Program	**:**	B. Pharmacy
Name of Unit	**:**	Drug Distribution, Hospital Formulary, Therapeutic Drug Monitoring, Medication Adherence
Subject /Course name	**:**	Pharmacy Practice
Subject/Course ID	**:**	BP 703T
Class: B.Pharm. Semester	**:**	VII
Module	**:**	II
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Learning Outcome of Unit

LO	Learning Outcome (LO)	Course Outcome Code
LO1	Students will learn about the drug distribution system in hospital.	BP703.1
LO2	Students will learn about the need of therapeutic drug monitoring.	BP703.3
LO3	Students learn about community pharmacy management.	BP703.2
LO4	Students will understand the importance of patient medication history	BP703.4

Module Content Table

No.	Topic
1	Drug distribution system in a hospital:- Dispensing of drugs to inpatients, types of drug distribution systems, charging policy and labeling, Dispensing of drugs to ambulatory patients, and dispensing of controlled drugs.
2	Hospital formulary :- Defination, contents of hospital formulary, Differentiation of hospital formulary and Drug list, preparation and revision and addition and deletion of drug from hospital formulary.
3	Therapeutic drug monitoring:- Need for TDM, factors to be considered during TDM, Indian scenario for TDM.
4	Medication adherence:- Causes of medication non- adherence, pharmacist role in the medication adherence, and monitoring of patient medication adherence.
5	Patient medication history interview:- Need for the patient medication history, medication interview forms
6.	Community pharmacy management:- Financial, material, staff and infrastructure requirements.

1. DRUG DISTRIBUTION SYSTEM IN HOSPITALS

Towards development of new and improved drug distribution system, traditional methods of distribution are now reconstructed into new system. In hospital, the procedure of drug distribution may be categorized into two groups:

- Ambulatory/Outpatient Service
- Inpatient Services

Inpatient: Inpatients are those who get hospitalized for the purpose of treatment of disease, surgery and rehabitation.

Drug distribution to inpatients falls within four categories are as follows:

1. Individual prescription order system.
2. Complete floor stock system (Charging Policy).
3. Combination of above 1 and 2.
4. Unit dose dispensing method.

1. Individual Prescription Order System:

- This system is generally used by the small and/or private hospitals because of the less manpower requirement and the appeal for individualized service.

Advantages:

- All medication orders are directly reviewed by the pharmacist.
- Easily interaction of pharmacist, doctor, nurse and patient in the medication matters. . Medication errors could avoid.

Disadvantages:

- Possible delay in obtaining the required medication and the increase in cost to the patient.
- This system cannot be used in big hospitals.
- Difficulty in dispensing of drug in absence of pharmacist.

2. Complete Floor Stock System (Charging Policy):

- Under this system, both pharmacy and nursing are responsible for drug distribution to patients.
- According to this system, the drugs are stored at the nursing station and administered by nurse according to order of physician.
- Commonly used drugs in significant quantity are stocked on the floor stock or in ward.

Drugs which are dispensed in complete floor stock system are categorized as:

(a) Charge floor stock drugs

(b) Non-charge floor stock drugs

This system is generally used by governmental and other hospitals in which charges are not made to the patient or when the all-inclusive rate is used for charging. It does not have applicability to the general hospital.

(a) Charge Floor Stock Drug:

- Charge floor stock drugs are those where patient is charged for every single dose administered to him.
- Selection of these drugs in various wards is decided by pharmacy and therapeutic committee.
- Examples of drugs in this stock are antibiotics, antihypertensive drugs, anticoagulant, antiepileptic, antidepressant, diphenhydramine.

(b) Non-charge Floor Stock Drugs:

3. Drugs are dispensed to all patients on floor on non-charged basis. Combination of Individual Prescription Order System and Complete Floor Stock System:
   - It is used in those hospitals, where patients have to pay for their hospitalization. In this system, their primary mean is to dispense the drugs according to individual prescription order system.

     Today most of the hospital uses this system. Some hospital modifies it to include the use of unit dose medications.
4. Unit Dose Dispensing
   - Unit dose medications are those which are ordered, packaged, and administered in single or multiple units containing predetermined amount of drug and doses.

Advantages of Unit Dose System

1. Patients receive better health service and have to charge for those drug and doses which are administered to them.
2. Nurses get more time for patient care because all doses of medication are prepared by the pharmacist.

Dispensing Procedure in Unit Dose System:

This system could be followed by two ways: Centralized Unit Dose Distribution System [CUDDS] and De-centralized Unit Dose Distribution System [DCUDDS].

(a) Centralized Unit Dose System:

In this system, all the drugs are stored in central area of pharmacy and the drugs are dispensed to all inpatients in unit doses.

To operate the delivery system effectively, various medication carts are used to transport unit doses to the patients and to forward a copy of the physician original medications order to the pharmacy for direct explanation and filling.

(b) Decentralized Unit Dose System:

Unlike the centralized system, decentralized unit dose system function through small satellite pharmacies which are located on each floor of the hospital.

In this system, the core pharmacy becomes a procurement, manufacturing, storage and packaging center which provides all medicine to all the satellites pharmacies.

The delivery process of this system is accomplished by the use of medication carts. Such type of system can be used for a hospital with separate buildings.

Following are the step by step outline procedure necessitated in a decentralized unit dose system.

1. During the admission of patient in hospital all the patients related data such as diagnosis profile, medication history, any allergies and other applicable data are entered on to the patient profile card.
2. Afterward direct copies of medication orders are sent to the pharmacist.
3. Entry of all medications ordered made into patient profile card.
4. Pharmacist verify the medication order for allergies, drug interactions, drug laboratory test effects, and rational of drug therapy.
5. Dosage time table is organized with nursing station.

Dispensing of drug to outpatient

It is also called ambulatory services and refers to those patients who are not occupying beds in hospitals or in clinics, health centers and other places when they come for consultation and diagnosis, treatment.

Categories of Ambulatory Services:

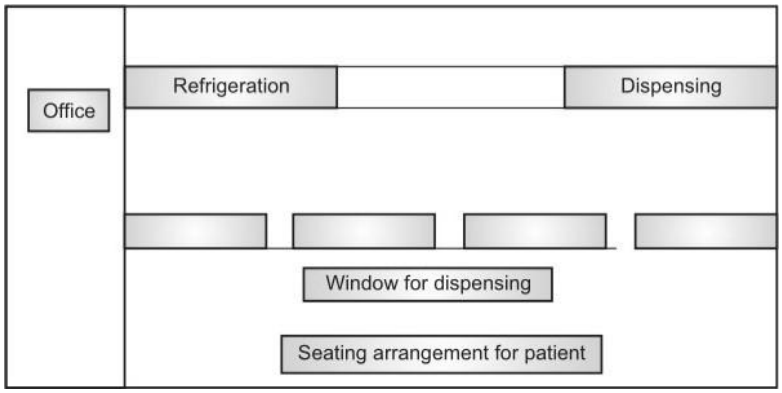
1. Emergency outpatients
2. Referred outpatients
3. Special outpatient
4. General outpatients

- Emergency Outpatients: For emergency outpatient, 24 hours services are given who requires immediate care for the survival.
- Referred Outpatient: These patients are referred to the hospital for a specific purpose due to lack of facilities available with the private clinic practitioners or patient needs extra care.
- Special Outpatient: After compilation of general check up, the patients are asked to go for accurate diagnosis by clinical, pathological or radiological examination. After receiving the test report of examination medicine is given to him.
- General Outpatient: These patients come for general checkup and medicines are prescribed to him. They may either undertake minor surgery, superficial surgery or dressing at hospital.

Outpatient decides the image of the hospital as per the services received by them. Thus, it is essential to look into the following aspects while designing the hospital care service.

1. Separate waiting room with appropriate seating facilities.
2. Sufficient number of service windows and separate facility for women.
3. Provision for adequate light and ventilation.

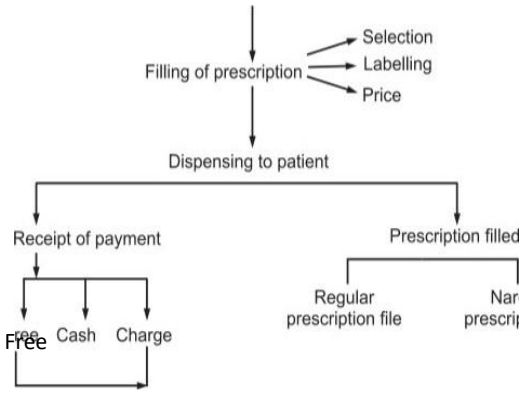
Social aspect must be considered to carry out dispensing services.



Typical layout for OPD

Routine Dispensing of Out-patient:

- Patients take written prescription by the Physician, which is given to the pharmacist where it is dispensed.
- Pharmacist guarantees that patient gets right medication. . Pharmacist gives instructions to patient about dispensed medicine.
- Labeling of medicine.
- Maintenance of payments by Pharmacist.
- Finally, payment by patient.



Layout for routine dispensing of out-patient

SATELLITE PHARMACY SERVICES

- Multispecialty hospitals are generally design for the diagnosis and treatment of number of diseases so the concept of satellite pharmacy is adopted in such hospital which have multistored building in a single premises.
- Every day in morning as well as evening it becomes very difficult to cope up with distribution of drug to all the wards. So, such cases hospital runs satellite pharmacy in the form of mini pharmacies, which is situated on each floor.
- According to hospital policies few days stock of medicines is stored in hospital. While main pharmacy supplies all medicine to satellites pharmacies.

Advantages:

- Efficiently drugs can be distributed.

- Time of drug distribution could be reduced.
- Errors in drug distribution could be stop.

Disadvantages:

Effect on the financial statement of hospital. • Additional manpower is required

BED SIDE PHARMACY

- Health authorities in countries like UK, USA, believe that it is responsibility of pharmacist to take part in the activities going on around the patient; apart from dispensing of drug.
- In 1972, survey was carried out by Noel Hall working group in UK and submitted a report with recommendation regarding the need of bed side services to public health.
- Life saving drugs like nitroglycerine tablet may be kept at bed side if it is order by physician. Not more than 1 strip shall be left with patient. Role of Pharmacist in Bed Side Pharmacy:
- A bed side pharmacist has to interact with nursing and medical staff.
- A bed side pharmacist recommends advice regarding the alteration and uses of frequently used drugs to the medical and nursing staff.
- He also gives his own expert evaluation/suggestion on prescribed drugs.
- In bed side pharmacy, pharmacist act as a key member of inter professional team of physician, nurse and patient.
- While serving as a bed side pharmacist, he works along with his capacity of compounding and dispensing of drugs.

He facilitates other with additional responsibility of drug usage and drug information. • A bed side pharmacist is essentially a drug consultant as he shares the healthcare responsibility with the physician

DISPENSING OF CONTROLLED DRUGS Controlled substance is a drug or chemical which ownership, manufacture, or use is absolutely regulated by a respective government of country such as illegally used drugs or prescription medications. These laws enforcement leads to prevention in the unauthorized use of such substances/drugs such as central analgesics (opioids), anaesthetics, steroids, etc.

Hospital Control Procedures:

Following procedure and person/department is responsible for maintenance and record of control substances in hospital.

- Pharmacist in chief: Responsible for the purchase, storage, accountability, and appropriate dispensing of the control substances in the hospital.
- Head nurse: Responsible for the record of proper storage.
- Administration head: Responsible for the proper safeguarding and handling of controlled substances.

Role and Responsibility of Administration:

During handling of control substances, following duties should be performed administration department.

Head nurse should use control drug form while ordering of the drug from the pharmacy. Head

nurse should enter the information of control substance administration within 24 hours in daily basis administration form.

Each nursing unit should maintain the monthly dispensing record of control substances. This called as storage record of nursing unit.

Policies and Procedures for Ordering of Controlled Substances

- Preparation of orders: Order of the control substance should be made by using Ink or indelible pencil, typing and duly sign by the respective doctor.
- Doctor's orders for administration of controlled drugs: Order of control substances for Ward stock must write on physician order sheet or patient chart. If the control substances are not in ward stock, then complete prescription is written on blank hospital prescription along with complete name and signature by the doctor. • Pro Re Nata orders (PRN Order): This type of order must be discouraged except under special circumstances.
- Telephone orders: Doctor may give telephonic orders of control substances in certain cases while it is necessary to take such order by nurse on doctor order sheet by mentioning complete name of doctor along with initial of nurse and later such order sheet must be sign by doctors within 24 hours.
- Verbal orders: In emergency cases a doctor may give a verbal order of control substances and the nurse may write such order on doctor order sheet and later duly sign by doctor within 24 hours.

Ordering non-ward stock-controlled drugs from pharmacy: Ordering of the control substances for non-ward stock done by doctor sign and if more substances are again needed then doctor may sign again. Prescribing of Control Drugs in Out Patient Department (OPD):

Dispensing of controlled drugs for outpatient from pharmacy must be made on the prescription only by clearly mentioning the strength and the quantity with duly sign of doctor. The information for such order includes:

1. Date.
2. Details of patients.
3. Patient's hospital number.
4. Amount Of drug ordered.
5. Strength.
6. Name of the prescriber and their signature.

Dispensing of Control Drugs for House use when Pharmacy is closed:

When the patients are discharge from hospital or emergency ward at the time of closed of pharmacy. Occasionally such patients require drugs for use at home and in such cases dispensing of drug can be done by only on prescription which must be signed by the staff who is a registered medical practitioner and also authorized to prescribe control substances for this purpose.

3. THERAPEUTIC DRUG MONITORING

Therapeutic drug monitoring (TDM) is generally defined as the clinical laboratory measurement of a chemical parameter that, with appropriate medical interpretation, will directly influence drug prescribing procedures.

It involves the use of drug concentration measurements in body fluids as an aid to the management of drug therapy for the cure, alleviation or prevention of disease.

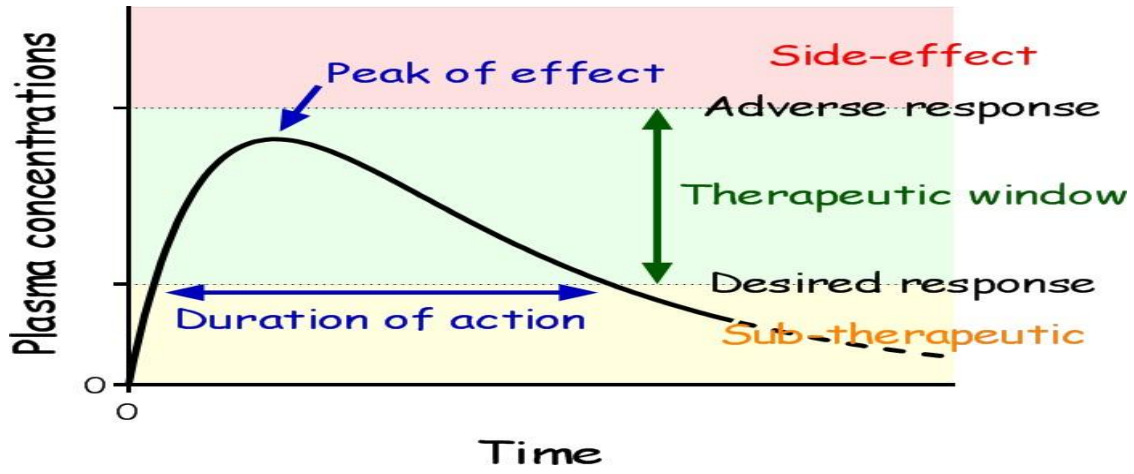
TDM enables the assessment of the efficacy and safety of a particular medication in a variety of clinical settings. The goal of this process is to individualize therapeutic regimens for optimal patient benefit.

CONCEPT OF THERAPEUTIC DRUG MONITORING (TDM):

- TDM is based on the principle that for some drugs there is a close relationship between the plasma level of the drug and its clinical effect.
- If such a relationship does not exit TDM is of little value.
- The clinical value of plasma level monitoring depends on how precisely the treatment outcome can be defined.
- When a precise therapeutic end point is difficult to define, monitoring of drug levels may be of considerable therapeutic assistance.

THERAPEUTIC RANGE/ THERAPEUTIC WINDOW:

The therapeutic range/ therapeutic window is the concentration range of drug in plasma where the drug has been shown to be efficacious without causing toxic effects in most people.



TARGET CONCENTRATION AND THERAPEUTIC RANGE:

- The therapeutic range concept suffers from two strategic deficiencies.
  – First the idea of a range introduces uncertainty into exactly how to prescribe the desired dose.
  – The second deficiency is the implicit assumption that all concentrations within the range are equally desirable.
- On the other hand, the target concentration is directly linked to a specific dose for an individual - not a range of doses.
- Selection of a target concentration requires an understanding of the concentration-effect relationship, i.e. pharmacodynamic, for both desired and undesired effects. The target concentration is chosen to optimize the balance between these effects.

NEED OF THERAPEUTIC DRUG MONITORING:

- Certain drugs have a narrow therapeutic range.
- In concentrations above the upper limit of the range, the drug can be toxic.
- In concentrations below the lower limit of the range, the drug can be ineffective.
- Not all patients have the same response at similar doses.

Indications for TDM Testing:

- Drug efficacy difficult to establish clinically (Phenytoin).
- Suspected toxicity.
- Inadequate therapeutic response.
- Compliance concerns.
- Dosage change.
- Change in patient's clinical state.
- Change in co-medications (quinidine decreases digoxin clearance).
- Manifestations of toxicity and disease state are similar (Theophylline).
- Drugs for which relationship between dose and plasma concentration is unpredictable, e.g Phenytoin.
- Drugs with a narrow therapeutic window:- will allow dosage alterations to produce optimal therapeutic effect or to avoid toxic effects. Ex: Lithium, phenytoin, and digoxin.
- Drugs with steep dose response curve: e.g. theophylline.
- Drugs for which there is difficulty in measuring or interpreting the clinical evidence of therapeutic or toxic effects:- Nausea & vomiting occur in both digitalis toxicity & congestive heart failure.
- Drug with saturable metabolism: Phenytoin.
- Drug with poorly defined end point or difficult to clinically predict the response. Example: immunosuppressant drugs.

- Renal disease: Alter the relationship between dose & the plasma concentration. Important in case of digoxin, lithium & aminoglycoside antibiotics.
- Drug interactions: When another drug alters the relationship between dose & plasma concentration e.g. plasma concentration of lithium is increased by thiazide.
- Drug with large individual variability at steady state PDC in any given dose.
- For diagnosis of suspected toxicity & determining drug abuse.
- To evaluate compliance of patient.
- Guiding withdrawal of therapy: Antiepileptics, Cyclosporine.

DRUGS THAT ARE NOT SUITABLE FOR TDM:

1. Drugs having wide therapeutic index.
2. Toxicity is not a realistic concern (Penicillin).
3. Effects can be measured using functional laboratory tests (Anticoagulants).
4. Plasma concentration not predictably related to effects (Anticoagulants).
5. Effect of the relationship remains undefined (Antidepressants).
6. Hit and run drugs: Omeprazole, MAO inhibitors.

BASIC PRINCIPLES OF THERAPEUTIC DRUG MONITORING:

The following are important considerations to ensure an optimum TDM service in any setting:

1. Measurement of patient's serum or plasma drug concentration taken at appropriate time after drug administration.
2. Knowledge of pharmacological and pharmacokinetic profiles of the administered drugs.
3. Knowledge of relevant patient's profile like demographic data, clinical status, laboratory and other clinical investigations.
4. Interpretation of SDC after taking into consideration all of the above information and individualizing drug regimen according to the clinical needs of the patient.

PROCESS OF TDM: Development of plasma profile in each patient

1. Administering a predetermined dose of drug.
2. Collection of blood samples.
3. Determination of blood samples.
4. Plasma profile and pharmacokinetic model development:
   – Clinical effect of drug
   – Development of dosage regimen
   – Diagnosis, dosage form selection, dosage regimen, initiation of therapy.

↓

Evaluation of clinical Response

FACTORS THAT AFFECT RESULTS:

- Pharmacokinetics
- Pharmacodynamics
- Dose
- Sampling time and type
- Testing methodology
- Genetic polymorphisms
- Other variables: Smoking, drug formulation and circadian effect, use of Alternative system ofmedicine. {shankhapushpi vs phenytoin}
- Interaction with conventional drugs have been documented for liquorice, ginseng, tannic acids,plantain, uzara root, hawthorn and kyushin.

MAJOR SOURCES OF PHARMACOKINETIC VARIABILITY:

- Patient Compliance – lack of
- Age – neonates, children, elderly
- Physiology – gender, pregnancy
- Disease – hepatic, renal, cardiovascular, respiratory
- Drug-to-drug interactions
- Environmental influences
- Sampling time is critical, since the drug concentration varies over the entire dosing interval and with the duration of dosing in relation to achieving a steady state.
- Trough values are the least variable concentrations and are most often used to establish therapeutic ranges. Drugs with short half-lives require trough concentration monitoring. Drugs with a long half- life can be monitored at any point in the dosage interval.
- Additional consideration should be given to the type of sample tested as some anticoagulants may interfere with results for certain drugs (lithium: heparin affects lithium results), while some gel separators interfere with the results of other drugs.
- The sensitivity and specificity of the testing methodology must also be considered.

FACTORS THAT AFFECT INTERPRETATION:

These vary from drug to drug.

Protein Binding

- TDM assays typically require serum or plasma and usually measure both the bound and unbound drug, even though it is the unbound drug that reacts with the receptor to produce a response.
- This is seldom an issue – unless the patient's binding capacity is altered due to disease-state, drug interaction, or non-linear binding. In such cases, the effect of the protein binding needs to be taken into consideration when interpreting results.

Active Metabolites: Many therapeutic drug metabolites, though not measured, contribute to a drug's therapeutic response. For example, primidone treatment is monitored by measuring phenobarbitone, an active metabolite, but primidone itself and other metabolites are also active.

Steady State: Unless a loading dose or i.v. infusion is used initially, steady state must be reached before meaningful TDM is possible for those drugs that are given long-term.

Turnaround Time: Turnaround time is important to ensure that the physician has time to evaluate the result before the patient is scheduled to receive the next dose.

• For most drugs this is not an issue, as assays for the most commonly tested analytes are available on several fully automated analyzers.

• However, for drugs without commercially available assays, highly specialized chromatographic and ultra-filtration assays are used. These methods require specially trained staff and are most often performed in a limited number of sites. Therefore, results tend to take longer to receive.

GUIDELINES TO SPECIMEN COLLECTION:

- Drawn blood, used for TDM, demonstrates a drug action in the body at any specific time. Therefore,blood testing is the procedure of choice when definite data are required.
- For adequate absorption and therapeutic levels to be accurate, it is important to allow for sufficienttime to pass between the administration of the medication and the collection of the blood sample.
- Blood specimens for drug monitoring can be taken at two different times: during the drug´s highesttherapeutic concentration ('peak' level), or its lowest ('trough' level).
- Occasionally called residual levels, trough levels show sufficient therapeutic levels; whereas peaklevels show toxicity.
- Peak and trough levels should fall within the therapeutic range.
- Patients receiving a drug at a dosing interval longer than the half-life of the drug will demonstratelarge fluctuations between peak and trough levels.
- Plasma concentrations of drugs dosed at intervals shorter than their half-lives would show lessfluctuation between peak and trough levels.
- For chronically administered oral medications the peak levels usually occur 1-2 hours after the doseand the trough serum concentration shortly after the dose is administered.
- Digoxin is one exception. The serum level to determine peak activity should be drawn after theserum digoxin has had time to equilibrate with the tissue i.e., 6-10 hours after the oral dose.

TIMING OF SAMPLE COLLECTION:

- The best sampling time is in the predose or trough phase, when a drug is administered by multipleoral doses.
- Trough conc. are commonly used for many drugs.
- Peak conc. may be useful for some antibiotics: Aminoglycosides

- Correct sample timing should also take into account absorption and distribution, eg digoxin samples are collected after 6 hours of administration. Drawing the trough level at the time the dose is given is usually sufficiently accurate.

TIMING OF SAMPLE COLLECTION:

- For short half-life drugs, more than one sample (three is ideal) is the most useful for determining individual pharmacokinetic parameters. Alternatively, a peak (CMAX) and a trough (CMIN) can be collected to determine the bounds of high and low concentrations at steady-state.
- For long half-life drugs (digoxin, phenobarbital), a single sample during the dosing interval is sufficient. If one suspects altered clearance rates, more samples can be collected to assess half-life. For cyclosporine, a single trough sample has been used for many years, but now recommendations arechanging to a single two hour sample (C2).
- For cyclosporine a “trough” usually refers to a 12 hour sample, even though this drug is used once a day, or once every other day in some patients.

SAMPLE TIMING FOR SOME IMPORTANT DRUGS:

a) Phenytoin: Since phenytoin has a long half life a single daily dose may be employed and so the timingof concentration monitoring is not critical.

b) Carbamazepine: Its half life may be as long as 48 h following a single dose. A trough concentrationtaken just after a dose together with a peak level 3 hours later is ideal.

c) Digoxin: The measurement must be made atleast 6 hours after a dose to avoid inappropriate highlevels.

d) Theophylline: This drug has a narrow therapeutic index and timing of sampling is not critical if the patient is receiving one of the slow release formulations, wherein trough levels should be taken.

e) Lithium: A 12 hr sample gives the most precise guide to dosage adjustment.
f) Gentamicin: Pre dose peak; 0.5 hr after i.v. And 1 hr after i.m. administration.

TDM OF CYCLOSPORINE

• Monitoring should take into account:
1) the blood level of cyclosporine and the therapeutic interval (different for renal, liver and heart transplantation) the correlation that exists between therapeutic interval and acute graft rejection and nephrotoxicity.
• Frequency of cyclosporine blood levels determination should be at 2-3 days (in the first 4 weeks post-transplant), then monthly after 3 months.

• Because cyclosporine binds significantly to red blood cells, whole blood is a better biological matrix forassessing cyclosporine concentration than plasma.

The purpose of monitoring is to prevent rejection and improve tolerance (avoidance of nephrotoxicity andtoo high immunosuppression).

• Ctrough residual concentration (C0, pre-dose concentration) is directly correlated with nephrotoxicity, but it is not a useful marker for prediction of acute rejection.

• Instead, both nephrotoxicity and acute rejection are better correlated with the area under the concentration-time curve measured between 0 - 4 h or 0-12 h (AUC0-4, AUC 0-12).

• These values can be better estimated using the value of C2 (blood level 2 h post-dose) than the residual concentration (C0). {greatest variability occurred in the absorption phase in the initial 4-6hr after the CsA dose}

• C2 concentration can be used as a surrogate index of CsA absorption and exposure.

TDM: THEOPHYLLINE g/ml□

• Therapeutic range - 5-20

•Time to steady state: 36 hours (average).

• Toxicity - manifest as tachyarrythmias, vomiting & convulsions. PK problems - Bioavailability varies widely between preparations. 90% eliminated by the liver & 10% unchanged in the urine (reversed ratioin dose in□neonates) i.e. No adjustment for renal failure required but presence of impaired hepatocellular function. Whenever possible establish drug level before administering IV and if in doubtdo not give bolus loading dose.

Drawing levels:

• a] Oral solution or immediate-release tablet: 1-2 hours after administration.b] Extended-release tablet: 4-12 hours after administration.

c] Injection: 30 minutes after completion of the intravenous loading dose; a second measurement should be obtained after one expected half-life- 4 hours in children age 1 to 9 years and 8 hours in nonsmoking adults.

TECHNIQUES FOR MEASUREMENT OF TDM

• **HPLC:** High Pressure Liquid Chromatography: The separation of a substance depends on the relative distribution of mixture constituents between two phases, a mobile phase (carrying the mixture) and a stationary phase.

• **LC/MS:** Liquid Chromatography Mass Spectrometry: All chromatography-based techniques work on the principle that different substances are absorbed differently in solution. Two “phases” or materials are used to separate the components of a solution. The mobile phase carries the sample along the stationary orsolid phase, which separates out the components in the sample.

• **GC/MS:** Gas chromatography is a separation method using very high temperatures to cause sample vaporization. In mass spectrophotometry the vaporized fractions are passed through an electrical field.The molecules can be separated on the basis of molecular weight. The pattern of separation is unique to each drug and therefore establishes a “fingerprint” for identification. GC/MS is the gold standard methodfor the identification of drugs of abuse.

EIA: Enzyme immunoassay. EIA uses a non-radioactive enzyme label. Most of the drug testing today isperformed using homogeneous EIA techniques. This refers to the fact that the assays are performed in a single step, i.e. only one antibody is used in the procedure. Therefore, the turnaround time for testing is reduced.

- **RIA:** Use radioactivity to detect the presence of the analyte. In RIA, the sample is incubated with an antibody and a radio-labeled drug. The amount of radioactivity measured is compared to the radioactivitypresent in known standards which are included in each run. Results are quantitative.

- **PETINIA:** An immunoturbidimetric method; Particle Enhanced Turbidimetric Inhibition Immunoassay.This method uses the creation of light scattering particles to measure drug levels.

- **EMIT:** Enzyme Multiplied Immunoassay Technique; based on competition for the target analyteantibody binding sites.

FPIA: Fluorescence Polarization Immunoassay. This method uses a fluorescent molecule as the labelinstead of an enzyme, making it more sensitive.

- **Chemiluminescence:** This is a chemical reaction that emits energy in the form of light. When used in combination with immunoassay technology, the light produced by the reaction indicates the amount of analyte in a sample. The most common chemiluminescent assay methods are either enzyme-amplified or direct chemiluminescent measurements.

- **ACMIA**: Affinity Chrome-Mediated Immunoassay. ACMIA is a technique to measure drug concentrations in which free and drug-bound antibody enzyme conjugates are separated using magnetic (chrome) particles.

- **CEDIA:** Cloned Enzyme Donor Immunoassay. CEDIA employs a recombinant DNA technology.

CLINICAL SIGNIFICANCE OF TDM

1. Maximizes efficacy.

2. Avoids toxicity.

3. Identifies therapeutic failure – Non compliance, sub therapeutic dose.

4. Facilitates adjustment of dosage New dose = Old dose X Desired Css/Old Css.

5. Facilitates the therapeutic effect of drug by achieving target drug concentration.

6. Identify poisoning, drug toxicity and drug abuse.

REQUEST FORM OF TDM

Name.....Date.....HN.....
...
Age.....Sex.....Wt.....Ht.....
.....
Ward.....Ordered by .....Phone No.....
DRUG LEVEL REQUESTED.....
.....

REASON FOR REQUEST:

( ) Suspected toxicity ( ) Compliance ( )Therapeutic confirmation ( ) Absence of therapeutic response

Please indicate when level is needed :

( ) within 24 h ( ) within 1-2 h ( ) stat ( )others.....

TIME AND DATE OF LAST DOSE:

Date..... Route : IV, IM, SC, PO, Others..... Time.....

Dose..... Freq.....

THIS DRUG LEVEL IS FOR : SAMPLING TIME :

( )Trough or predose level Date..... Time.....

( ) Peak level Date..... Time.....

DOES THE PATIENT HAVE ORGAN-SYSTEM DAMAGE ?

( ) Renal ( ) Hepatic ( ) Cardiac ( ) GI ( ) Endocrine ( ) Others.....….

OTHER DRUG(S) PATIENT IS TAKING :.....

DRUG LEVEL & USUAL THERAPEUTIC

RANGE.....
.....

INTERPRETATION.....
.....
.....
.....
...Date..... Technologist..... Time.....……..

TDM in our hospital and elsewhere in India

Our TDM service began in a small way in 1988 with a single high performance liquid chromatograph (HPLC.) and one research assistant in a tiny laboratory tucked away in a corner of an 1800 bed teaching public hospital. In 1992 we reported our experiences in the management of epilepsy in a developing country . Over the last 10 years the laboratory has grown and is now part of a fully fledged department of Clinical Pharmacology with a total staff of 30, three HPLC, and an automated immunoassay laboratory.

Our TDM service started with the monitoring of three anticonvulsants—phenytoin, phenobarbitone and carbamazepine as an adjunct to the epilepsy clinic run by the Neurology Department. Today the TDM outpatient clinic is run twice a week and has an annual attendance of 1500 new cases and 3000 old cases. The laboratory has three technicians, one pharmacist, and one medical officer who are involved in initial history taking, sample collection and analysis by HPLC. The 'monitoring', not 'measuring', service is manned by three senior Clinical Pharmacologists who provide advice on dosage adjustment, non responsiveness, compliance, managing and identifying adverse reactions and using anticonvulsants in pregnancy. In developing countries TDM services are broadly of two types: one is like ours in large teaching hospitals where the service is available through departments of Clinical Pharmacology, while the other is in the private sector, where the drug estimations are performed by the clinical biochemistry departments. The HPLC. technique, which is used by teaching hospitals, is labour intensive, technically demanding and the turnaround time is high. However, as the consumables are available locally, the recurring cost is low. As the TDM service is provided by utilizing the same infrastructure as for other academic and commercially required studies (e.g. new drug pharmacokinetics, bioavailability); it can be offered at very low charge to the patient. For example we charge £0.5 per sample which includes simultaneous estimation of phenytoin, phenobarbitone and carbamazepine. This is a cost effective proposition particularly for patients taking multiple anti convulsants. Most clinical biochemistry departments use automated equipment and ready to use kits using the fluorescence polarization (FPIA) and enzyme mediated immunoassay (EMIT) techniques. The kits have to be imported and storage conditions properly ensured and the cost per drug test is usually £3–4. The advantage here is short turnaround times and ease of use. However, these laboratories provide no clinical interpretation of data.

TOPIC-4 MEDICATION ADHERENCE

MEDICATION ADHERENCE DEFINITION: It is defined as the exact or extent to which a patientmedication taking behavior concedes with the intention of the health advice he/she has been given.

- Medication adherence is the one of the most important factors that determines the therapeutic out comes, especially in a patient suffering from chronic illness/diseases. Whatever the efficiency of the drug, it can't act unless the patient takes it.
- Low medication adherence has consumed importance as it seriously undermines the benefits of current medical care and imposes a significant financial burden on individual patient and health care system as a whole.
- The word 'compliance' can imply an authoritarian attitude on the part of health care professionals andmay suggest yielding and submission by the patient.
- 'Non-compliance' is failure or refusal to comply with advice and can imply disobedience on the part of patient.
- Adherence to treat/treatment is the key link between treatment and outcome in medical care.
- Many variables which may influence adherence have been studied, but none of them have beenshown to consistently predict adherence.
- Research into medication adherence has been piecemeal, and as there is no gold standard formeasuring adherence, it is difficult to draw conclusions from the studies which have been done.
- Further research is needed in this complex field, especially taking into account the various factors thatcan be controlled to improve adherence.
- Medication adherence richly deserves attention and much impetus is needed to develop new ideas andtheories to improve it.

IMPORTANCE OF ADHERENCE:

- **Replacement therapy:** For example, thyroxine and insulin are essential for maintaining the body metabolism and must be used regularly as prescribed**.**
- **Maintenance of pharmacological action:** For example, anti hypersensitive and hypoglycemic action control of blood pressure throughout the body and maintaining blood sugar levels within normal range are necessary to obtain optimal treatment benefit**.**
- **Maintenance of serum drug concentration to control particular disorder:** For example anticonvulsant, sub-therapeutic level of anticonvulsant may increase the risk of convulsions in epileptic patients.
- **Some disease of public health:** It is important where non adherence is a major obstacle to achieving control. For example, tuberculosis, human immune deficiency virus and hepatic infections preventive strategies such as immunization programs**.**
- **In chronic disease such as diabetes and hypertension:** where adherence is important to prevent short and long term complications such as diabetes.

CAUSES OF MEDICATION NON ADHERENCE:

Patients demonstrate medication non-adherence in many different situations. These have been categorized based on whether the prescription was honored the medication was **underused or overused** or whether **nonprescription** medicines were used.

- **Primary:** Not having a prescription dispensed.
- **Secondary:** The patient does not adhere to the prescription on his own volition. **For example** the patient may take less than the prescribed dose with the assumption that the prescribed dose is high or take more than the prescribed dose expecting quicker recovery from the disease.
- **Unintentional:** this is typically occurs when the patient has misunderstood or forgotten the doctor direction or fails to adhere to the prescribed dosage regimen due to cognitive problems such as memory loss or confusion.

For example, patient may cease to take antibiotic after two days or anti-tubercular drugs after two months if any forget that the doctor had advised them that a full treatment course should be completed.

MEASUREMENT OF ADHERENCE:

1. Social/economic factors
2. Provider-patient/health care system factors
3. Condition-related factors
4. Therapy-related factors
5. Patient-related factors

1. SOCIAL AND ECONOMIC DIMENSION

- Limited English language proficiency
- Low health literacy
- Lack of family or social support network
- Unstable living conditions; homelessness Burdensome schedule
- Limited access to health care facilities
- Lack of health care insurance
- Inability or difficulty accessing pharmacy
- Medication cost
- Cultural and lay beliefs about illness and treatment
- Elder abuse

2. HEALTH CARE SYSTEM DIMENSION

- Provider-patient relationship
- Provider communication skills (contributing to lack of patient knowledge or understanding of thetreatment regimen)

- Disparity between the health beliefs of the health care provider and those of the patient
- Lack of positive reinforcement from the health care provider
- Weak capacity of the system to educate patients and provide follow-up
- Lack of knowledge on adherence and of effective interventions for improving it
- Patient information materials written at too high literacy level
- Restricted formularies; changing medications covered on formularies
- High drug costs, copayments, or both
- Poor access or missed appointments
- Long wait times
- Lack of continuity of care

3. CONDITION-RELATED DIMENSION

- Chronic conditions
- Lack of symptoms
- Severity of symptoms
- Depression
- Psychotic disorders
- Mental retardation/developmental disability

4. THERAPY-RELATED DIMENSION

- Complexity of medication regimen (number of daily doses; number of concurrent medications)
- Treatment requires mastery of certain techniques (injections, inhalers)
- Duration of therapy
- Frequent changes in medication regimen
- Lack of immediate benefit of therapy
- Medications with social stigma attached to use
- Actual or perceived unpleasant side effects
- Treatment interferes with lifestyle or requires significant behavioral changes

5. PATIENT-RELATED DIMENSIONPHYSICAL FACTORS:

- Visual impairment
- Hearing impairment
- Cognitive impairment
- Impaired mobility or dexterity
- Swallowing problems

Psychological/Behavioral Factors:

- Knowledge about disease
- Perceived risk/susceptibility to disease
- Understanding reason medication is needed
- Expectations or attitudes toward treatment
- Perceived benefit of treatment
- Confidence in ability to follow treatment regimen
- Motivation
- Fear of possible adverse effects
- Fear of dependence
- Feeling stigmatized by the disease
- Frustration with health care providers
- Psychosocial stress, anxiety, anger
- Alcohol or substance abuse

ROLE OF PHARMACIST IN EDICATION ADHERENCE:

- Pharmacists are in unique position to improve medication adherence because they can actually show the medication to the patient and relate any information to the medication itself.
- Pharmacists often provide verbal education and written individualized information for the patient although the benefits of these strategies alone are unclear.
- A few studies provide evidence of level II or improved patient medication adherence as a result of patient education given by pharmacy.
- Macdonald studied the effects of patient education by pharmacists on medication adherence in post- discharge patients, which demonstrated a clear benefit in the patients receiving education frompharmacists.
- In an unpublished study by authors, clear benefit was demonstrated in a randomized control trial in both asthma and COPD patients with a follow-up period of two months in improving medication adherence along with the inhalation technique following pharmacist- based educational interventionalprogram.
- It was interesting to note that the improvement in the inhalation technique continued with each educational sitting.
- The patients received both oral education and written instructions in the local language about their diseases, need for regular medication and the importance of each medication in an educational programme lasting 45 minutes in each sitting.
- **The information that patients need to know which pharmacists can impart includes:**

  •Name and purpose of the drug.

  •When and how to take the medication.

•Possible side effects.

•Precautions.

•Interaction with food or other drugs.

•Duration of therapy.

•Action to take if a dose is missed.

•How to tell if the medication is working or not working.

Strategies to improve the patient-pharmacist relationship are in table.

- Apart from patient education, a pharmacist may contribute towards improving medication adherence by other means including advice to prescribers on the simplification of drug regimens, providing patients with medication cards or medication aids such as a dosette, and by identifying the predisposing, enabling, and reinforcing factors which may contribute towards medication non- adherence.
- In hospitals, clinical pharmacists have many opportunities to assess factors which may assist the patient's medication adherence.
- Though patient interviews, the pharmacists can assess the patient's knowledge of their drug therapy and usual medication habits.
- For example, does the patient have a set of routine and is family support available to supervise medication use?
- The pharmacist is also able to identify if the patient has any specific problems with medication, such as a problem swallowing large tablets, or difficulty opening child-proof containers.
- The pharmacists can also assess the patient's ability to comprehend and recall information, and if an adverse drug reaction may discourage medication adherence.

Strategies to improve the pharmacist-patient relationship**:** Be friendly and approachable to the patient.

•Improve communication skills.

•Take into account the spiritual and psychological needs of the patient.

•Improving patient education.

•Encourage the patient to discuss their main concern without interruption (or) pre mature closing.

•Elicit the patient perception of the illness and associated feelings and expectations.

•Learning methods of active listening and empathy.

•Give clear explanation.

•Check the patient understanding.

•Simplify the therapeutic regimes.

•Monitor the side effects.

•Monitor the beneficial effects.

•Speak the same language of patient.

•Involvement of patient treatment discussion.

•Through the patient interviews the pharmacist can assist the patient knowledge of their drug therapy and usual medication habits.

Example: Dose of patient has a set routine and his family support available to supervise the medication use. The pharmacist has any specific problem with the medication such as swallowing ofa large tablets, difficulty of opening child proof containers.

At the end of process the pharmacist should be able to determine the patient's own assessment of theiradherence to medication and make a professional assessment of the ways in which this can be improved.

For example, this may involve counseling for any specific problems with medication and preparation of individualized medication information sheets.

MONITORING OF PATIENT MEDICATION ADHERENCE:

- Full adherence to the medication is required as the drug can effective only where it is taken.
- A number of approaches have been used for the aim of monitoring medication adherence because it has been shown that improving adherence to medical therapy would substantially lead to both health and economic benefits.
- In general two key factors should be considered when discussing the medication adherence.
- **The first factor is monitoring,** which is alternative referred to as assessment, qualification, measurement or evaluation. Medication monitoring means using some methods for observing if the patient has taken a medication or not.
- **The second factor is intervention**, interventions refer to the means that can be used for improving adherence to the medication or correcting it once erroneous or drift is detected.

MEASURING ADHERENCE

There are several ways to measure medication adherence.

1 .Medication event monitoring systems (MEMS):- These are the most accurate method of measuring adherence because they record the date and time the medication bottle was opened through microprocessor technology embedded in the cap.

Advantages with microprocessor:-

1. Very expensive & different devices are needed for each medication.
2. Therefore it is an impractical way to determine adherence in clinical practice.

2. Patient self-reports: it is easiest method when adherence is being assessed, open-ended questions should be asked. Instead of asking, "Are you taking your medications?" the HCP should phrase the question along the lines of, "How many times in the past week (month) have you skipped your medications?"

3. Pill counts

4. Pharmacy databases or refill rates.

5. Blood levels which also are employed in research, are more feasible options for clinical practice.

6. Morisky's Medication Adherence Scale (MMAS): It was designed to distinguish poorly adherent patients from those with mediumto-high adherence to their antihypertensive regimen. MMAS consists of questions addressing multiple reasons for non-adherence. e.g., because regimen complexity can lead to noncompliance. The scale contains a question assessing whether the patient feels hassled (trouble/Tense) about his or her regimen.

Since patients tend to give their HCPs positive answers to please them, the questions in Morisky's study were phrased to avoid this bias. Each question measures a specific medication taking behavior rather than adherence or compliance behavior.

Q1 – I will ask you few questions about your medication that you were using after Heart Failure

SNO	MMAS–8 Adherence Questions	Patients Response
Q1_1	Do you sometimes forget to take your prescribed medicines?	☐ Yes[0] ☐ No[1]
Q1_2	Over the past 2 weeks, were there any days when you did not take your prescribed medicines?	☐ Yes[0] ☐ No[1]
Q1_3	Have you stopped taking medications because you feel worse when you took it?	☐ Yes[0] ☐ No[1]
Q1_4	When you travel or leave home, do you sometimes forget to bring along your meds?	☐ Yes[0] ☐ No[1]
Q1_5	Did you take your prescribed medicine yesterday?	☐ Yes[0] ☐ No[1]
Q1_6	When you feel like your health is under control, do you sometime stop taking your meds?	☐ Yes[0] ☐ No[1]
Q1_7	Do you feel hassled about sticking to your prescribed treatment plan?	☐ Yes[0] ☐ No[1]
Q1_8	How often do you have difficulty remembering to take all your prescribed medicine?	☐ Never/rarely[1] ☐ Once in a while[0] ☐ Sometimes[0] ☐ Usually[0] ☐ All the time[0]
	Total Score	_____

DOSING CARD

5. PATIENT MEDICATION HISTORY INTERVIEW

A medication history is a detailed, accurate and complete account of all prescribed and non-prescribed medications that a patient had taken or is currently taking prior to a newly initiated institutionalized or ambulatory care.It provides valuable insights into patients' allergic tendencies, adherence to pharmacological and non- pharmacological treatments, social drug use and probable self-medication with complementary and alternative medicines.

Interviewing a patient in collecting the data medical history is called **medication history interview.**

GOALS OF MEDICATION HISTORY:

The goal of medication history interview is to obtain information on aspects of drug use that may assist inover all care of patient. The information gathered can be utilized to: ‰

- Compare medication profiles with the medication administration record and investigate the discrepancies.
- Verify medication history taken by other staffs and provide additional information where appropriate.
- Document allergies and adverse reactions.
- Screen for drug interactions.
- Assess patient medication compliance.
- Assess the rationale for drug prescribed.
- Assess the evidence of drug abuse.
- Appraise the drug administration techniques.
- Examine the needs for medication aids.
- Document patient initiated medication administration.

Importance of accurate drug history:

- Medication histories are important in preventing prescription errors and consequent risks to patients.
- Apart from preventing prescription errors, accurate medication histories are also useful in detecting drug-related pathology or changes in clinical signs that may be the result of drug therapy.
- A good medication history should encompass all currently and recently prescribed drugs, previous adverse drug reactions including hypersensitivity reactions, any over-the counter medications, including herbal or alternative medicines, and adherence to therapy for the better health care plan.
- A full medication history.
- Identifies patients' needs.
- Explores the patient's perspective of illness and its treatment (needs and concerns).

The following information is commonly recorded:

1. Currently or recently prescribed medicines
2. OTC medication
3. Vaccinations
4. Alternative or traditional remedies
5. Description of reactions and allergies to medicine
6. Medicines found to be ineffective
7. Adherence to past treatment and the use of adherence aids

Question to Ask

- Which community pharmacy do you use?
- Any allergies to medications and what was the reaction ?
- Which medications are you currently taking
- The name of the medication
- The dosage form
- The amount (specifically the dose)
- How are the taking it(by which route)
- How many times a day
- For what reason
- What prescription medications are you taking on a regular basis or as needed basis?
- What over the counter medications are you taking on a regular or as needed basis?
- What herbal or natural medicines are you taking on a regular or as needed basis?
- What vitamins or other supplement are you taking?
- Have you recently started any new medicines?
- Did a doctor change the dose or stop any of your medications recently?
- Did you change the dose or stopped any of your medications recently?
- Are any of the medications causing side effects
- Have you change the dose or stopped any medications because of unwanted effects ?
- Do you sometimes stop taking your medicine whenever you feel better?
- Do you stop taking your medicine if it makes you feel worse?

Patient counseling : Patient counseling is defined as providing medication information orally or in written form to the patient or their representatives on direction of use ,advice on side effects precautions, storage, diet and life style modifications.

Objectives of Patient Counseling:

•Patient should recognize the importance of medication for his well being.

- Patient's understanding of strategies to deal with medication side effects and drug interactions shouldbe improved.
- Patient becomes an informed, efficient and active participant in disease treatment and self caremanagement.
- Drug interactions and adverse drug reactions should be prevented.
- Should ensure better patient compliance.

Patient counseling consist of 3 stages

•Introduction
•Process content and issue regarding
•Conclusion

Introduction

- Review the patient's record.
- Introduce yourself (pharmacist).
- Explain purpose of counseling.
- Obtain drug related information such as allergies, use of herbals etc.
- Assess the patient understanding of the reasons for therapy.

Issues Regarding manner

- Use language that the patient understands.
- Present facts and concepts in simple words logical order.
- Use open ended questions.

Conclusion

- Verify the patient's understanding by feedback.
- Summarize by emphasizing key points.

Counseling area: The patient should be counseled in a semiprivate, private area away from the other people and distractions . The patient perceive the counseling area as confidential , secure and conducive to learning .This helps ensure both parties are focused on the discussion and minimizes interruptions and distractions . It provides an opportunity for patients to ask questions they may be hesitant to ask in public. Give an opportunity to the patient to put forward any concerns.

Functions of Patient Counseling:

- Effective patient counseling aims to produce the following results:
- Better patient's understanding of their illness and the role of medication in its treatment •Improvedmedication adherence.
- More effective drug treatment.
- Reduce incidence of adverse effects and unnecessary healthcare cost.

- Improved quality of life for the patient.
- Better coping strategies to deal with medication related adverse effects.

Medication History Form

Patient:_____Bed #_____Date of Birth:_____

A) Check in with nurse (or chart) and ask if he/she has a medication list
B) Wash hands
C) Verify patient name/date of birth, introduce yourself and why you are there
D) Verify allergies in the computer are accurate and up-to-date. Obtain any missing information.
E) Ask the patient if he/she has a medication list
F) Ask if the patient knows what medications he/she is taking (if not, obtain pharmacy/nursing home, or MD office and location:_____)

Is anyone at home who can answer questions about your medications? _____ **phone** _____
Which pharmacy do you use? _____ **phone** _____
Who is your primary doctor? _____ **phone** _____
Is it OK if I call your home, pharmacy or doctor if I need more information?

Obtain medications and last date/time taken

Medication	Strength	Route	Directions	Prn or Routine	Last date/time taken

G) Ask if the patient uses any of the following:

	Yes	No		Yes	No
Vitamins:	☐	☐	Injections:	☐	☐
Antibiotics:	☐	☐	Creams/Oint/Lotion	☐	☐
Supplements/herbals:	☐	☐	Anything for sleep:	☐	☐
Aspirin:	☐	☐	Birth control (female)	☐	☐
OTC for pain:	☐	☐	Male enhancement:	☐	☐
Other OTC:	☐	☐	Eye or ear meds:	☐	☐
Inhalers/Nose sprays:	☐	☐	Medication samples:	☐	☐
Patches:	☐	☐	Investigational meds:	☐	☐

H) Recent vaccinations?
   a. Flu, When?
   b. Pneumonia, when?

I) Ask if there is anything else they can think of, thank the patient, ask if they need anything (can refer to nurse/patient care technician, wash hands).

6. COMMUNITY PHARMACY MANGEMENT

Community Pharmacy: It is the place where most pharmacists practice the profession of pharmacy. It consists of a retail store front with a dispensary where medicines are stored and dispensed.

Functions of Community Pharmacy:

- Providing health information to patient and public.
- Prescription handling.
- Patient counseling.
- Patient medication record.
- Pharmacy administration.
- Compounding.

The community pharmacy medicines management (CPMM) is a unique point with an objective to introduce a structured intervention process into the relationship study between the community pharmacist, the patient and the general practitioner. The study is designed as a randomized controlled trial (RCT).

The primary objectives of the CPMM are:

(a) Compare the proportion of the patients receiving appropriate treatment, as defined by currently available evidence and guidelines, between intervention and control groups at baseline and follow up.

(b) Quantity "Health gain" by describing the change in patients overall health status after the interventionas defined by standard measures, both general and condition specific.

(c) Conduct an economic evaluation of the medicines management intervention (including estimates ofdrug cost changes).

The secondary objectives are to:

(a) Describe the opinions of the stakeholders (patients, general practitioners and their staff andcommunity pharmacists) of medicines management before and after its introduction.

(b) Describe the role of over the counter (OTC) medicines in the overall patient management of thiscondition.

FINANCIAL REQUIREMENTS:

Financing is required to set up a new community pharmacy in order to maintain the medicines stock and cover the expenses.

Purpose of Finance:

- To purchase land, building, machinery and equipment.
- To purchase raw materials and other materials.
- To pay salaries, wages and incidental charges.
- To maintain stock and supply products.

Types of finance:

1. **Equity Finance/capital:** Fixed/Tangible assets that are free from financial obligation or debts.
2. **Burrowed Finance/capital:** Assets that are taken as loan from banks or other sources.

Sources of Finance:

- **Owned finance**: The capital is generated by owner, partner or shareholders. As long as business runit remains and surplus is returned to the shareholders.
- **Loan (Burrowed) Finance:** The capital is generated from bank or other financial institutions. Interest is paid periodically at a fixed rate and then payment of loan capital. Loan can be obtained against mortgage or pledge of the property.

MATERIAL MANGEMENT:

Function of materials management:

1. Procurement of raw materials and other inputs required for production.
2. Maintaining stores and stock levels.
3. Receiving and issuing of the materials.
4. Transportation and material handling.
5. Disposal of scrap and surplus material.

Material Management is a basic function of the business that adds value directly to the product itself. Material Management is the planning, directing, controlling and coordinating the activities concerned with material and inventory requirements from the point of their inception to their introduction into the manufacturing process.

The two important aspects of material management includes:

1. STOCKING
2. CODING

1. **Stocking**: The drug store should have adequate space for storage of drug with proper lighting, ventilation and temperature controls. Special locked storage space provided to meet the legal requirements for storage of narcotics, alcohol and prescribed drugs. The drugs are stored in such away that they should not be damage due to high temperature. It is a fact that more than 70% of the capital of an enterprise is invested in stores.

Objectives of stocking:

(a) Easy location of the items in store.
(b) Proper identification of items.
(c) Speedy issue of materials.
(d) Efficient utilization of space.
(e) Reduction in needs of materials handling equipment.

Functions of stocking:

(a) Receiving, handling and speedy issue of material.
(b) Custodian of goods in store against damage and pilferage.
(c) To establish regular supply of materials.
(d) Physical stocking and its checking.
(e) Efficient utilization of store space.
(f) To provide service to the organization in most economic way.
(g) Proper identification and easy location of items.

Arrangements of Drugs in Drug Store The drugs may be arranged in the following manner:

- **According to manufacturer**: The drugs are arranged in a drug store, manufacturer-wise for example,the drug manufactured by Glaxo (India) Ltd. are place in one cup-board and so on.
- **According to pharmacological action:** The drugs may be arranged in order of their pharmacological action for example, all analgesics drugs are placed in one cupboard. All multivitamin preparations arekept in another cupboard and so on.
- **Alphabetical order**: The drugs may also be arranged alphabetically. The drugs starting with letter "A" are placed in one row of the cupboard. Similarly with other drugs based on their first alphabet.
- **As per old stock and date of expiry**: Drugs are stored in such a way that the older stock must besold first, so that the old stock is stored in front row and the fresh stock is stored on the backside.
- **Location of stores for stocking**: The location of stores in an enterprise should be at a place where handling, transportation and movement of the material is at a minimum level. If there is only single plant or many plants situated at the same area, then it is profitable to have one centralize store to serveall production operations.

The following are some of the advantages and disadvantages of centralized storing

Advantages

(a) Economy in investments.
(b) Reduction in incidental expenses.
(c) Less storage of space.
(d) Less manpower required, due to which reduction in administrative costs.
(e) More bargaining power due to buying in bulk.

Disadvantages

(a) More materials handling operations.
(b) The chances of delay are likely to be more.
(c) More exposed to loss due to natural calamities like fire, rain, dust etc.

2. Coding or Codification

It is the process of assigning a code number or code symbol to a particular material for easy identification. Usually manufacturers, distributors and wholesalers have large merchandise in the stores. Itis difficult to locate the items in the store unless some system is evolved to store them. There should be place for everything and it should be place at their right place. Therefore code numbers are allocated to various items to facilitate easy identification.

Advantages of codification

(a) It helps in easy identification of items.
(b) It helps in grouping the similar items together.
(c) The ambiguity in description of the materials can be avoided.
(d) The detailed description of the materials is minimized.
(e) It helps in avoiding duplication of items.
(f) It helps in physical counting.
(g) It helps in inspection of the materials.
(h) The coding helps in maintaining the secrecy of the items.

Methods of codification: The various methods employed for codification includes:

- Alphabetical order method
- Mnemonic method
- Numerical method
  - (a) Decimal system
  - (b) Block system
- Combination method or alphanumerical method
- Location coding
- (a) Fixed location
- (b) Random location
- (c) Zonal location

- **Alphabetical order method**: This method is also known as "Letter Code" system. In this system all items are on the code number alphabetically for example Code "C" represents capsules Code "T" represents tablets.
- **Mnemonic method:** In this method, coding letters assigned to each items so that they can be very easily identified for example "APC" represents aspirin, paracetamol and caffeine. The main disadvantage is that the items cannot be identified without refers code index book.
- **Numerical method:** This method is also known as 'sequence system method'. Under this method separate numbers are assigned to different classification of store items. The method has the following sub-systems-

  (a) **Block system:** In this method the numbers are reserved for specified items. Example let the number 10-50 is allotted to various types of tablets. 10.1, 10.2, 10.3, 10.4, 10.5 represents antipyretic,analgesic, anti-inflammatory, decongestants and cold remedies respectively.

  (b) **Decimal system:** In this system, the numbers are assigned in such a way that each digit representsthe separate name under same heading. example- Let the code for tablet is 10, then 10.1 (Paracetamol- antipyretic), 10.2 (Analgin-analgesic).
- **Combination method:** In this method both mnemonic and numerical methods are combined to assign a code to different items of the store example Code number "CPC" is allotted from chloramphenicol capsules. Code number "PAT 11" is allocated to paracetamol with analgin tablets. This method is used when store items are quite large.
- **Locating coding:** In a large organization, there are a large number of stores. The store rooms are divided in blocks and each block is identified by lateral block letter and longitudinal block letter. The location of items can be identified from ware-house number, block number, row number, rack number and shelf number etc. Location of any item inside the store rooms can also be done in the following manner-

  (a) Fixed location: In this method each and every group of items is allotted a fixed place inside thestore according to either-

  (i) Supplier wise

  (ii) Item wise

  (iii) According to the utility of the item.

  (b) Random location: This is most widely used method in almost all kinds of retail shops but eachgroup items are stored, in a particular shelf for its easy location.

  (c) Zonal location: According to this system, available space is divided into different zones and eachzone is allotted to different kinds of items. The zones can be named as-

  (i) Bulk Zone

  (ii) Reserve Stock Zone

  (iii) Spare part Zone

  (iv) Consumable Item zone

STAFF REQUIREMENTS: Staff Management The right type of organization is selected, then it becomes necessary to fill in the various job positions with right kind of people, who can effectively performed their assigned activities. This is the management function of staffing.

The process of hiring and developing the required personnel to fill in various positions in the organization. It involves the scientific and systemic procurement, allocation, utilization, conversation and development of human resources.

The main objective of the staffing is to ensure the optimum utilization of human resources as well as to provide personal and social satisfaction to the employees.

Salient features of staffing:

- Staffing is a function of management.
- It is a continuous function.
- It is a pervasive function.
- It is an integral part of the management process.
- It is a difficult function because it deals with human beings who have their own needs, emotions andaspiration.
- It is concerned with the human resources of an organization.

Importance of staffing:

(i) Staffing helps to build up a healthy organization in which the job performance and satisfaction ofevery employee can be high.

(ii) Staffing injects life into the organization by providing right person for every job. The effectiveness of directing and control functions also depends upon staffing.

(iii) Employees in the organization are the most valuable asset of an organization. The quality ofhuman assets largely determines the success and growth of the organization.

INFRASTRUCTURE REQUIREMENTS:

Space Layout: Plant layout is a method of allocating machines and equipments, various production processes and other necessary services involved in transformation process of a product with the availablespace of the factory, so as to perform.
Various operations in the most efficient and convenient manner providing output of high quality and minimum cost. Planning the layout of a plant is a continuous process as there are always chances of making improvements over the existing arrangements.

Objectives of an ideal plant layout

(i) Material handling and transportation is minimized and efficiently controlled.

(ii) Work stations are designed suitable and properly.

(iii) Suitable spaces are allocated to production centers and service centers.

(iv) The movement made by workers is minimized.

(v) Waiting time of the semi furnished product is minimized.

(vi) There are improved work methods and reduced production cycle means or times.

(vii) There is increased flexibility for changes in product design and for the future expansions.

(viii) A good layout permits materials to move through the plant at the desired speed with the lowercost.

Types of layout : There are mainly following types of layout:

1. Process layout
2. Product layout
3. Combination layout

1. **Process layout:** It is also known as functional layout and is characterized by keeping similar machines or similar operation at one location. The arrangement of machines of a particular class doing a particular type of work or process as a separate department e.g. cutting machines may be placed under cutting department.

Advantages

(i) Better machine utilization.

(ii) Greater flexibility.

(iii) Better supervision which ultimately leads to better production.

(iv) Less number of machines is needed involving reduced capital.

Disadvantages

- Functional Layout type may not be possible in the pharmaceutical and chemical industries, because a number of unit operations should be performed in sequence.

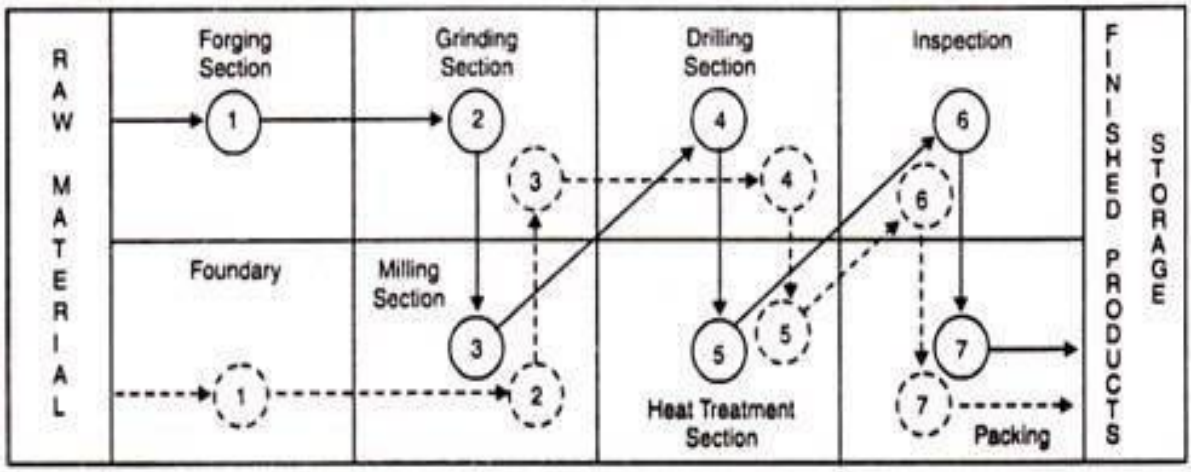


Fig. 8.4.

Product layout: It is also called as straight line layout and according to the product manufactured. This set up of product layout is standardized in beginning. The product can be manufactured in large quantity by repetitive operation.

Advantages:

(i) Less space requirements for the same volume of production.

(ii) Less in-process inventory.

(iii) Smooth and continuous work flow.

(iv) Processing of work is quick and smooth.

(v) Cost of material handling can be reduced by using conveyors.

(vi) Manufacturing time is reduced and manufacturing cycle can be speeded up.

(vii) Floor space can be properly utilized. This type of layout is more suitable for the Pharmaceutical Industries.

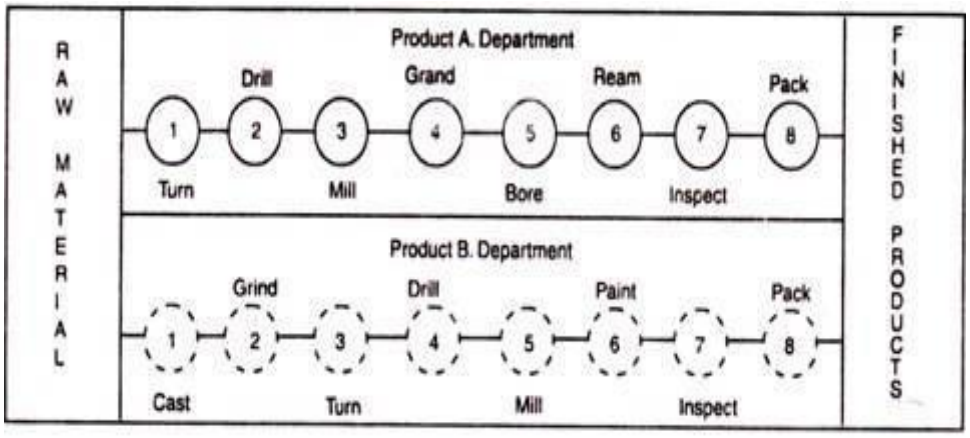


Fig. 8.3.

Importance of plant location or site: The selection of appropriate location is important due to the following reasons:

1. Location of plant partially determines operating and capital cost. It determines the nature of investment costs to be incurred and also the levels of many operating costs.

2. Location fixes some of the physical factors of the overall plant design example heating and ventilation requirements, storage capacity of raw material taking into consideration their local availability.

3. Each prospective location implies a new allocation of capacity to respective market area.

Government some-times play an important role in the choice of the location keeping in view the national benefits.

Plant Location-Factors Influencing

The selection of a location for the construction of a pharmaceutical plant is a vital decision to be taken, because it determines the balancing of investment and profit. Hence the location of the planthas a strong influence on the success of an industrial venture. Primarily the plant should be located where the minimum cost of production and distribution can be achieved. But other factors such as room for expansion and general living conditions are also important.These factors may be described as follows:

1. Fundamental (Primary) Factors

2. Derived (Secondary factors)

Combination layout: A combination of process and product layout combines the advantages of both types of layout. The layout should be efficient by keeping material handling at a minimum level. Suitable layout planning is required to keep the cost of product minimum.

Selection of Site: A plant is a place where men, materials and equipment are brought together for manufacturing procedures

1. **Fundamental (Primary) Factors:**

- **Raw materials:** The availability of raw materials and cost of its transportation are the major determinants. Pharmaceutical industry uses the following types of raw materials: crude drugs, inorganic and organic chemicals etc. It would be economical to locate the plant nearer to the source of raw materials particularly when they are consumed in large volumes. If the raw materials are not readily available or a dangerous chemical, the freight charges and risk of dangers increase enormously. If raw materials are stable, other factors gain more importance over this factor.
- **Market of products:** Market exercises a strong influence on the establishment of industries. When market is regional, the industry is located nearer to the market. The bulk drug industry is located in a place where drug formulation industries are located, since bulk drugs are the feed for the formulations and buyers are found nearby.
- **Energy availability:** Fuel and power are the energy sources, which exert the same kind of influence as the raw materials. Now a days, electricity and diesel engines are developed and available widely. In many cases, plant produces power on their own for the smooth functioning of the industry. Therefore, it is possible to locate the industry remote to the power generation plants.
- **Transportation facility**: Transportation is the lifeline of modern industry. Transport facilities are needed for bringing raw materials and sending the finished products. An industry tends to be localized at places, which have a developed means of transport such as railway, road and seaport. These facilities are normally available in metropolitan cities.
- **Labour supply**: Low wages and abundant labour help in localization of certain industries. However, pharmaceuticals and chemical plants require skilled labour, who are better paid and often highly mobile. Therefore, industries can be located away from the areas of labour concentration. Consideration should be given to prevailing pay rates, restrictions on number of hours per week, competing industries etc.

2. **Derived (secondary) factors:**

- **Climate and soil:** Climate and soil is very important for industries depending on agriculture. In pharmaceutical industry, many operations are carried out in air-conditioned rooms, in dust free environments and under strict control and regulations depending upon the nature of formulation. Industries producing antibiotics are normally located in a place wherein the microbial contamination in environment is low and the ambient temperatures throughout the year are cool.
- **Government concessions**: Government has been providing subsidies and tax concessions for the industries located in certain notified areas. These areas have been declared as industrially backward and the government offers incentives, namely cheaper power, tax concession etc.

Water supply: The processing industries use larger quantities of water for cooling, washing and steam generation and also as a raw material (liquid orals). The plant therefore must be located in a place where a dependable supply of water is available.

Waste disposal: In recent years, many legal restrictions have been imposed on the methods for disposing of waste materials from the processing industries. The site selected for a plant should have adequate capacity and facilities for correct waste disposal. Attention should also be given to potential requirements for additional waste treatment facilities.

Site characteristics: The topography of the land and soil structure must be considered, since either both may have a pronounced effect on construction costs. The cost of land, local building construction costs and living conditions are important. Future changes for expanding the plant facilities make it desirable or necessary.

- **Flood and fire protection:** Many industries are located along large bodies of water and there are risks of flood or hurricane damage. Before choosing a plant site, the regional history of natural events of this kind should be examined. In case of major fire, assistance from the outside departments shouldbe easily available.
- **Community factors:** The character and facilities of a community can have quite an effect on the location of the plant. Cultural facilities of the community are important for sound growth. Churches, temples, libraries, schools, theaters and other similar groups, if active and dynamic, do much to make a community progressive.

Special provisions of Factory Premises:

- **Location**: It is important to recognize that the pharmaceutical industry has some special requirement that need to be interpreted. The factory shall be located in a sanitary place remote from filthy surroundings. The factory shall be situated in place which:

  (a) shall not be adjacent to an open sewage, drain or public lavatories.

  (b) Shall not be adjacent to a factory, which produces disagreeable or obnoxious odours or fumes.

  (c) Shall not be adjacent to a factory, which emits large quantities of soot, dust or smoke.

IMPORTANT QUESTIONS

2 MARKS QUESTIONS.

1. Define hospital formulary.
2. Significance of hospital formulary.
3. Define OPD.
4. Explain activity chart for OPD.
5. Define TDM.
6. What is therapeutic window?
7. What is need of TDM?
8. Define medication adherence.
9. What is medication non-adherence?
10. Write the importance of adherence.
11. What are the causes of medication adherence?
12. What are the dosing cards?
13. Define medication history.
14. What are the goals of medication history?
15. Write the importance of drug history.
16. What is community pharmacy?
17. Write the function of community pharmacy.
18. Define Coding.
19. Define Stocking.

5 MARKS QUESTIONS.

1. Write a note on:
    a) Distribution of formulary
    b) Revision of formulary
2. Differentiate between hospital formulary and drug list.
3. Write a note on addition and deletion of hospital formulary.
4. Write a short note on dispensing of drugs to ambulatory patients.
5. Draw the layout plan for OPD.
6. Explain the different techniques for therapeutic drug monitoring.
7. How we measures the medication adherence?

8. Explain the Indian scenario for TDM.
9. Write a short note on patient counseling.
10. What are requirements staff management?
11. Write a note on finical management.

10 MARKS QUESTIONS.

1. Discuss in detail “contents of formulary”.
2. Write guiding principles of hospital formulary.
3. Discuss in detail unit dose dispensing system.
4. Explain types drug distribution system for in-patient department.
5. Give a detail note on charging policy for drug distribution system.
6. Write a note on therapeutic drug monitoring.
7. Write the principles of TDM.
8. Explain role of pharmacist in medication adherence.
9. Explain the different methods used for monitoring the patient medication adherence.
10. Detail note on medication history form.
11. Discuss in detail about the infrastructure management.
12. Write a note on material management.