver the best training to you. Your evaluations, comments and suggestions will help us to improve our performance

Feedback Form

	Strongly agree	Agree	Neutral	Disagree	Strongly disagree
1. The course met my expectations.	○	○	○	○	○
2.I will be able to apply the knowledge learned.	○	○	○	○	○
3.The course objectives for each topic were identified and followed.	○	○	○	○	○
4.The content was organised and easy to follow.	○	○	○	○	○
5.The quality of instruction was good.	○	○	○	○	○
6.Class participation and interaction were encouraged.	○	○	○	○	○
7.Adequate time was provided for questions and discussion.	○	○	○	○	○

8.How do you rate the course overall?

- ○ Excellent
- ○ Good
- ○ Average
- ○ Poor
- ○ Very poor

9. The aspects of the course could be improved?

10. Other comments?

Signature of the student:
Date:

Annexure- V

Student Feedback Form

Course Name: "CLINICAL PHARMACOLOGY"

Subject Code: VAC04/AHS/2019-18/11

Name of Student: AJITH KUMAR Roll No.: VAH18011130.

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9. The aspects of the course could be improved? Good enough its more intellectual

10. Other comments? overall teaching level Good.

Signature of the student: V. Ajithkumar

Date: 13/12/2019

Annexure- V

Student Feedback Form

Course Name: "CLINICAL PHARMACOLOGY"

Subject Code: VAC04/AHS/2019-18/11

Name of Student: Alaguri Sandeep Roll No.: UAH1801189.

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Signature of the student:
Date: 13/12/2019.

Annexure- V

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Annexure- V

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Date: 13.12.2019

From

Dr.G. Somasundaram
Principal of Allied Health Science,
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Through Proper Channel

To

The Dean,
Sri Lakshmi Narayana Institute of Medical Sciences
Bharath Institute of Higher Education and Research,
Chennai.

Sub: Completion of value-added course: CLINICAL PHARMACOLOGY

Dear Sir,

With reference to the subject mentioned above, the department has conducted the value-added course titled: **CLINICAL PHARMACOLOGY** November to December 2019 for 30 AHS Students. We solicit your kind action to send certificates for the participants that is attached with this letter. Also, I am attaching the photographs captured during the conduct of the course.

Kind Regards,

Dr. G. Somasundaram

Encl: Certificates

Photographs