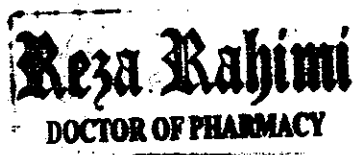


Rajiv Gandhi University Of Health Sciences

Karnataka Bangalore

Clinical Pharmacy



KIMS HOSPITAL

2014-15

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DOCTOR OF PHARMACY

1.3 CLINICAL PHARMACY (THEORY)

Theory: 3 Hrs. /Week

1. Objectives:

Upon completion of the subject student shall be able to (Know, do, appreciate) –

- a. monitor drug therapy of patient through medication chart review and clinical review;
- b. obtain medication history interview and counsel the patients;
- c. identify and resolve drug related problems;
- d. detect, assess and monitor adverse drug reaction;
- e. interpret selected laboratory results (as monitoring parameters in therapeutics) of specific disease states; and
- f. retrieve, analyse, interpret and formulate drug or medicine information.

Text books (Theory)

- a. Practice Standards and Definitions - The Society of Hospital Pharmacists of Australia.
- b. Basic skills in interpreting laboratory data - Scott LT, American Society of Health System Pharmacists Inc.
- c. Biopharmaceutics and Applied Pharmacokinetics - Leon Shargel, Prentice Hall publication.
- d. A textbook of Clinical Pharmacy Practice; Essential concepts and skills, Dr.G.Parthasarathi, Karin Nyfort-Hansen and Milap Nahata Orient Langman Pvt.Ltd. ISSN8125026

References

- a. Australian drug information -Procedure manual. The Society of Hospital Pharmacists of Australia.
- b. Clinical Pharmacokinetics - Rowland and Tozer, Williams and Wilkins Publication.
- c. Pharmaceutical Statistics. Practical and clinical applications. Sanford Bolton, Marcel Dekker, Inc.

2. Detailed syllabus and lecture wise schedule:

Title of the topic

1. Definitions, development and scope of clinical pharmacy
2. Introduction to daily activities of a clinical pharmacist
 - a. Drug therapy monitoring (medication chart review, clinical review, pharmacist interventions)
 - b. Ward round participation
 - c. Adverse drug reaction management
 - d. Drug information and poisons information
 - e. Medication history
 - f. Patient counseling
 - g. Drug utilisation evaluation (DUE) and review (DUR)
 - h. Quality assurance of clinical pharmacy services

3. **Patient data analysis**
The patient's case history, its structure and use in evaluation of drug therapy & Understanding common medical abbreviations and terminologies used in clinical practices.
4. **Clinical laboratory tests used in the evaluation of disease states, and interpretation of test results**
 - a. Haematological, Liver function, Renal function, thyroid function tests
 - b. Tests associated with cardiac disorders
 - c. Fluid and electrolyte balance
 - d. Microbiological culture sensitivity tests
 - e. Pulmonary Function Tests
5. **Drug & Poison information**
 - a. Introduction to drug information resources available
 - b. Systematic approach in answering DI queries
 - c. Critical evaluation of drug information and literature
 - d. Preparation of written and verbal reports
 - e. Establishing a Drug Information Centre
 - f. Poisons information- organization & information resources
6. **Pharmacovigilance**
 - a. Scope, definition and aims of pharmacovigilance
 - b. Adverse drug reactions - Classification, mechanism, predisposing factors, causality assessment [different scales used]
 - c. Reporting, evaluation, monitoring, preventing & management of ADRs
 - d. Role of pharmacist in management of ADR.
7. Communication skills, including patient counselling techniques, medication history interview, presentation of cases.
8. Pharmaceutical care concepts
9. Critical evaluation of biomedical literature
10. Medication errors

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Reza Rahimi
DOCTOR OF PHARMACY

Definitions, Development and Scope of Clinical pharmacy

1

Clinical pharmacy:

Definition:

- Is the branch of Pharmacy where pharmacists provide patient care that ^{gives rise to} optimizes the use of medication and ^{achieves} promotes health, wellness, and disease prevention.

Pharmaceutical Care:

Pharmaceutical Care is defined as the care a patient requires to assure safe and rational drug use.

Clinical Pharmacy Practitioner:

Clinical Pharmacy Practitioner refers to a clinical pharmacist working within the healthcare system as ^{one of} experts in the therapeutic use of drugs who are primary sources of scientifically valid information and advice and who generate, disseminate and apply new knowledge that contributes to improved health and quality of life.

Development of clinical Pharmacy In India:

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- During the 1980's and 1990's the consequences of drug misuse, such as poor health outcomes from drug treatment, antibiotic resistance, A.D.R, and economic loss to patients and the wider healthcare system were acknowledged not just by the pharmacy profession, but also by the medical profession, consumer, and patient organizations and the government.

- The 1990's were a period of awaking when the profession recognized clearly that an urgent need existed for pharmacist to contribute to improving medication use in our community.

- The existing education of degree pharmacist emphasized knowledge and skill in pharmaceuticals, pharmaceutical chemistry, pharmacology and industrial pharmacy. But a different set of knowledge and skills is needed by pharmacists wishing to contribute to patient care. These include pathophysiology, applied therapeutics,

clinical pharmacokinetics, and practice skills such as drug information and drug therapy review.

-Very significantly, these teaching programs were based at local hospital with students participating in patient care activities on a daily basis, using case-based learning.

-The result of this expansion is that the pharmacy profession in India is in transition. It is moving from being a technical, industry-oriented profession to one that also has significant role to play in the healthcare system.

Some of the early Institutions which initiated Masters program in Pharmacy Practice:

1. Delhi College of Pharmacy (Delhi University) 1982
2. JSS College of Pharmacy, Mysore 1996
3. JSS College of Pharmacy, Ooty 1997

The Need For Clinical Pharmacy In India:

- Clinical pharmacy practice is concerned with the promotion of effective, safe and econo-

mical drug therapy.

- Pharmacy practice is a broader term, which includes clinical pharmacy, and other activities performed by pharmacists in the hospital and community settings. These include dispensing and drug distribution, drug information, health promotion, patient counseling, pharmacovigilance, medication review, academic detailing and sterile and non-sterile manufacturing.

Pharmaceutical Industry:

- Around 60,000 formulations are available in the market today.

- Most pharmaceutical companies in India do not have fully fledged medical information departments. Package inserts provided by pharmaceutical companies may contain only technical information about drugs and this information is not useful to patients.

- Consumer product information is not provided. This practice of clinical pharmacy can address

these industry-based problems by providing unbiased, independent drug information to doctors and by providing patient counseling to patient.

Prescribers:

-The patient load for prescribers is very high. A busy practitioner may spend only around 5-10 mins per patient. Outpatient departments (OPD) in government hospitals are always overcrowded. During a short time, it may be very difficult to make a clear diagnosis of the disease.

- Some doctors may give a prescription "a pill for every ill" which may lead to unnecessary drug-related problems such as ADR's. This is because they have not received adequate pharmacotherapeutic training in the medical curriculum, and rely on handouts from pharmaceutical companies as a source of drug information.

- Most doctors prescribe drug by brand names with the risk of duplication of therapeutics equivalents.

Infectious diseases at primary and secondary healthcare levels are often treated empirically. Definitive therapy after assessing culture and sensitivity data is not regularly practiced. Broad-spectrum antibiotics are used for simple infections at primary and secondary healthcare levels because of wide spread antibiotic resistance.

- Clinical pharmacist can help by providing doctors with advice and information to deliver safer and more effective drug therapy.

□ Pharmacist:

- Pharmacist in medical stores do not offer any professional services to patients such as patient counseling, labeling of medication with directions for use or advising patients or their doctors about possible drug interactions or other prescription problems. This is mainly because of a poor knowledge base, lack of financial benefits. This control on medical stores by statutory bodies is far from satisfactory.

□ Hospital pharmacist manages drug inventory, drug dispensing at OPD dispensaries, and record keeping with appropriate education and training, graduate pharmacist can help to improve medication use, by providing services such as drug therapy monitoring, patient counseling, drug information services, ward round participation and ADR reporting and monitoring.

□ Government:

- Government drug policies are mainly aimed at the pharmaceutical industry rather than the patient.

Technical and commercial matters such as price control and licensing of manufacturers have taken precedence over initiatives to ensure that medications are used wisely.

Advertising and promotional claims by the pharmaceutical industry are not strictly regulated.

A functional national ADR reporting system remains to be established.

Clinical pharmacist can play an important role in monitoring and reporting ADR, this will improve medication safety, specially amongst pediatrics and geriatrics patients. Much can be done by the government to develop pharmacy practice in India, so that pharmacists can play a meaningful role in the healthcare system.

- Patients:

- The majority of Indian patients, perhaps 50%, cannot read and understand English, the language used on medicine labels on containers and closers.

- Clinical pharmacists can assist medication compliance through patient counseling in the local language, and identifying and helping to resolve factors, which contribute to non-compliance.

- Patient information leaflets and advisory labels provided in local language would also assist medication use, and clinical pharmacist in consultation with other healthcare providers can develop these.

- The low income of many Indian patients means that every rupee used to purchase medication should be well spent. Clinical pharmacist can advise patients and their doctors on the most cost-effective medications for particular conditions, and help to reduce spending on unnecessary and traditional medication.

□ Scope For Clinical Pharmacy Practice In India:

- Based on physician ^{surveys} at JSS hospital, Mysore, the service that are most appreciated by medical staff include: ^{cream did up}

- drug information services
- clinical pharmacy input on ward rounds
- information about new drugs
- patient counseling
- advice on individual patient management
- detection and management of ADR
- choice of antibiotics
- Drug interaction
- preparation of treatment guidelines or protocols
- education of nurses about the preparation and administration of parenteral drugs
- support for clinical research activities.

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After visiting regular visit to hospital in Mysore by medical staff for the purpose of making decisions concerning patient care.

-In community pharmacy, knowledge of clinical pharmacy can be used to counsel patient about their medications, identify drug interactions and other drug-related problems.

-In particular, diploma pharmacists must be trained to provide these services and the public needs to be educated to expect a professional service whenever a prescription is filled.

□ Aims of Clinical Pharmacy:

1. To assist the physician in doing a better job of prescribing and monitoring drug therapy for the patient.
2. To assist medical and paramedical staff and documenting medication incidents correctly
توثيق الحوادث
3. To maximize the patients compliance in drug process.
تحسين الامتثال

Qualities of clinical Pharmacist:

1. Communication Skill:

-The clinical pharmacist should have good communication skills in order to communicate with the patient and co-professionals freely and effectively.

2. Clinical skills:

-The clinical pharmacist should have thorough knowledge about etiology of a disease, signs, symptoms, pathophysiology, laboratory tests and pharmacokinetics.

3. Professional relationship:

He should be able to understand and appreciate the role of medical and paramedical staff where ever possible.

He must accompany physician drug informations.

The physician, pharmacist and nurses should develop an inter-profession relationship with each other to enhance the quality of the patient care.

4. Empathy:

Clinical pharmacist should possess a deep sense of shared responsibility towards medical care of patients.

It will help to take medication history and gaining patients confidence.

5. Monitoring Drug Therapy:

Clinical pharmacist must help in monitoring drug therapy because it is an ongoing process and keeps on changing depending on patients' condition.

SHPA Standards of Practice For Clinical Pharmacy:

The society of hospital pharmacist of Australia code of ethics provides guidance in relation to professional conduct.

-The principle of the code of ethics form the basis of the roles and responsibilities of pharmacists practicing in hospital and related areas.

Objective:

The objective of clinical pharmacy practice is to optimize patient outcome by providing best possible quality use of medication.

Definition:

Clinical pharmacy practice is defined as the practice of pharmacy in multidisciplinary healthcare team directed at achieving patient treatment goal.

-Operation of clinical pharmacy Services:

-A pharmacy service should be provided by a well trained and qualified pharmacist.

Services:

- ① Medication history interview
- ② Drug therapy monitoring
 - ③ Medication order review
 - ④ ADR management
 - ⑤ Clinical review
 - ⑥ Therapeutic Drug Monitoring (TDM)
- ③ Participation in ward rounds and meetings
- ④ Selection of drug therapy
- ⑤ Provision of drug information
- ⑥ Prevention, assessment, and management of drug interactions.
- ⑦ Patient medication counseling

1. Medication History Interview:

includes:

- Establish the identity of the patient.
- Introduce yourself
- Explain the purpose of the interview
- Adopt a suitable physical position to enable the interview to take place comfortably and effectively
- In the event that the patient is not involved in the administration and management of their medication, the interview should be continued with relevant persons, e.g. relatives.

At the conclusion of the interview:

- Summarize the important information for the patient.
- Ask the patient if they have any question related to their medication.
- Encourage patient to provide more information
- Explain when the next opportunity for discussion with pharmacist will arise.

2. Drug Therapy Monitoring:

DTM includes activities such as:

- a. Medication order review
- b. ADR management
- c. Clinical review
- d. Therapeutic drug monitoring

a: It is the fundamental responsibility of pharmacist to ensure the appropriateness of medication orders.

-The goal of medication order review is to optimize the patient's drug therapy.

This includes ensuring that the patient receives the most appropriate drug, dose, and dosage form; that the timing of dosage and the duration of therapy is optimized and that drug related problems are minimized.

b: The WHO defines ADRs as "any response to a drug which is noxious and unintended, and which occurs at normally used dose in man for prophylaxis".

c: Clinical review is an integral component of drug therapy monitoring and should be performed routinely.

Clinical review is the assessment of the patient for the purpose of evaluating the nature of the response therapy. This may include the review of patient signs, symptoms, and results of investigations.

d: TDM is the application of pharmacology, pharmacokinetics, pathology and clinical medicine in the interpretation of measured drug concentration in body fluid.

The aim is to optimize drug therapy by using this information in the patient care. Pharmacology consist of detailed study of drugs particularly their action on living animals, organs, and tissues. The action may be beneficial or harmful.

3. Participation in ward rounds and meetings.

-Participation in ward rounds and meeting enable pharmacist to contribute to patient care through the provision of drug information and promotion of rational drug therapy.

4. Selection of Drug Therapy:

-The medical staff normally carries out the selection of drug therapy. Pharmacist can only provide guidance and recommendation in the form of information and opinion.

5. Prevention, Assessment, And Management of Drug Interactions:

-A drug interaction when administration of or exposure to a substance which modifies a patient response to a drug. The substance may be a drug or another factor such as blood products, enteral feeds, food stuff, chemicals, therapeutic devices, or the environments.

6. Provision of Drug Informations:

- A Fundamental responsibility of the clinical pharmacist is to provide information on drug related matters.

7. Patient Medication Counseling:

- Pharmacists have a responsibility to provide sufficient information and counseling to patient which enable patients and/or their care givers judicious use of their medicines, thereby enhancing therapeutics outcomes.

Objectives:

- To maximize the effectiveness and safety of drug therapy.
- Used to identify those patients requiring medication counseling
- To minimize the risk of medical errors and also to identify patient with specific pharmaceutical care.

□ Drug therapy review (DTR) refers to a process by which a pharmacist review a patient medication regimen to make sure that the drug therapy meets these objectives.

- The most important responsibility of a clinical pharmacist is to ensure that each patient receives effective, safe and cost effective drug therapy.

- DTR is a complex process involving the assessment and ^{تفسير} interpretation of clinical information from a ^{مختلف} diverse range of source.

- The review process ^{درجہ بندی} draws upon the clinical pharmacist knowledge and skill in pharmacotherapeutics, ADR, drug interaction, interpretation of lab

data and also communication skill.

→ DTR can take place in both hospital as well as community settings.

→ Pharmacist should follow the patient progress from the day of admission till the day he is been discharged from the hospital.

^{C-MIAMZ} Components:

- 1- Collection and interpretation of patients-specific information.
- 2- Assessment of therapeutic goals
3. identification of drug-related problem
- 4- Individualizing medication regimen
- 5- Monitoring of treatment outcomes
- 6- Medication chart endorsement

1. Collection of Patient specific Information:

- Includes the patient's age, sex, body weight, social history, current and recent medication, allergy and sensitivity status, present complaints, past medical history and other investigation.

- This enables the pharmacist to understand the patient's disease condition.

: Sources like case, notes, medication chart, nursing notes, observational charts, lab results and also by patient's interview.

- Pharmacist need to communicate with patient in language that the patient can understand should pay close attention to what the patient is saying and response to his or her comments.

□ Steps involved in Medication History Interview:

- Patient selection:

Establish the identity of the patient who are likely to benefit from the interview.

- Self-preparation:

Understand the patient's medical condition and therapy before commencing the interview.

- Introduction: Introduce yourself and explain the purpose of interview.

- Conduct interview: Obtain all relevant information using a combination of open and close ended questions.

- Conclusion: Summarize the important issues and clarify if necessary.

- Documentation: Document the information obtained during the medication history interview for future reference.

^{2.2.2} 2. Assessing Therapeutic Goal:

- In this to determine the appropriateness of drug therapy it is essential to understand the therapeutic goals for individual patient.

These may include one or more of the following cure of the disease, reduction/elimination of signs and symptoms, preventing disease/symptoms or arresting or slowing disease progression.

- Therapeutic goal should be patient specific

and established in consultation with patient, medical staff and other health care professionals. The desired clinical outcomes should be measurable (e.g. B.P) or else observable (e.g. enlargement of lymph node) or objective (e.g. improvement in sign and symptoms).

- In case of multiple disease pharmacist should understand the therapeutic goals for each individual disease.

3. Identification of Drug Related Problem:

- A drug related problem is an event or ^{ارضاع واصرار} circumstance involving drug treatment that interferes with patient achieving an optimum outcome of medical care.

- If one or more problem are identified this should be brought to the notice of concerned physician.

- Identification of drug related problem involves the systemic review of each drug order on the patient medication chart this process is some time called as MEDICATION or DRUG CHART

REVIEW.

-To identify drug related problem during medication chart review the pharmacist should consider the following possibilities:

1. Untreated indication
2. Inappropriate drug selection
3. Sub-therapeutic dose
4. Over dosage
5. Adverse drug reaction
6. Failure to receive drug
7. Drug interaction
8. Drug use without indication

② It is important to ensure that the most appropriate drug has been selected to treat the patient medical condition and also to ensure that the drugs prescribed are able to achieve the therapeutics objectives.

⑤ First step the pharmacist should check that

the patient is not allergic to the drugs prescribed or has an adverse reaction to any drug in the past.

- Secondly important to assess the patient for any evidence of adverse effects.

- Patient who are most susceptible to develop ADR should be identified and monitored on a daily basis these include:

- Patient with poly pharmacy
- Patient with multiple disease
- Patient with renal and hepatic impairment
- Patients those who are treated with highly toxic drugs.
- Drugs which have a narrow therapeutic index

6. Failure to receive drug: This may be due to medication error, non adherence, poor administration technique, sub standard drug, or the patient inability to pay for the prescribed drugs.

7. Does the patient have a current or potential medical condition that is the result of a drug-drug or drug-food interaction. Pharmacist need make a judgement whether change in therapy is necessary.

8. Does the patient have a current or potential medical condition that is the result of taking the drug for which there is no valid indication.

4. Individualising Medication Regimens.

- Once the drug related problems related to individual drugs on the medication chart have been resolved, the next step is to consider the patient's overall medication regimen. This is particularly important to patients with chronic disease who are taking many drugs on a long term basis. The aim should to ^{over the} simplify the regimen as much as possible and to adjust the regimen to maximize long term adherence.

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affordable: ^{جائز}

- Affordability of drug therapy should be considered for individual patient.

- Sometimes a combination formulation should be used to replace two drug which are being taken at similar dose as in combination product. This should only be done after the doses for the individual drugs have been stabilized.

5. Monitoring of Treatment Outcomes:

- Monitoring of treatment outcomes is the key to assessing whether the therapeutic goals of drug treatment are achieved. It is an ongoing process and involves review of patient's clinical status from various sources as mentioned before and also by direct interviewing the patient.

6. Medication Chart Endorsement:

- Another important goal of medication chart review is to minimize the risk of medication error that might occur at the level of prescribing and/or drug administration.

- A medication error is any preventable event that may lead to inappropriate medication use or patient harm.

- So to prevent this errors pharmacist should review medication chart systemically and write annotation (comments) on the chart where medication order are unclear.

- Pharmacist should never try to guess the prescriber's intention from an illegible, poorly written or confusing prescription. These types should be referred back to the doctor for confirmation of his or her prescribing intention.

- The types of annotations that may be needed are determined by considering the following:

- o Identity of the patient (name and medical record number).

- o Is the allergy status of the patient documented on each medication chart if not NIL. KNOWN ALLERGIES should be annotated on the chart.

- o Is the medication name clear? Abbreviations should be avoided.

◦ Is the route and time of drug administration clear? If not pharmacist should check this with the prescriber.

◦ Is the prescription signed by the doctor etc.

Medication Chart review:

- A medical chart is a ^{class} confidential document that contains detailed and ^{at} comprehensive information on an individual and the care experience related to that person.
- The review of such orders serves as a starting point for other clinical pharmacy activities including patient medication counselling, therapeutic drug monitoring and assessment and management of adverse drug reactions (ADR).

Aim:

- to optimize the patient's drug therapy.
- This includes ensuring that the patient receives the most appropriate drug, dose, dosage form, the timing of dosage and the duration of therapy and that the drug related problems are minimized.

Procedure:

- The patient's medical record should be reviewed in conjunction with the medication administration

record and medication history obtained.

Recent ^{opinions} consultations, pathology results and ^{investigations} investigations, treatment plans and daily progress should be taken into account when determining the appropriateness of current medication orders.

-Components of medication chart review include:

→ Checking that the medication order is written in accordance with the legal and local ^{requirements} requirements

→ Ensuring that the medication order is comprehensive and unambiguous

→ Detecting orders for medication to which the patient may be hypersensitive.

→ Ensuring that the medication order is appropriate with respect to the patient's previous medication specific considerations like pregnancy, age, renal function, liver function etc.

→ Checking for medication duplications, interactions, or incompatibilities

→ Ensuring that administration times are appropriate e.g. With respect to food, other drugs and procedure

→ Ensuring appropriate therapeutic monitoring is implemented.

→ Reviewing medication for cost effectiveness

→ Endorsing the medication orders comprehensively with info. such as dilution/flow rates for IV infusion, generic drug names and trade names, allergies and ADR.

consultation regarding suggested and necessary changes must be undertaken with the relevant healthcare professional and the patient. Consultation and interventions in patient care must be documented in the patient's history and pharmacy records where appropriate.

□ Clinical Review:

- Clinical review is an ^{important} integral component of drug therapy monitoring and should be performed routinely.

Clinical review is the assessment of the patient for the purpose of evaluating the nature of the response to therapy. This may include the review of patient signs, symptoms and results of investigations.

-Goals:

1. Determine the priorities of treatment with respect to the therapeutic outcomes desired by the patient and to co-relate these with strategies employed by the healthcare team.
2. Monitor the patient's therapy
3. Review the outcomes of treatment.

□ Procedure:

- The collection of patient specific data should be

undertaken routinely.

- The data collected should be clinically relevant and documented in the pharmacy patient profile when required.

- To evaluate a patient's therapy the pharmacist may review the results of biochemical, haematological, microbiological, radiological and other investigations.

→ Information regarding to a patient's signs symptoms and progress may be obtained from:

- An accurate medication history interview
- Review of the patient's clinical progress notes
- Discussion with other health care team
- Discussion with the patient.

→ The information obtained must be interpreted and evaluated with reference to:

- The clinical features and pathophysiology of the condition being treated.

-The indication for an investigation, its sensitivity and specificity

-The time frame of drug related effects

-The patient's medication history

-The planned outcome(s) of treatment

Pharmacist Intervention:

- Any action that directly results in a change in patient management or therapy.

- Forms:

- Active (e.g. use of guidelines)
- Passive (e.g. Drug information services)
- Reactive (monitoring prescriptions and seeking amendments to those that are unclear, erroneous, inadequate or inappropriate).

- Interventions may be classified according to clinical or economic.

- Recording of the following details of all pharmacist interventions is recommended in:

- Drug involved
- Brief description of the intervention
- Brief details of response to the intervention
- Patient name and unit record number
- Date, ward, pharmacist

-Other Activities include:

- Supply of drug information
- Patient medication counseling or education
- Cost saving initiatives
- Recommendations for patient monitoring and TDM
- Reporting ADR
- Review of laboratory results
- Patient interviews and taking medication histories
- Participation in ward rounds

2.b

□ Ward Round Participation:

- A ward round is a visit made by a medical practitioner, alone or with a team of health professionals and medical students, to hospital inpatients, at their bedside to review and follow up the progress in their health.

□ Use of ward rounds to pharmacist:

1. Ward round provides many learning opportunities for pharmacist like how drugs are been used and prescribed and also the effects of these drugs on patients.
2. The influence of social, cultural and economic ^{circumstances} on therapeutic or drugs selection.
3. Ward rounds provides identification of cases (or) selection of topics for academic and research work.
4. It strengthens the inter-professional relation-

ship among various health professionals.

- Pharmacist participation is to ensure the safe, effective and economic use of drugs.

- The new role of pharmacist in ward round has been resulted

→ Decreased adverse drug event

→ Improved patient care

→ Reduced length of hospital stay

→ Reduced the health care cost.

□ Requirements of clinical pharmacist to attend ward round:

- Should have good knowledge of:

1- Availability of drugs in the market and the respective hospital pharmacy.

2. Availability of drugs with their different brand names and costs.

3. Complete monograph of drugs, its include

class, how to supply, pharmacological actions, pharmacokinetic profile, adverse drug reactions, drug interactions, uses etc.

Goals and objectives:

-For clinical pharmacist on ward rounds:

1. gain an improved understanding of patients clinical status and progress, current planned investigations and therapeutic goals.
2. Provide relevant information on various aspects of the patient's drug therapy such as pharmacology, pharmacokinetics, drug availability, cost, drug interactions and adverse reactions.
3. Optimize therapeutic management by influencing drug therapy selection, implementation, monitoring and follow-up.
4. Investigate unusual drug orders or doses.

5. Detect adverse drug reactions and interactions.
6. Participate in patient discharge planning.

Classification:

- 1. Pre-rounds
- 2. Registrar/resident rounds
- 3. Professor/chief rounds
- 4. Teaching rounds

1. Pre-rounds:

- During these rounds, the interns or medical postgraduate students in teaching hospitals perform a daily review of patients in their unit or ward.

This is largely a learning opportunity and very few management decisions are made during these rounds. Trainee clinical pharmacists may join the interns or postgraduates in their pre-rounds and complete the patient medication and clinical review at this time.

2. Registrar/resident rounds:

- In teaching hospitals, the registrars and residents, individually or as a team conduct ward rounds, at least once a day at a fixed time, usually in the morning.

In the intensive care unit (ICU), rounds may be conducted several times a day. These rounds are extensive and may also involve clinical teaching to medical postgraduate students and interns. There are useful rounds for clinical pharmacists of all levels of experience.

3. Professor/chief rounds:

- In teaching hospitals, the chief of unit or ward, or the professor in a specialty conducts rounds together with their registrars, residents, postgraduate students and interns for all patients under the care, on a daily basis or a few days of each week.

- These rounds may be extensive, with time devoted to addressing more complex issues regard-

ing diagnosis or management which the registrar or residents have encountered. These rounds may be more challenging for clinical pharmacist in terms of their clinical knowledge.

- Some consultant in teaching hospitals do not get involved in regular teaching activities and may only be doing referrals on request by professors or unit chiefs. It may be difficult for clinical pharmacist to join these consultant rounds due to timing. In such instances, recommendations or advice on patient management may be conveyed verbally through other members of the medical team or written in the patients case sheets, if permitted.

4. Teaching round:

- In teaching hospitals, academic medical staff conduct bedside clinical teaching rounds for residents, medical postgraduate students, interns

and medical undergraduate students.

These are very extensive rounds and are usually conducted only a few times a week.

Though these rounds provide an opportunity for pharmacist to improve their clinical knowledge, they are generally not the best rounds for making interventions or recommendations. Some clinical pharmacists with joint college or university appointments may use these rounds to reach therapeutics.

Pre-ward round preparations:

- > Pharmacist need to prepare well before participating in ward rounds.
- > Accurate and up-to-date information on the patients health status, disease management and past medical history is essential for effective participation in clinical decision-making.
- > Should carry latest CIMS
- > Clinical pharmacist maintain individual patient

profiles which summarise information relevant to the patient's drug therapy. It includes allergies or hypersensitivities, the reason for admission, relevant social history, laboratory data, other relevant investigations and reports and other information such as medication compliance.

- > These details are collected by reviewing charts as by interviewing the patient or carers.

- > During pre-ward round preparations, issues may arise that need to be clarified by looking at appropriate references.

- > Pre-ward round preparation allows the pharmacist to be well-informed and organised before discussing patient management and contributing to the decision-making process.

□ Ward round follow-up:

- Clinical pharmacist often encounters issues

during a ward round that requires some follow-up. Pharmacist should prioritise these issues according to their urgency and relevance.

- Some of the outstanding issues that may arise during a ward round include:

o Responding to enquiries:

- All unanswered queries raised during ward rounds should be recorded and followed-up at earliest convenience. Response may be given over the telephone, by email, in print or in person, as appropriate. If necessary, the information should be supported with adequate references.

o Completing documentations:

- In some situations recommendations or interventions made by the pharmacist during a ward round may need to be documented appropriately. If the clinical pharmacist has permission to record on the patient's case sheet, relevant details should be entered with the name, contact details and signature of the pharmacist.

o Making necessary alterations:

-The pharmacist may need to make alterations to the patients care plan to meet the requirements resulting from changes in patients management.

Ex: monitoring of drug levels and recommending doses after dialysis.

o Discussion with patients:

-If appropriate, the pharmacist should discuss drug-therapy issues with patients.

Ex:

the reasons for alteration in therapy, drug administration or self-monitoring techniques and caution regarding likely adverse effects.

Adverse Drug Reaction Management:

The WHO defines an adverse drug reaction as "A response to a drug which is ^{ies} noxious and ^{accidental} unintended and which occurs at doses normally used in man for ^{بیماری} prophylaxis, diagnosis or therapy of disease or for modification of physiological function".

Adverse drug event or experience:

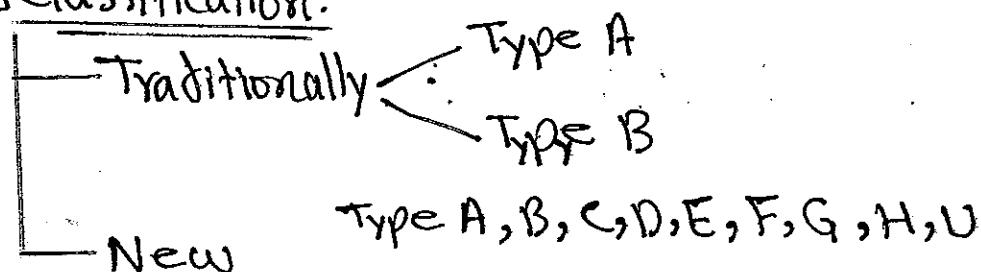
WHO: Any ^{تأثیر} untoward medical ^{اثر} occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

مفهوم، تشخیص

Suspected adverse drug reaction:

Suspecting a causal relationship b/w the untoward occurrence and an administered medicine.

Classification:



— based on Practice aspects:

	Based on administration
	" " intensity
	" " Preventability
	" " causality

^{افزایش}
Type A (Augmented) reactions:

- 80% of ADR

- These reactions are usually ^{افزایش کردن} aggravates the pharmacological effects of drugs and thus are dose dependent.

Ex:

Insulin induced hypoglycemia

Propranolol → heart block

- These reactions are predictable and preventable

Thus, reactions of this type can be nullified by reducing dose or discontinuation of the drug.

- The mortality rate is relatively low, occurrence is common.

Type B reactions (Bizarre):

- 20% of ADRs ^{غیرمنتظره}

- These reactions are hypersensitivity reactions and are not dose dependent.

Ex:

penicillin → hypersensitivity

anesthesia induced hyperthermia

- These reactions are not predictable and preventable (unless the patient has a known history of this type of reaction).

- The mortality rate is high but the chances of this reactions are rare.

Wills and Brown have proposed another classification on the basis of mechanism into 3 new categories:

class	category	Example
Type A	Augmented	Insulin induced Hypoglycemia
Type B	Bizarre/Bugs	Bee sting bite
Type C	Chemical/chronic treatment effects	antimalarial causing ocular toxicity

-Type D: Delayed reactions (Dose-independent)

- Appears after long period of exposure
- Caused by mtd of administration or nature of formulation

Ex: Drug induced cancer

-Type E (Exit/End of treatment effects):

- Begins only when medicine is stopped or dose reduced.

Ex:

Withdrawal Syndromes (Headache, anxiety etc after stopping paroxetine).

Type F (Familiar/Failure of therapy):

- unexpected failure of therapy due to drug interaction (second cancers in those treated with alkalyting agents for Hodgkin's disease).

Type G (Genetic / Genotoxicity):

- Cause irreversible genetic damage

Ex:

carcinogens.

-Type H (Hypersensitivity):

- requires activation of immune system.

Ex:

penicillin $\rightarrow$ hypersensitivity.

Type V (Unclassified):

Mechanism is not understood.

Characteristic	Type A	Type B
Predictability	Yes	No
Dose dependency	Yes	No
Frequency	Common	Rare
Morbidity	Higher	lower
Mortality	Rare	common
Management	reduce the dose and stop the drug.	Stop drugs

Based on intensity:

_____	Minor (mild)
_____	Moderate
_____	Severe (major)
_____	lethal

Based on Preventability:

	Predictable
	Unpredictable
	Preventable
	Unpreventable

Predispose:

مسند کردن ،
باعث شدن

Predisposing/Risk factors of ADR:

1. Polypharmacy:

- Patients with multiple drug therapy are more prone to develop an ADR either due to alteration of drug effect through an interaction mechanism, or by synergistic effect.

2. Multiple And Intercurrent Disease:

- Patients with multiple diseases are at an increased risk of developing an ADR due to multiple drug use for their multiple diseases.

- Similarly, patients with impaired hepatic or renal status are also at a high risk of developing an ADR to drug which are eliminated by these organs.

3. Age:

- Elderly and pediatric patients are more vulnerable to develop ADRs.

- Elderly patients are more susceptible to ADRs due to the physiological changes.

Ex: Nitrate or ACE inhibitors induced postural hypotension in an elderly.

Ex= Grey Baby syndrome with chloramphenicol (in pediatric)

4. Gender:

It has been reported that women are susceptible to develop an ADR, for unknown reasons.

Ex:

Chloramphenicol induced aplastic anaemia

5. Drug Characteristics:

Some drugs are highly toxic in nature and patients who are treated with these agents are at an increased risk of ADRs.

Ex:

Nausea and vomiting is a common ADR seen in patient treated with anticancer drugs.

6. Genetics:

- Patients who are genetically deficient of glucose 6-phosphate dehydrogenase (G6PD) enzyme are at higher risk of developing hemolysis due to primaquine than those who are not.

Mechanisms of Adverse Drug Reactions:

Type A:

- Any type A reaction, which occurs in an individual, may be attributed to any one or more of the following mechanisms.

1. Pharmaceutical causes:

i- Changes in drug quality present in particular product.

ii- Changes in drug release properties.

Ex:

The corrosive effects on the esophagus caused by certain doxycycline salts.

By changing to another salt, the risk may be reduced dramatically.

2. Pharmacokinetic Causes:

- Alterations in the absorption, distribution, metabolism and elimination of drugs may alter drug effects by changing the concentration of

Drug present in the site of action.

a. Absorption:

-The extent of drug absorption (the total amount of drug reaching the general circulation) plays an important role in altered response. etc.

b. Distribution:

-There are several factors, which determine the extent of distribution of a drug including regional blood flow, membrane permeability and protein/tissue binding. etc.

c. Metabolism:

-In an individual who has a reduced metabolic rate, accumulation of drug in the body may be higher, leading to increased risk of ADRs, while therapeutic failure may occur in an individual who has an enhanced metabolic rate.

Ex:

'Slow acetylators' are highly prone to develop

type A reaction to drug which are metabolized by acetylation, such as isoniazid, dapson etc.

δ. Elimination:

- Drug accumulation due to reduced elimination may predispose to ADR, as a result of increased drug concentration in plasma and tissue.

- Conversely, reduced concentration of drug in plasma and tissue due to enhanced drug elimination may lead to therapeutic failure.

3. Pharmacodynamic Causes:

a. Drug Receptors:

- Most drugs elicit their response by combining with receptors.

- The amount and sensitivity of receptors of one individual may differ from another individual, which can greatly affect the drug effect, when the drug acts through these specific receptors.

b. Homeostatic mechanisms:

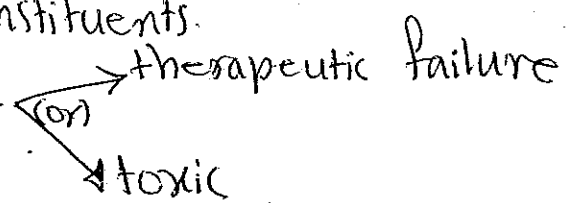
- Many physiological factors may determine the extent of drug's effect in an individual as drug effect occurs within the environment of the body physiological mechanisms.

c. Disease:

- The pharmacological effects of a drug which are not apparent in a healthy individual may be unmasked by intercurrent diseases.

□ Mechanisms of Type B Adverse Drug Reactions:

- The major sources for type B reactions include decomposition of the active ingredient, the effects of non-drug excipients (additives etc) and synthetic byproducts of active constituents.

- Decomposed drug product 

ⓔ Penicillin

- Hypersensitivity are caused by the degradation products of penicillin, mainly penicilloic acid which combine with host protein and become antigenic. Ex: skin rash and fever, acute anaphylactic shock, which may in some cases be fatal.

Detection and monitoring of ADRs ^[5M, 2M]

1. Pre-marketing studies (prospective):

The safety of new medicines

↓ tested in

Animal models

↓

information (level of acute toxicity, organs affected, cell injury etc) obtained

↓

specific animal tests for mutagenicity, carcinogenicity and teratogenicity carried out

↓

But no sufficient knowledge to extrapolate information collected from animals into human risks.

↓

if no worrying results in animals, safety tests proceed onto testing in humans in clinical trial programmes.

o Clinical trials have the power to identify adverse reactions of a frequency greater than 0.5 - 1.0 percent.

o Clinical trials are carried out in three

phases prior to the submission of a marketing authorization application with a stepwise increase in the number of individuals being exposed.

- Only dose related (type A) ADRs will be known.

2) Post marketing Studies: (Retrospective or concurrent)

- To assist the detection of ADRs healthcare professionals should closely monitor patients who are at high risk:

- Patients with renal or hepatic impairment
- Patients taking multiple drug
- Patients who have had previous allergic reaction.

-Detection of ADRs includes:

- Collection of data (presenting complaints, past medication history etc).
- Detail of the suspected ADR such as time of onset and duration of reaction, nature and sensitivity of a reaction.

- Data can be obtained from:

- Patients case notes and treatment charts
- Patient interview
- Laboratory data sources.

Under reporting of ADRs:

Under reporting varies with a number of factors:

- 1- reporting is higher for new drugs than for old.
2. Serious reactions get reported to a higher degree.

Not-reporting of ADRs:

Reasons:

- 1- lack of time
2. lack of knowledge on what, how or where to
3. reaction is already well-known: report.

Assessing Causality:

Causality assessment is the method by which the extent of relationship between a drug and a suspected reaction is established based upon an individual clinician's assessment.

Approaches:

- Opinion of the individual ^{or team} experts
- Opinion of a ^{group} panel of experts
- Formal algorithms

Scales (Ex) ^(2m) x_{new}

WHO Scale (common)

Naranjo's scale

European ABO system

Kramer

WHO scale categorizes the causality relationships into:

- | | |
|------------|--------------------------------|
| - Certain | - Unclassifiable |
| - Probable | - Unlikely ^{possible} |
| - Possible | - Conditional/unclassified |

- Event or laboratory test abnormality, with plausible time relationship to drug intake

1. Certain:

- A clinical event including laboratory test, abnormality occurring in ^{years} plausible time relationship to drug administration.

- It can not be explained by concurrent disease or drugs.

- responsible to withdrawal plausible

- rechallenge if necessary.

2. Probable

- Event of lab test abnormality with reasonable time relationship to drug administration.

- Unlikely to be attributed to concurrent disease or other drugs.

- Rechallenge not necessary.

3. Possible:

- Event of laboratory test abnormality with reasonable time relationship to drug administration.

- Could also be explained by disease or other drugs.

- Information on drug treatment withdrawal lacking or unclear.

4. Un assessable/unclassifiable:

- A report suggesting an adverse reaction.
- Can not be judged because of insufficient information.
- Report cannot be supplemented or verified.

5. Unlikely:

- A clinical event including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable.
- Diseases or other drugs provide plausible explanations.

6. Conditional/unclassified:

- Event or laboratory test abnormality.
- More data for proper assessment needed or additional data under examination.

HARTWIG ADR SEVERITY ASSESSMENT SCALE

Level 1	An ADR occurred but required no change in treatment with the suspected drug.	
Level 2	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. No antidote or other treatment requirement was required. No increase in length of stay (LOS)	
Level 3	The ADR required that treatment with the suspected drug be held, discontinued, or otherwise changed. AND/OR An Antidote or other treatment was required. No increase in length of stay (LOS)	
Level 4	(A) Any level 3 ADR which increases length of stay by at least 1 day OR (B) The ADR was the reason for the admission	
Level 5	Any level 4 ADR which requires intensive medical care	
Level 6	The adverse reaction caused permanent harm to the patient	
Level 7	The adverse reaction either directly or indirectly led to the death of the patient	

Mild	Level 1 & 2	
Moderate	Level 3 & 4	
Severe	Level 5, 6 & 7	

Management of ADRs:

1) Discontinue the offending agent if:

- It can be safely stopped.
- There is reasonable alternative

2) Continue the medication if:

- It is medically necessary.
- There is no reasonable alternative
- The problem is mild and will resolve c time.

3) Discontinue non-essential medications:

4) Administer appropriate treatment:

5) Provide supportive care:

Ex: analgesics

Warm / cold compression.

6) Consider rechallenge or desensitization.

Role of pharmacists in the Management of ADR:

- 1- Monitoring the patients who are at greater risk of developing ADRs.
- 2- Monitoring the patients who are prescribed with drugs highly susceptible to cause ADRs.
- 3- Assessing and documenting the patients previous allergic status.
- 4- Assessing the patient's drug therapy for its appropriateness.
- 5- Assisting health care professionals in detection and assessment of ADRs.
- 6- Educating patients.
- 7- Follow up of patients to assess the outcome of the reaction and management.

8. Educating health care professionals about the importance of reporting of an ADR
9. Creating awareness about ADRs among health care professionals, patients and public.
10. Presentation of reports in meeting and conferences.
11. Conducting workshops or conferences or seminars on ADRs for health care professionals.
12. Dissemination of signals generated through publications of reports in bulletin or journals.
13. Encouraging or stimulating health care professionals in reporting ADR.

Under reporting of ADRs:

- One of the major deficiencies of spontaneous reporting program is the failure of health professionals to identify and report drug related injuries.

- Under reporting varies with a no. of factors:

1. reporting is higher for new drugs than for old
2. Serious reactions get reported to a higher degree.
3. Reporting is affected by promotional claims of the drug sponsors.
4. Type B reactions are reported more commonly than their share of events in practice.

- The reasons most often given by the health professionals for not reporting are:

1. lack of time
2. lack of knowledge on what, how or where to report
3. guilt or fear of litigation.
4. Belief that all registered medicines are safe.

The Naranjo's scale: (2M)

The Naranjo's scale: categorizes the reaction as either definite, probable, probable or unlikely.

NARANJO ADR PROBABILITY SCALE (Not done)

	Yes	No	Do Not Know	Score
1. Are there previous <u>conclusive reports</u> on this reaction?	+1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4. Did the adverse reactions appear when the drug was readministered?	+2	-1	0	
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	0	
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	+1	0	0	
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	
			Total Score	

Total Score

ADR Probability Classification

9

Definite/Highly Probable/Certain

5-8

Probable

1-4

Possible

0

Doubtful/Unlikely

□ Drug Information:

- Drug Information refers to the provision of unbiased, well-referenced, and critically evaluated up to date information on any aspect of drug use.

- The information may be specific to an individual patient or relative to a group of patients.

- Drug Information Service refers to activities that are part of the overall pharmacy service or pharmaceutical care process.

Drug Information Center (DIC) refers to the specialized facility that provides drug information to those who need it.

- The first drug information centre was established at the University of Kentucky in 1962.

□ location of some drug information centers in India.

1. Victoria Hospital, Bangalore, Karnataka
2. JSS College of Pharmacy, Ooty, Tamilnadu
3. Kempegowda Institute of Medical Sciences, Blore, Karnataka
4. Pharma Information Centre, Chennai, Tamilnadu

Drug Information Resources: (TAD, dis 5M)

- 3 types:

1. Primary Resources:

- It consists of research studies or clinical experience, which has not been previously published.

- This includes clinical trials, short reports, case reports and letters to the editor which describe clinical events such as ADRs.

- It give information of latest drug only not other old drugs.

Ex:

- British Medical Journal
- Drugs and Therapeutics Bulletin
- Lancet
- Australian Prescriber
- Indian Journal of Medical Sciences.

Advantages:

1. It offers the most current information on any given subject.
 2. Best source of unbiased information.
 3. Provide the specific details on comparative drug studies.
 4. Source for answering therapeutic questions.
- Journals enables pharmacists to
- a. keep abreast of professional news
 - b. Enhance communication with other health-care professional.

Disadvantages:

1. Getting access to the sources is difficult.
2. As thorough knowledge of the organization and types of literature is necessary for efficient search practice.

2. ^{2m}Secondary Resources:

- Secondary resources provide an ^{80%}overview of previously published work, and include indexing

and ^{مختص} abstracting services of the primary ^{أصلية} literature.

- An indexing system provides only bibliographic information that is indexed by topic and provide the original abstract or full text with no interpretation.

- On the other hand, an abstracting service provides content by ^{تفسير} interpreting the original reports and creating ^{ملخص} summaries based on the abstracting service's editorial guidelines.

- Secondary resources provide access to primary literature.

Ex:

Medline

Drugdex

poisindex

Chemical abstracts

-Advantages:

1. It does not require a large library space.
2. Remote access too many data bases at any time of the day or night.

3. You may download information.

-Disadvantages:

1. Online search is expensive
2. involved a finite number of journals.

3. Tertiary Resources:

-These consist of general literature including textbooks and full text computer database like micromedex.

Adv:

1. Easily accessible
2. Information that is collected and evaluate from multiple references and expressed in a practical way.

-Dis:

require long time
Biased information may not be completed.

Ex:

Standard references and Textbooks.

Medical Dictionaries Ex: Dorland's

Drug Bulletins

Medical
Dictionary

Ex { Drug information
Handbook

{ Drug Interactions
Stockley

Poison Information

- It refers to a specialized area of drug information that provides information on the toxic effects of an extensive range of chemicals, including plant and animal toxins. This task is handled by specialized centers known as poison information centers.

- Poison Information Services (PIS)

Are activities that deal with the

- risk assessment	} of exposure to
- Diagnostic	
- Management	
and prevention	
	any poison
	in patient of any
	age.

Poison information Center (Poison ^{PCC} Control center)

Functions:

1. They assess and make treatment recommendations during possible poisoning via a twenty-four-hour emergency telephone service.

2. They provide public and professional education programs.

3. Collect data on poisoning

4. Perform research.

→ The main function of a poison information center is to provide information and advice concerning the diagnosis, prognosis, treatment and prevention of poisoning, as well as about the toxicity of chemicals and the risk they pose.

Equipment and Facilities:

- Suitable office furniture and facilities
- Specific areas should be set aside for answering telephone enquiries, consultation with patients, and preparation of documents, staff meetings etc.
- Additional desk space is needed at centers using computer equipment and online database.
- Own libraries
- Substances records: To provide advice on management of a patient poisoned by a specific substance.

Centers must have information on the physical, chemical and toxicological properties of the substance, its effects on various organ systems and body functions etc.

Communications records:

includes: incoming and outgoing enquiries, by telephone, fax, telex, letter etc, and of personal consultations.

Annual reports:

Library requirements:

- i- Books or other publications on the animal and plant toxins of the region.
- ii- Standard text books of medicine, chemistry
- iii- Journals of medicine and toxicology etc.
- iv- Dictionaries relating to...

□ Staff:

1- The team may include physicians, nurses, analysts, pharmacists etc.

ii - An administrative director and administrative assistants.

Research and development:

- Appropriate research on antidotes is also essential and should include kinetic, toxicological and pharmacodynamic studies in both animals and humans.

Prevention:

1. Encouraging manufacturers to employ less toxic formulations and to improve the packaging and labeling of their products.
2. Giving special warnings to professional health care workers concerning specific toxic risks.
3. Labeling of toxic products or special packaging to reduce the risk of exposure to toxic substances.
4. Informing the general public, as well as special

groups at risk, about recognized or emerging risks to the community posed by the use, transport, storage and disposal of specific chemicals and natural toxins.

□ Poison Information resources:

1- Primary resources:

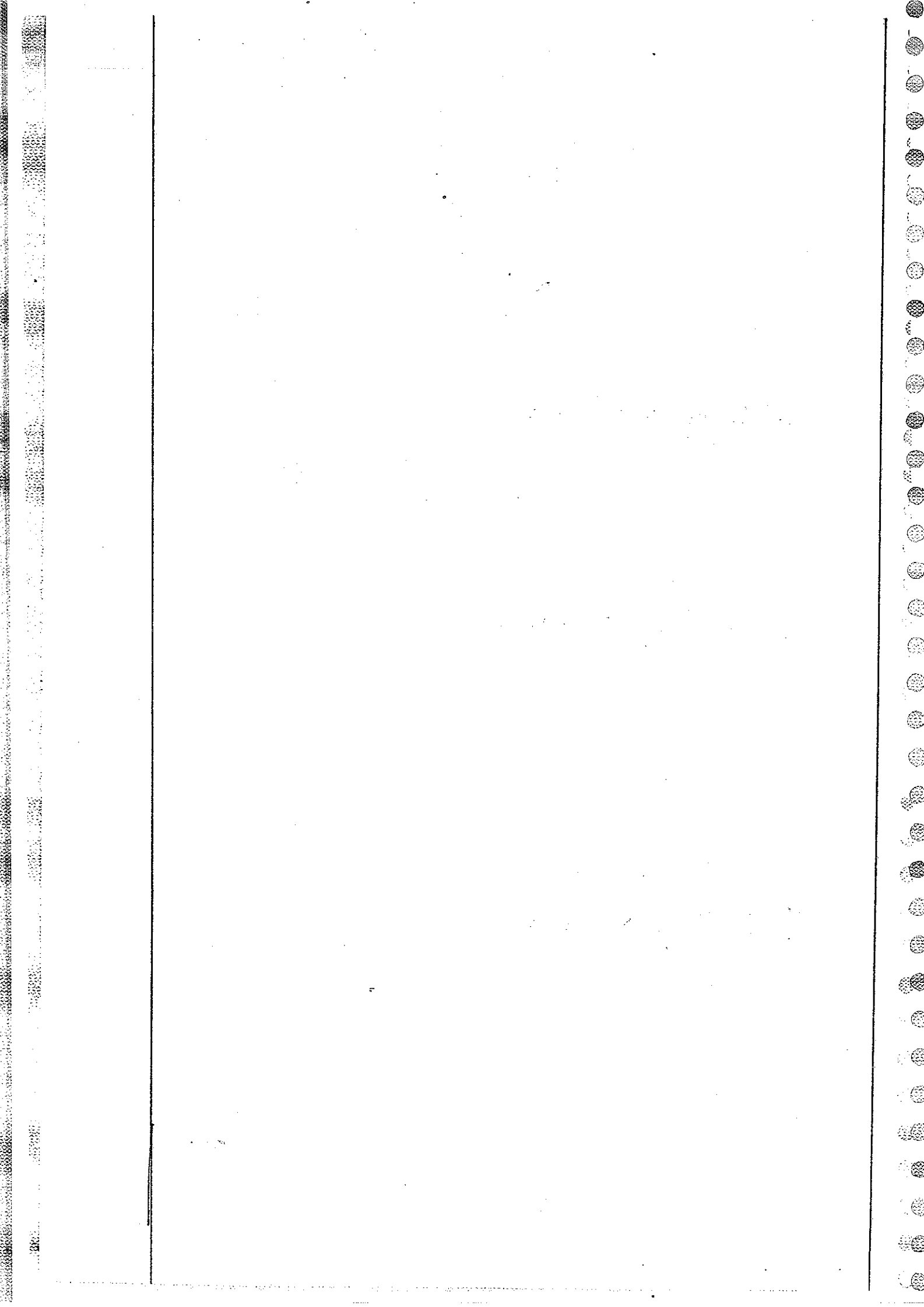
Ex: Journal of medical toxicology
Indian Journal of toxicology

2. Secondary resource:

Ex: poison dex
Medline
Toxbase
Toxline

3. Tertiary resource:

Indian pharmacopoeia
United states pharmacopoeia



□ Medication History Interview

MHI is a vital tool, the pharmacist can use to gather information and improve overall patient outcomes

- Medication History is defined as the information regarding the medications taken by the patient previously.

- Information may collected by the pharmacist or other health care professionals.

- Goal:

- 1- To identify significant past medical conditions.
- 2- Document allergies and adverse reactions
3. Screen for drug interactions
4. Examine the need for medication aids

- Importance/significance of MHI:

→ The information obtained can be utilized to:

- Compare medication profiles $\bar{c}$ the medication administration record and find out discrepancies ^{تفاوت}

- Document allergies and ADRs.
- Screening for drug interaction
- Document patient-initial medication administration.
- Assess drug administration techniques

→ Medication history interview is conducted for inpatients as well as outpatients.

Practically speaking it is not possible to conduct interviews for all the patients hence, it is important to select those patients where maximum benefit is likely to be obtained. This special patient group includes:

1. Patients with serious and/or unstable disease states.
2. Patient receiving specific medications, ex-drugs with narrow therapeutic index
3. Patient treated with complex drug regimens
4. Elderly or paediatric patients
- etc.

Procedure:

- Documentation relevant to the MH may includes:

- Current medication administration record
- Previous prescriptions
- current admission details (medical and nursing notes)
- Referral letter from local doctor or other source (nursing home)
- The patient's own medication list

- After determining the ability of the patient to communicate appropriately and choosing the most suitable environment to conduct the interview:

- ① Establish the identity of the patient
- ② self preparation
- ③ Introduce yourself
- ④ Explain purpose of interview
- ⑤ Conduct interview
- ⑥ conclusion: summaries the important issues

7. Documentation

- Document the information obtained during MHI for future reference.

- Using appropriate interview techniques (e.g. open ended questions), seek information on the following:

- Prescription medication use
- Non-prescription medication use
- Allergies, previous ADR and their manifestation
- Use of alternative therapies
- Social drug use (alcohol, tobacco etc).

Patient Counselling

Definition:

Patient counselling is a process of educating the patient regarding the

- Medication

- Drug interaction

- ADRs etc by the community

pharmacist so as to improve the patient ^{compliance} compliance.

Objective / aim of counselling:

1- To improve patient compliance

2- To prevent therapeutic errors

3- To give maximum therapeutic benefits to the patient

4- To advise the patient regarding:

- Route of administration

- Time of "

- Side effects

- Drug interaction

- Storage condition

Need For patient Counselling:

-The need for patient counseling is apparent from both the pharmacists and patient's point of view.

-For the pharmacist, patient counseling provides legal, personal, professional and economic benefits; for the patient, it reduces errors in medication use, drug interactions, adverse drug reactions.

II Communication skills for effective counselling:

counseling process uses:

A-Verbal communication skills

B-Non-Verbal " "

A-Verbal communication skills:

1- language:

while speaking to patient use simple language and avoid using unnecessary medical words.

-If possible speak the patient own language.

2. Tone:

Changes in the level and range of pitch convey information about the feelings and attitude of the person speaking; the tone of the voice should be caring and reassuring.

3. Volume:

- Ideally, counseling should be conducted in quiet private setting where it is unnecessary to raise ones voice.

- Although it may be necessary to speak more loudly to patients with hearing problem.

4. Speed:

The clarity of our communication depends on our rate of speech.

Patients may be ^{reluctant} to interact with a pharmacist who speaks quickly because they may feel the pharmacist is busy too.

B-Non-verbal communication:

Proximity:

This refers to the distance that people maintain between themselves during the counseling process.

- Classified into 4 zones:

	intimate (45cm or less)
	personal (45 cm to 1.2m)
	Social (1.2 - 3.6)
	public (more than 3.6m)

→ Generally counselors or health care professionals use intimate or personal proximities.

Eye contact:

- The duration of time that people look at one another during a conversation varies depending on whether they are speaking or listening.

- Listeners look at the speaker more often and for longer periods.

3. Facial expression:

These can be used during counseling to demonstrate empathy towards the patient.

- Head movements such as nodding, and gestures and body postures can be used to advantage.

□ Barriers to patient counselling:

- 1- Lack of time
- 2- Lack of knowledge (about drugs and patient history)
- 3- Lack of confidence
- 4- Poor communication skills
- 5- Lack of awareness by the patient of the need for counseling and its availability.

□ Requirements For Removing The Barriers:

1- Availability:

- The pharmacist must be available to the patient even if things are busy and hectic.

2- Atmosphere:

-An atmosphere is needed where the patient can feel comfortable asking advice, discussing his prescription or illness with the pharmacist.

-Through an unhurried manner and through your availability you can create an atmosphere that shows interest in patients.

-In order for effective and efficient patient counselling to be conducted, the dispensary lay out should provide a number of counseling areas, including a semi private and private area.

3. Approach:

-involves the pharmacist's approach to each individual counseling situation. This involves eliminating time and personal barriers.

4. Attitude:

-The attitude towards patient counseling and the individual patient are important in providing optimum counseling.

- Personal barriers such as passiveness and lack of self-confidence in knowledge must be overcome.

Steps During Patient Counselling:

- Introduce yourself:

It is important for patients to know they are speaking with the pharmacist.

- Pharmacists should greet the patient.

- Extend your hand, and state your name:

"Hello, I'm Reza R, your pharmacist". This begins the relationship.

Identify to whom you are speaking:

If you are talking to the patient directly, information is less likely to be confused or distorted than if you are talking to the patient's agent, who must pass the information on to the patient.

Explain the purpose/importance of the counseling session:

Ex

- Patients are less likely to take tetracycline with food or dairy products if they are told that decreased absorption and effectiveness of the drug may result.

- Ask the patient what the physician told him/her about the drug and what condition it is treating:

- The purpose of the session is to ensure that patients leave the pharmacy with knowledge about the proper use of the medication.

It really doesn't matter whether the patient gets this information from the pharmacist or physician.

- Prior to providing information, ask the patient if he/she has any concerns:

- The pharmacist should make every effort to understand the concerns of the patient and treat the concerns with the attention they deserve.

- Listen carefully and respond with appropriate empathy:

- These skills are absolutely essential to an effective counseling session.

- Tell the patient the name, indication, and route of administration of the medication:

- Inform the patient of the dosage regimen:

Ex:

Not everyone eats three meals a day:

Patients with diabetes may eat six or seven mini meals each day. Therefore, directions that state, "Take one tablet after meals and at bedtime", may prompt some patients to take their medications more than the intended four times per day.

- Ask the patient if she/he will have a problem taking the medication as prescribed:

→ Pharmacists should attempt to resolve problems related to the dosage regimen, either through tailoring the regimen or working with the

physician to change the medication to a less complicated dosing schedule.

- Tell the patient how long it will take for the drug to show an effect.

If patients are not told when to expect onset of action, they may believe the medication is not working. Patients may cease taking a medication, or they may take too much because they believe one dose did not work.

- Tell the patient how long he/she might be taking the medication.

- Emphasize the benefits of the medication:

- Discuss major side effects of the drug:

- Discuss precautions (eg: activities to avoid) and beneficial activities (eg: exercise, ~~used~~ salt intake etc).

- Discuss drug-drug, drug-food, drug-disease interaction

- Discuss storage recommendations, ancillary instructions (e.g. shake well, refrigerate)

- Explain to the patient in precise terms what to do if he/she misses a dose:

- Advise patients to always check their medicine before they leave the pharmacy.

- Use appropriate language throughout the counseling session:

- Organize the information in an appropriate manner:

Generally speaking, the most important information should be provided at the beginning of the counseling session and repeated at the end.



Department of Pharmacy Practice

Visveswarapura Institute of Pharmaceutical Sciences
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PATIENT COUNSELLING FORM

Patient name:

date :

Age/sex :

Past medical history:

Family history :

Personal history ,(lifestyle, occupation):

Current illness :

Allergies (drug/food/others):

Medication:

Counseling given on :

Patient perception with respect to disease and medication:

Patient compliance and evaluation:

Poor ☐ satisfactory ☐ good ☐

Major side effect and management :

Provision of written information :

Precaution

Diet and exercise

Interaction (drug- drug ,drug- food,drug -disease)

Storage

Information on missed dose

Any communication barriers :

Yes ☒ No ☐

If Yes:

Language ☐ literacy ☐ physical/sensory impairment ☐
Anxiety ☐ age ☐ time ☐ non co-operative ☐

Comments:

Signature of Patient

Signature of clinical pharmacist

Drug Utilization Review/Evaluation:

-DUE is an ongoing, authorized and systematic quality improvement process which is designed to:

1. Review drug use or prescribing pattern
2. provide feed back of results to the prescribers
3. develop criteria and standards which describe optimal drug use
4. promote appropriate drug use through education and other interventions

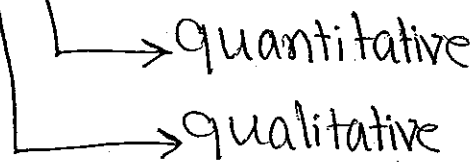
-DUE is a discipline which aims to understand how and why drugs are being used as they are so that drug use and health outcomes can be improved.

DUE can help the health care system to understand, interpret, and improve prescribing, administration and use.

DUE can be

- Drug or class of drugs focused
- indication focused

classification



- Quantitative analysis involves collection, organization and display of estimates or measurements of drug use which is help for purchasing departments but it gives only a suggestive data and unilateral pharmacy function.

- Qualitative analysis involves collection, organization, and analysis and report information on actual drug use.

- The main difference b/w qualitative and quantitative analysis is the inclusion and the use of criteria in qualitative analysis.

- Criteria are predetermined elements against which the aspects of quality, medical necessity appropriateness of medical care may be compared.

-This may be based upon indication of use, dose, dosing, frequency and duration of therapy.

-It is possible to combine both qualitative as well as quantitative analysis together.

Establishment of DUE program:

- DUE program is composed of professionals with an interest in improving drug therapy and have ready access to experts in medicine, surgery and major hospital specialties. So it can be either PTC or separate DUE committee.

- Pharmacist play a key role in delivery of DUE.

- DUE programme should be multidisciplinary to avoid some of the problems such as:

- physician may perceive DUE as pharmacy budget management program.

- the involvement of doctors and nurses are restricted which reduce the effectiveness of DUE.

the pharmacy department may keep aside this function of DUE when there is a shortage of staff.

The committee should

1. Draft and approve the policies and procedures that govern its work.

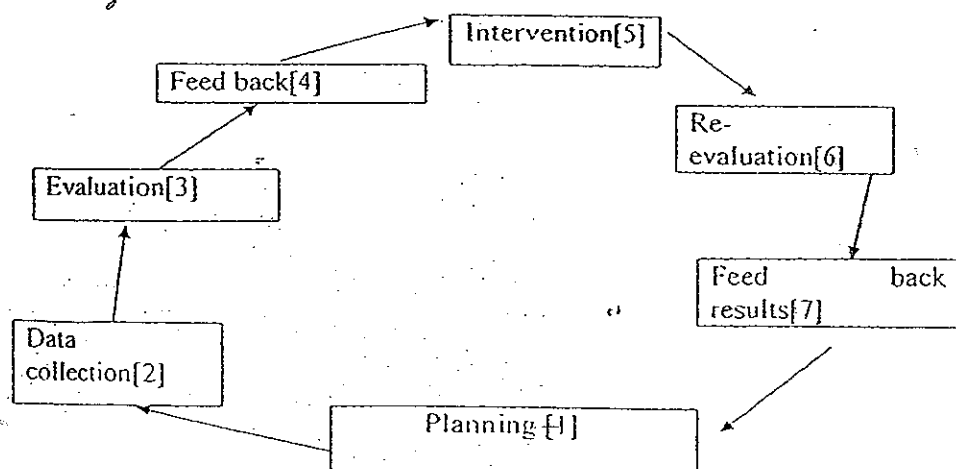
2. establish and maintain adequate means of communication with administration and other committees.

3. the committee should prepare a schedule including a yearly planning meeting, evaluating data, meetings for selecting and approving criteria etc.

P D E F I R F

The DUE cycle

DUE operates in a repeating cycle.



1. planning:

Step 1 - identify drugs or therapeutic areas of practice for possible inclusion in program.

- The areas can be identified from medication error reports, ADR reports, feed back reports from the doctors, clinical pharmacists, microbiological data, medical and pharmaceutical literature.

- Common target for DUE include:

1. Commonly prescribed drugs eg antibiotics
2. drugs associated with significant interactions
e.g phenytoin
3. expensive drugs. eg: LMWH
4. new drugs
5. Drugs with narrow therapeutic index eg:
digoxin
6. drugs used in high risk patients eg ICU etc.

Step 2: design of study

- DUE studies can be prospective,
planned

در بوطیک گزیده
concurrent or retrospective depending on the timing of data collection.

- Prospective means patient's drug therapy is planned before the start of therapy.

- Concurrent studies are performed during the course of treatment.

- Retrospective - in this case the therapy is reviewed after the patient complete the therapy.

Adv: the doctors and others are unaware of data collection so it gives an unbiased result.

Dis: Some data unclear or missing and reviewed patients do not gain immediate benefit.

Step-3: Define criteria and standards:

- It is important to conduct a comprehensive literature review.

- The steps involved are:

• Perform an exhaustive literature search for the chosen drug or therapeutic area using

more than one search mechanisms eg. medline
◦ assemble full copies of all relevant
original research papers.

◦ Critically evaluate the studies directly relevant
to the chosen drug or therapeutic area
identifying strengths and weakness in the
study design and deciding whether appropriate
conclusion have been made from the
data presented

◦ Briefly summarize the literature review,
identifying the key papers in chosen area
and the drug use criteria.

- Criteria are those predetermined statements
describing optimal drug use against which
the quality of actual drug use is compared.
◦ Standards are professionally developed
expressions of the range of acceptable
variation from a criterion.

- The criteria should be scientifically based

be supported by clinical or research literature. They must be valid, realistic, easily measured and outcome oriented.

Step 4. Design the data collection form

Common aspects of drug use studied in DUE are:

1. patient demographics
2. prescriber details
3. disease severity
4. contraindications
5. indication for drug use
6. side effects
7. dosing information
8. preparation and administration
9. drug-drug or drug-food interactions
10. cost of therapy
11. patient education.

Data collecting form for a DUE examining the monitoring of renal functions during amino glycoside therapy:

Name: _____		Hospital name _____	
DOA: _____		age _____	
DOD: _____		Sex _____	
		consultant _____	
		inpatient # _____	
		weight _____	
		previous hospital Yes/no	
Indication		Details of aminoglycoside therapy	
UTI, pneumonia, septicemia, endocarditis		reasons for cessation	
Others-----[specify]		infection resolved/toxicity	
Drug	dose in mg	route	frequency
Gentamycin		IV/IM	QD/QID/TID/
Tobramycin			BD/Others
amikacin			
date-----			date
serum creatinine----			started
comments---			date
data collectors sign			cease

-Step 5- data collection:

-Data collection should be chosen carefully and should be ^{data} familiar with information which is arranged in patient case notes.

-Step 6- Evaluate results:

-Data evaluation is the most critical steps in DUE.

- Summarize the major categories of results and to identify where exactly the data shows deviation from the guidelines and reason should be evaluated

- The reasons for deviation may include:

1. drug used for new indications
2. out dated procedure
3. inadequate resources
4. misinformation or misunderstanding

Step 7. provide feed back of results:

- The success of DUE depends on feed back to prescribers, other hospital staffs, administrative heads.

- The results may be circulated to hospital staffs via news letters, DUE meeting or academic meetings.

Step 8. develop and implement intervention:

- The intervention to improve drug use can be educational or operational and can target

groups or only those prescribers who did not meet drug use criteria.

- Educational intervention consist of educational meetings, circulation of protocols, academic detailing, feed back of study results.

Step-9:

Reevaluate to determine if drug use and prescribing patterns need to be monitored to determine the success of interventions.

Usually done 3-12 months after the intervention.

Step 10: reassess and revise the DUE program:

-The questions addressed should include:

1. Did the program address important aspects of care?
2. Were the criteria developed appropriate? etc.

Step 11: Feed back results:

-The results of the DUE to clinicians and other involved hospital staff to get opinion and otherwise the intervention.

★

The pharmacist's role intervention DUE:

1. program development, ^{or/with} supervision and co-ordination.
2. education of hospital staff about DUE
3. promotion of the goals and objectives of DUE
4. Development of data collection instruments.
5. pilot test, data collection, analysis and report writing.
6. Documentation of program outcome
7. presentation of DUE results at meetings and conferences.
8. publication of results intervention peer-reviewed journals.

#Drug Utilisation Review (DUR):

-DUR is a tool to identify problems in the medication use process i.e. drug prescribing, dispensing, administration and monitoring, according to the formulary and STG.

-As problems are identified, strategies are developed and implemented to improve the use of drugs.

-DUR also helps to monitor the rational use of drugs by knowing which drugs are properly used (according to the formulary) and for how long they are used (as described in STG).

The approach to develop a DUR programme, varies, but there are nine important steps to follow which are now well accepted.

Step 1: Establish responsibility for DUR process:

The DTC committee usually takes the responsibility for DUR process.

- It can be allotted to a sub committee also if

DTC is preoccupied with other hospital responsibility

Step 2: Establish the scope of each study:

- Hospital pharmacists, nurses and physicians are major sources of suggestions for focusing DUR studies.

- For ex, DUR may study one medication such as ranitidine or a condition [^{like} use of antibiotics as prophylaxis medication for caesarean section].

- DUR might also focus on one step in medication use process such as prescribing, drug labeling or drug administration].

- The focus may shift from one area to another, from quarter to quarter or as and when one DUR study gets over.

- DUR usually focuses on drugs or therapies that are of high use, high cost, high risk to prone to a problem.

- May use A.B.C analysis to choose.

Step 3: Establish Criteria or Indicators for how the drug should be used or the condition treated:

-Criteria usually include the following components:

Use:

Appropriate indication, treatment of underlying conditions, appropriate treatment of symptoms in treating underlying diseases.

Selection:

Efficacy, safety, total cost,

Dosing: Indication-specific dosing (age), indication-specific duration, dosing intervals.

Interaction: Disease, food, drug

Administration: Dosing interval, loading dose, maintenance dose, duration and withdrawal of medication.

Step 4: Collect and organise data:

- Data collection forms can be designed based on the criteria and made into a simple 'yes-or-no' or 'fill-in-the-blanks' questions format.

- Data collection for a DUR study within the hospital is often done by hospital pharmacist and his group or head nurse and her team.

- The most common data sources are patient charts, dispensing records, medication administration records and laboratory test records.

- It is important not to collect too much data, but to focus on specific indications related to the problem.

Step 5: Analyse the data:

- The data must be tabulated and reported in a standard format for comparison with benchmarks. It is often necessary to create simple tables usually sorted by the most important indicator.

Step 6: Develop conclusions:

-The DTC committee would review the results and decide what needs to be done. DTC may also develop conclusions regarding reasons for differences between results and benchmarks.

Step 7: Make recommendations:

-The DTC committee reviews the results of the data analysis and develops conclusions regarding reasons for differences between results and benchmarks.

Step 8: Take Action:

-The DTC committee may recommend changes based on the audit to improve knowledge or change behaviour.

Step 9: Follow up:

-It is important to follow up actions decided

in Step 8.

What is Peer Review? 2M

QA can be defined as the procedures which are used to set, promote, maintain and monitor the desired standards for services and products.

Quality Assurance of clinical pharmacy services

Objectives And definition:

-The objective of clinical pharmacy practice is to optimise patient outcomes by working to achieve QUM:

Definition:

Clinical pharmacy practice is the practice of pharmacy as part of a multidisciplinary healthcare team directed at achieving QUM. This may include:

- Participation in the management of individual patients;
- Contribution of clinical knowledge and skills to the healthcare team;
- Identification and reduction in risks associated with medicines use;
- Involvement in the education of patients, carers and other health professionals and
- Involvement in research.

Extent and Operation:

- Clinical pharmacy services must be supported by management to enable pharmacists to achieve QUM (Quality use of medicine).

A pharmacy service should provide suitably trained and qualified pharmacists supported by appropriately supervised technicians to facilitate the most effective, efficient and economical use of medicines with the aim of optimising patient care.

Clinical pharmacists should be involved in activities directed to individual patients and more broadly to support the objectives of the National Medicines Policy, especially its QUM arm.

- Clinical pharmacy should not be restricted to hospital practice. Communication and cooperation between institutional and community-based pharmacists is an essential element of a patient's ongoing care.

□ Clinical Pharmacy Services to Support the National Medicines Policy:

- Pharmacists must be involved in activities that support the objectives of the National Medicines Policy, especially its QUM arm.

1- Pharmacists should be involved in contributing to processes involved in selecting new medicines, approving institutional procedures and guidelines.

2- Pharmacists should be involved in the identification, formulation, implementation and evaluation of decision support tools for medicines management.

3. Drug use evaluation

4. Patient information and education programs.

5. Research

□ Procedures for clinical pharmacy services For individual patients:

1. Medication Action plan:

The medication action plan focuses on overall patient outcomes and in order to carry out this plan, the pharmacist will perform a number of specific clinical activities:

→ The 6 fundamental components of a Medication Action Plan for an individual patient are:

1. interpretation of patient-specific data
2. identification of clinical problem
3. establishment of therapeutic goals
4. evaluation of therapeutic options
5. individualisation of therapy
6. Monitoring of patient outcomes.

→ The ten specific clinical activities that contribute to the components of a Medication Action plan:

1. Accurate medication history

2. Assessment of current medication management
3. Clinical review
4. Decision to prescribe a medicine
5. Therapeutic drug monitoring
6. Participation in multidisciplinary ward rounds and meetings
7. Provision of medicines information to health professionals.
8. ADR management
9. Information for ongoing care
10. Provision of medicines information to patients.

□ Training And Education:

- The training and education of pharmacists providing clinical services must ^{و شاملة} encompass orientation, clinical competency assessment and performance appraisal supported by a structured and documented program.

- A policy and procedure manual should

contain the SHPA standards of practice for clinical pharmacy, describe the duties and responsibilities of pharmacists at the site and be regularly updated to reflect changes in clinical practice within and outside the workplace.

- An experienced clinical pharmacist or clinical education pharmacist should have ^{وقت}dedicated time to provide clinical pharmacist education.

Staffing Structure And levels:

- The staffing structure required to deliver clinical pharmacy services will be determined by the size and type of institution, patient casemix, and local resources.

- Adequate technicians and support staff must be available to perform non-clinical functions, such as medicine acquisition and distribution, manufacturing and data entry.

□ Primary Goals:

The primary goals of a clinical pharmacy quality assurance program should be to:

- Ensure the ^{توفير} provision of an appropriate clinical service to patients (and others involved in their care);
- Monitor and evaluate the clinical pharmacy services and standards of practice;
- identify and minimise risks associated with practices;
- Ensure patient medicine needs are addressed.
- Identify areas for improvement, including staff development programs,
- Provide a mechanism through which action is taken to make and maintain these improvements and:
- Motivate clinical pharmacists by involving them in the ^{التقييم} assessment and evaluation of these services.

#The components of developing a quality program include:

- i- Establishment of a quality program.
 - The aims and practices of clinical pharmacists should be in accordance with the overall pharmacy department and the large framework of the institution.

Where existing institutional procedures and requirements are inadequate, establishment of clinical pharmacy quality practices may provide impetus or even serve as a model for other areas.

- ii- Development and documentation of clear objectives:

- iii- Development of clear and effective strategies and supporting plans to achieve objectives.

The strategies should be explained, detailed and understood.

iv: Encouragement of effective employee participation.

- Participation by appropriate staff (and stakeholders) in the development and implementation of quality plans is likely to lead to the plan being better received and adopted by the participants.

Methods:

→ Standards and criteria established should reflect the range of activities for clinical pharmacists.

• Suggested performance indicators for clinical pharmacy services:

Clinical activity	Performance indicator
Accurate medication History	Percentage of patients interviewed by a pharmacist by the end of the following working day after admission

Assessment of current medication management	Number of assessments of current medication managements per total patient bed days.
Clinical review	Number of clinical reviews per number of total pt bed days
Provision of medicines information to patients	Percentage of patients receiving discharge medicines who also receive medicines information

Documentation:

This section relates to the documentation of patient-specific clinical pharmacist activities.

- Documentation of the various aspects of clinical services should only be considered in situations where the information is useful and the time required in documentation does not detract from

الوقت.

the provision of the clinical pharmacy service.

-The method of documentation should be determined by the pharmacist recording the information and influenced by those accessing the information.

Access: دست یافتن

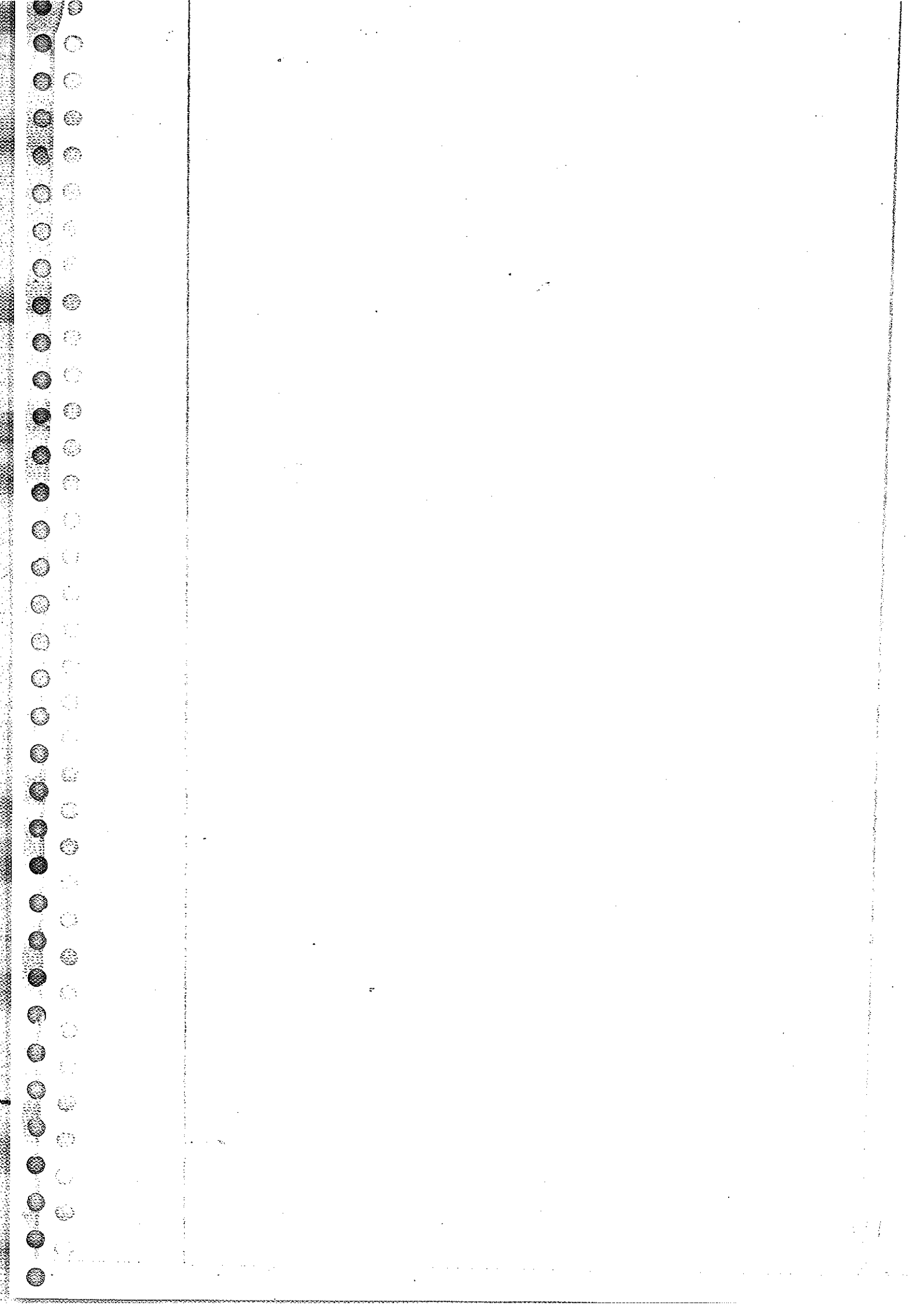
-The time taken for both recording and accessing information documented should be reduced through developments in technology.

Conclusion:

-QA Programme ^{نظارت کردن} ensures that quality of Health care is achieved and maintained in the given clinical setting.

-It also provides professional satisfaction to the pharmacists.

-Quality Assurance should be an integral part of clinical pharmacy services.



Patient Case History

- Pharmaceutical care:

"the responsible provision of drug therapy to achieve definite outcomes that are intended to improve a patient's quality of life".

- Patient case history is a part of pharmaceutical care.

Organizing the patient care:

- Those who provide pharmaceutical care should develop standardized forms to record patient information.

- Advantages of standardized forms:

- Quick ^{بارباری} retrieval of information
- Minimizes the ^{غیر عمدی} inadvertent ^{مذنی یا ناگزاشتی} omission of data
- Enhances the ability of other practitioner to ... records

→ For ^{سہولت} convenience, the Pt record can be divided into sections such as:

- The patient case history

- ▢ Medical history
- ▢ Drug history
- ▢ Social history

- Assessment

- Plan

1. Medical History:

- The medical history is essential to the provision of pharmaceutical care.

- The purpose of the medical history is identify significant past medical conditions or procedures; identify, characterize and assess current acute and chronic medical conditions and symptoms and gather all relevant health information that could drug selection or dosing.

Eg: function of major organs such as the GI tract and kidney that are involved in the absorption and elimination of drugs, height and weight, including recive changes in either age and.

gender, pregnancy and lactation status and special diets.

2. Drug History:

> After the initial visit patients often present themselves to community pharmacists in one of the three ways:

- I. With a self diagnosed condition for which non-prescription drug therapy is sought.
- II. With a newly diagnosed condition for which a drug has been prescribed.
- III. With chronic condition that requires refill of a previously prescribed drug or the preparation of a new drug.

- The goals of the therapeutic history are to obtain and assess the following information:

- The specific prescription and non-prescription drugs the patient is taking (the latter includes over the counter drugs medications, vitamins and dietary or nutritional ^{the} supplements, alcohol, cigarettes etc).

- The intended purpose or indications for each of these medication; how (route, ingestion in relation to meals).

- How much, how long, how often these medications are used whether the patient believe any of these agents are providing therapeutic benefits, whether the patient is experiencing or has experienced any adverse effects that could be caused by each of these agents (idiosyncratic reactions, toxic effects adverse effects) and allergic reactions and any history of hypersensitivity or other severe reactions to drugs.

- This information should be as specific as possible including a description of the reaction, the treatment and the date of its occurrence.

3. Social History:

- The social history is used to determine the patient's ^{life} occupation and life style; important family relationships or other support systems.

any particular circumstances (e.g. disability) or stresses in her life that could influence the pharmaceutical care plan that is developed to achieve the agreed-on therapeutic outcome, and attitudes: values and feelings about health, illness and treatments.

- A patient's occupation, lifestyle, insurance status, ability to pay, and attitudes often can determine the success or failure of drug therapy.

B. Assessment:

- An examiner's evaluation of the disease or condition based on the patient's subjective report of the symptoms and course of illness or condition and the examiner's objective findings, including data obtained through laboratory tests, physical examination, medical history etc.

C. Plan:

- A detailed description of recommended or intended further workup (laboratory radiology, consultation), treatment (e.g. continued observation; physiotherapy, diet, medications, surgery),

patient education (self care, goals of therapy, medication use and monitoring), monitoring, and follow-up relative to the above assessment.

- After the problem list is generated, subjective and objective data are reviewed, and the severity and acuity of the problems are assessed and prioritized, the next step in the problem-oriented (i.e. SOAP) approach is to create a plan, which at the minimum should consist of a diagnostic plan and a MAP that includes patient education.

VISVESWARAPURA INSTITUTE OF PHARMACEUTICAL
SCIENCES



DEPARTMENT OF PHARMACY PRACTICE

SEMINAR TOPIC : **Medical Abbreviations**

SUBJECT : Clinical Pharmacy

SUBMITTED TO :

Meera N.K.

SUBMITTED BY : Reza Rahimi

1TH YEAR PHARMA D(PB)

ABG	arterial blood gas
ACCU	acute coronary care unit
ADDU	alcohol and drug dependence unit
AED	automatic external defibrillator
AFB	acidfast bacillus, aflatoxin B; American foulbrood, aorto femoral bypass
AG	analytical grade (Organic chemistry); antiglobulin; antigravity; atrial gallop; axiogingival
A/G ratio	albumin-globulin ratio
AIDS	acquired immune deficiency syndrome
ANDA	Abbreviated New Drug Application
ANOVA	analysis of variance
AO	acid output;
AOM	Master of Obstetric Art
ART	Accredited Record Technician; acoustic reflex test
AST	angiotensin sensitivity test ; aspartate aminotransferase; Association of Medical Technologists; audiometry sweep test (Brit)
ATCC	American Type Culture Collection

ALT	alanine aminotransferase; alternate; altitude
BBT	basal body temperature
BCG	bacille bilié de Calmette Guérin (vaccine)
BMI	Body mass index
BNF	British National Formulary
BP	blood pressure;
BPPV	benign paroxysmal postural vertigo
BPH	Bachelor of Public Health; benign prostatic hypertrophy
BS	Bachelor of Science ; Bachelor of Surgery; bismuth subsalicylate; blood sugar; Blood syndrome Blue Shield; bowel sound; breath sound; British Standard; Bureau of Standards
CABGS CAD	coronary artery bypass graft surgery computer-assisted diagnosis; coronary artery disease
cAMP	cyclic adenosine monophosphate
CAPD	continuous ambulatory peritoneal dialysis
CBA	chronic bronchitis and asthma

CBG	corticosteroid-binding globulin (transcortin)
CC	calciumcyclamate; cerebral commissure; choriocarcinoma; chief complaint classical conditioning; clean catch (of urine); closing capacity; coefficient of correlation; commission certified (with reference to stains); compound cathartic computer calculated; corpora cardiaca; corpus collum; critical care; critical care; current complaints
CCA	cephalin cholesterol antigen; chick cell agglutination (unit); chimpanzee coryza agent
CCB	calcium channel blocker (s)
COPD	chronic obstructive pulmonary disease
CD 4	helper T lymphocytes
D&C	Dilation and curettage
CIBD	chronic inflammatory bowel disease
CK-MB	creatine kinase MB band
CMP	Competitive Medical Plans; Comprehensive Medical Plans; cytidine mono phosphate

CBC	A complete blood count (CBC) test
CST	cavernous sinus thrombosis; contract ion stress test (gynaccology); convulsive shock therapy
CT	calci tonin; carpa l tunne l; Ce llular Therapy; cer ebra l thrombosis; chole ra toxine; chymotrypsin; clot t ing; (coagula t ion) t ime; coated tablet ; compressed tablet ; computerized tomography; connect ive t issue ; cont inue t reatment ; continuous-flow t ube; cont racept ive techniques; controlled temperature ; corneal t ransplant ; coronary thrombosis; correct ive the ra pist (-apy) ; cyst ine t ellura te (medium) ; cytotechnologist
CXR	chest X-ray
DC	De nt al Corps; diagnost ic ce nt re ; digit copying; diphenyl cyanoarsine; donor's cells (Corpuscles); Decrease
D and C	dilatation and curettage; Drugs and Cosmetics
DDD	Defined Daily Doses Degenerative Disk Disease
D and I	debridement and irrigation; dry and intact
DIC	diffe rent ial inter ference cont rrast (microscope); 5-(3, 3, dime thyl-1- t ria ze no) imina zole-4- ca rboxamide (da carba zine); disseminated intravascular coagulopathy or

	coagulation
DKA	diabetic ketoacidosis
DM	dexromethorphan; diabetes mellitus, diastolic murmur; diphenylaminearsine chloride (Adamsite); Doctor Medicina (L) Doctor of Medicine
DIC	Disseminated intravascular coagulation
DNA	deoxyribonucleic; acid; did not attend
DOB	date of birth; doctor; order book
DOT	date of transcription; date of transfer
DRESS	<i>Drug Reaction (or Rash) with <u>Eosinophilia</u> and Systemic Symptoms</i>
DUB	dysfunctional uterine bleeding
ELISA	enzyme-linked immunoabsorbent assay
ECG	electrocardiogram (-ograph)
EEG	electroencephalogram; electroencephalograph
ED	effective dose; electrolysis; Emergency Department; Enter-Doudoroff (metabolic pathway); enzymatic deficiencies; epidural; erythema dose; ethynodiol; ethyl dichlorarsine; extra- low dispersion

ED50	median effective dose
E and E	Emergency and evaluation
EENT	eyes, ears, nose and throat
EF	edema factor; ejection fraction; Emergency Facilities; eosinophilic fasciitis; equivalent focus; extra fine; extrinsic factor
ESR	electron spin resonance; erythrocyte sedimentation rate
EMG	electromyograph (-gram); exomphalos, macroglossia and giantism (syndrome); eye movement gauge
ESRD	end stage renal disease
FNAC	fine_needle aspiratory cytology
FEV	forced expiratory volume
FEV1	forced expiratory volume in one second
FBG	fibrinogen
FDA	Food and Drug Administration; frontodextera anterior (L) right frontoanterior (position of fetus)
FDE	fixed drug eruption
FL	fluid

FMH	fat_mobilizing hormone
FRC	Federal Radiation Council; frozen red cells; functional residual capacity (of lungs)
GAD	generalized anxiety disorder
GC	ganglion cells; gas chromatography; Geriatric Care; glucocorticoid; gonococcal infection (gonorrhoea); gonococcus (-al); granulocyte cytotoxic; guanine_cytosine
GE	gastroenterology (-enteritis); gel electrophoresis; gentamicin
GERD	gastroesophageal reflux disease
GFR	glomerular filtration rate
GMP	General Medical Practitioner; guanosine monophosphate
GTCS	generalized tonic_clonic seizure
GYN	gynaecologist (-ology)
HAART	highly active antiretroviral therapy.
HB	bundle of His; Health Board; heart block; hepatitis B
HbA1c	glycosylated hemoglobin
HCG	human chorionic gonadotrophin

HEENT	head, ears, eyes, nose and throat
HELLP SYNDROME	• H- hemolysis (breakdown of red blood cells) • EL- elevated liver enzymes (liver function) • LP- low platelets counts (platelets help the blood clot)
HF	ha emorrhagic fact or; Hageman fact or (in blood plasma); hard filled (capsule s) ; hay feve r; he ar t failure ; high fa t (die t) ; high frequency; human fibroblasts
H/O	history of
FMAC	Find, Meet, Attract, <u>C</u> lose
HRQOL	Health-Related Quality of Life
HRT	heart rete; heparin raponse test ; hormone replacement therapy
IBD	inflammatory bowel disease
IBW	ideal body weight
ICD	immune complex disea se; I nst i tute for Cr ippled and Disa ble d; Int er nat ional Ce nte r for t he Disabled; I nte rnät ional Classification of Diseases; International College of Dentists; intrautrine contraceptive device

ICU	Intensive Care Unit
IDDM	insulin - dependent diabetes mellitus
IHD	ischaemic heart disease
ino	inosine
ins	insurance
IV	int e r v e n t r i c u l a r ; int e r v e r t e b r a l ; int r a v e nous (ly) ; intraventricular
KDA	Known Drug Allergies
LFT	La t e x f i x a t i o n t e s t ; l e f t f r o n t o t r a n s v e r s e (l e f t mentotra nsverse) (posit ion of fe tus); liver funct ion test ; low frequency transduction
LBD	Left border of dullness (of heart to percussion)
LBW	Low birth weight
LD50	median lethal dose
Lf	Limit of flocculation
LMWH	Low molecular weight heparin
LRTI	Lower respiratory tract illness or infection

MCV	mean corpuscular volume
MCHC	mean corpuscular haemoglobin concentration
MCH	Maternal and Child Health; mean corpuscular haemoglobin
MeSH	Medical Subject Headings (MEDLARS)
MICU	Mobile Intensive Care Unit
MMR	Mass Miniature Radiography; maternal mortality rate; measles - mumps - rubella; monomethylolrutin
MRSA	methicillin - resistant staphylococcus aureus
MR	may repeat; measles - rubella ; medial rectus (muscle); Medical Record; mentally retarded; metabolic rate; methyl red; mitral regurgitation
MRI	Medical Research Institute ; Member of the Royal Institution; Mental Research Institute; moderate renal insufficiency
MTC	medical test cabinet; Medical Training Center; medullary thyroid carcinoma; mitomycin C
NVBS	
NF	National Formulary; nephritic factor; neurofibromatosis; neutral fraction; noise factor; none found; nonfiltered;

	non white female; normal flow
NIDDM	noninsulin - dependent diabetes mellitus
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
N/M	Not Meaningful
NKDA	no known drug allergies
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NTT	nasotracheal tube
OBG	obstetrician-gynaecologist
OD	Doctor of Optometry; occupational disease; oculus dexter (L) right eye; open drop; optical density; originally derived; out-of-date; outside diameter; overdose
OENT	Ongoing Education and Training
OGTT	oral glucose tolerance test
o/o	Office Of
P/A	Per Annum
PSB	phosphorus-solubilizing bacteria; protected specimen brush
PEFR	peak expiratory flow rate
PPS	personal preference scale; post-partum sterilization

PCR	polymerase chain reaction
PEF	peak expiratory flow; Psychiatric Evaluation Form
PFT	pancreatic function test; phenylalanine mustard (melphalan)- fluorouracil- tamoxifen; pulmonary function test
aPTT	activated partial thromboplastin
Pt	patient
OCD	Obsessive-compulsive disorder
PPB	positive pressure breathing
PPF	pellagra -preventive factor (niacinamide); plasma protein fraction
PR	panama red (type of marijuana); parallax and refract ion; partial remission; partial response; patient relations; percentile rank; peripheral resistance; per rectum; phenol red; pityriasis rosea; pregnancy rate; pressure receptor; pressure; prevention; proctologist; progestone receptor; progressive resistance; prolactin; prosthetic- group removing (enzyme); prosthesis; pulse rate
PSA	prolonged sleep apnea; prostate specific antigen

P and T	Pharmacy and therapeutics
PTC	percutaneous transhepatic cholangiogram; phenylthiocarbamide (phenylthiourea); plasma thromboplastin component (factor IX, Christmas factor); posterior trabeculae cornea; prothrombin complex
puD	pulmonary disease
PV	paraventricular (nucleus); paromycin- vancomycin blood agar; per vaginam; plasma volume; polycythaemia vera; polyoma virus; portal vein; pressure volume; pulmonary vein
QALE	Quality-adjusted Life Expectancy
QBC	query by case
REM	rapid eye movement (in sleep); roentgen equivalent man
RCT	randomized clinical trial; Rorschach content test
RFT	right frontotransverse (position of fetus)
RF	radial fibres (of the cochlea); receptive field (of visual cortex) Reitland-Franklin (unit); relative flow rate; releasing factor; replicative form; resistance factor; respiratory failure; reticular formation; rheumatic fever; rheumatoid factor; riboflavine

RFID	Radio Frequency Identification Device
RIA	radio-immunoassay
RTI	respiratory tract infection
RS	Rauwolfia serpentina; reading of standard; recipient's serum; rectal sinus; reducing sugar; reinforcing stimulus; renal specialist; resorcinol-sulphur; respiratory syncytial (virus); response to stimulus (ratio); review of symptoms; Reye's syndrome; right sacrum; right side; Ringer solution
RUE	right upper extremity
RV	reinforcement value; residual volume; retroversion; right ventricle; rubella vaccine
SAE	short above elbow (cast)
SAD	sugar-acetone-diacetic acid (test)
SC	Schwan cell; sciatic nerve; science; scientific; scilicet (L) naemy; scrupulus (L) scruple; secretory component; self-care; service connected; sex chromation; sickle cell; sickle cell; silicone coated; skin conductance; slow component (neurology); squamous cancer; Stepped Care; stimulus

	conditioned; subcutaneous; sugar coated.
SOS	speed of sound; supplemental oxygen system
SLE	Saint Louis encephalitis; systemic lupus erythematosus
SNPS	Single Nucleotide Polymorphisms
SSNB	Schizophrenia Society of New Brunswick
ST	speech threshold
stat	statim (L) at once - immediately; statistics
SVC	superior vena cava
TSH	thyroid - stimulating (thyrotrophic) hormone
TIBC	total Iron - binding capacity
TB	thromboxane B; thymol blue ; total base ; tracheal bronchiolar (region); tracheobronchitis; trapezoid body; tubercle bacillus; tuberculosis
TBW	total body water; total body weight
TC	tetracycline ; thermal conductivity; thoracic cage ; thyrocalcitonin; tissue culture; to contain; total cholesterol; total colonoscopy; transcobalamin; transcutaneous; tuberculin contagious; type and cross match
TBG	testosterone - binding globulin; thyroxine - binding

	globulin
tid	ter in die (L) three times daily
TEN	total faecal nitrogen
TG	t e t r a glycine ; t hio glyco la t e b r o t h ; t hio gua n ine ; thromboglobulin; thyroglobulin; triglyceride
TPN	tha lamic project ion neurons; tota l pa rent eral nut rit ion; triphosphopyridine nucleotide
TRH	thyrotrophin - releasing hormone
TT4	Total T4 Total Thyroxine
UI	Urinary Incontinence Uniformity Index Uptake Index
U/L	upper and lower
URTI	upper respiratory tract infection
VC	colour vision; vaso constrictor (-construction); venereal case; Veterinary Corps; visual capacity; vital capacity
WBC	whloe blood cell count; white blood cell
WNM	well-nourished male
XDR	extremely drug resistant

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CLINICAL LABORATORY TESTS AND ITS INTERPRET HAEMATOLOGICAL TESTS

INTRODUCTION

Laboratory test abnormalities are values outside the normal range or reference range of population. True abnormalities are reproducible and they are associated with signs and symptoms of a disease state.

Laboratory test abnormalities are not themselves disease, but increases or decrease in the values are associated with various diseases.

Abnormal values may also be because of some drugs due to their interferences during the lab analysis and be lead to wrong interpretations. Diseases associated with renal and liver dysfunction, diabetes mellitus, gout, myocardial infarction, malnutrition, inflammatory diseases, anemia, and other disease conditions.

PHARMACIST ROLE IN MONITORING THE LABORATORY TEST RESULTS:

1. Firstly, to diagnose and to interpret the disease condition.
2. To assess the therapeutic and adverse effect of the drug. (e.g: monitoring the serum uric acid level after allopurinol is administered)
3. To measure the effectiveness of the drug or therapy given (e.g: assessment of serum creatinine value before use of a renally excreted drug)
4. To assess the need of additional or alternate drug therapy (e.g: assessment of WBC after administration of penicillin)
5. To determine the proper drug dose
6. Prevent the test misinterpretation resulting from drug interference (e.g: determination of false positive for urine glucose test after cephalosporin administration)

NORMAL LABORATORY TEST:

- Normal laboratory test results fall within a predetermined range of values and abnormal values fall outside that range.

- Normal limits are defined arbitrarily; hence sometimes the values outside the range may not necessarily indicate any disease condition.
- Some of the factors to be considered during the lab tests are sex, age, time since last meal etc
- Normal values may differ from institution to institutions, also vary in different places
- Normal values may also differ due to the different methods used to analyze
- Lab error: sometimes lab errors may occur due to various reasons and is should be prevented as much as possible or reduced. Lab errors must always be considered when test results do not correlate with expected results of the patient.

TYPES OF TEST

Depending on the way results are reported, laboratory tests are called as:

- QUANTITATIVE TEST: it is the AMOUNT of substance present in the sample test. (e.g.: concentration of glucose in the blood sample or concentration of potassium in the serum)
- QUALITATIVE TEST: it is the type of substance or tests with only positive or negative results (e.g.: in case of infections to detect the organism infected or pregnancy test in case of women whether the women is pregnant Is pregnant or not)

NORMAL OR REFERENCE RANGE:

The normal range of a lab test is usually determined by applying statistical methods to results from a representative sample obtained from the study of general population. the normal range represents the (95%) large percentage of the normal people fall. The mean average value plus or minus two standard deviation is usually takes as normal range (5% is considered).

FACTORS AFFECTING NORMAL RANGE ARE:

1. Sample or specimen to be analysed:

Whether its blood, serum, urine etc: the normal range for a substance in ne body fluid is quite different from the other. (e.g. when a diabetic patient is measured for the concentration of glucose in the serum its normal range is 70-120mg/dl where as the concentration of glucose in CSF is 50-75mg/dl)

2. Population under study:

Even if the assay and equipment used are the same, reference ranges may differ among laboratories. This difference occurs because some laboratories determine their own normal ranges from local population. However variabilities are not much significant. (e.g.

in one lab the sodium range in the serum may be 136-145mEq/L and in another lab it may be 134-143mEq/L)

3. Demographics:

In addition to population characteristics, the normal range of a given test may vary depending on patient's demographics like age, sex, height, weight and body surface area. E.g. with respect to gender a women's normal retaining clearance is typically less compared to men at any age. Some of the electrolytes like sodium, potassium, chloride, carbon dioxide, magnesium, calcium and phosphorus do not move significantly out of the normal range as one age. Calcium level may be increase in postmenopausal women. Enzymes such as creatine kinase decreases after the age of 60 -70 years in most of the groups.

4. Nutritional status:

Malnutrition is usually associated with hypoalbuminemia. This may lead to large concentration of unbound drugs in the plasma.

5. Food and time of the test:

It includes time of the day, last meal taken or last dose taken before test. Timing refers to which time of the day or the time of blood draw to administration of exogenous substance (food or drug) a fasting glucose concentration may appear abnormally high if patient eats just before blood sample is drawn.

6. Drugs:

Drugs also may interfere in the laboratory test results.

RATIONALE FOR ORDERING LABORATORY TESTS:

Laboratory tests are performed with the expectation that results will aid the practitioner or patient in the following:

1. Discovering occult disease.
2. Confirming suspected diagnosis after signs and symptoms appear.
3. Differentially diagnose possible diseases.
4. Determining the stage or activity level of the disease.
5. Detecting the reoccurrence of the disease.
6. Measuring the effectiveness of therapy and guiding its course.

UNITS USED IN REPORTING LABORATORY DATA:

As already mentioned one cause of normal range variation among laboratories in the use of different assay methods. Another cause is the reporting of results with different units. For e.g. one lab may report magnesium concentration in mg/dl and another lab may report in mEq/L. now s.i units has been standardized in most of the lab so that it can be standard.

SENSITIVITY, SPECIFICITY AND PREDECTIVE VALUE

The clinical usefulness or clinical performance of a test varies with its sensitivity, specificity and predictive value. These variables especially predictive value, depend on the prevalence of the disease in the population tested.

SENSITIVITY: the sensitivity of a test refers to its ability to show positive results in patients who actually have the disease.

SPECIFICITY: the specificity refers to the percentage of negative results among people who do not have the disease in question.

PREDECTIVE VALUE: the predictive value of a positive result is the percentage of positive results that are actual (true) positives.

GUIDELINES FOR INTERPRETATION OF THE RESULTS:

- Does the measured or isolated entity exist naturally or normally in the body? If so where?
- How might entity get into the body fluid or tissue being tested? What is its usual destiny?
- Is entity preferentially stored or concentrated in anybody compartment or organ?
- Does the entity have normal function in the body? If so what is it?
- Does the assayed entity reflect pathophysiology in question directly or indirectly?

MECHANISM OF ABNORMAL RESULTS

The specific mechanisms of truly abnormal results of quantitative tests are as diverse as the type of pathophysiology the mechanism reflects.

- Excessive or insufficient intake, production, release or secretion into the body fluid of the substance being measured.
- Excessive or insufficient outflow from the body or metabolism within the body of the substance being measured.
- Dilution or concentration of the substance being measured, secondary to an increase or decrease in the usual amount of fluid in the compartment from which specimen is taken.

TIPS FOR INTERPRETATION AND UTILISATION:

Clinicians should remember the following checklist when interpreting the results.

- Test results versus signs and symptoms
- Isolated results versus trends
- Baseline studies

HAEMATOLOGICAL TESTS

Blood has 3 formed elements RBC'S, WBC'S and PLATLETS. Some of the tests to determine the concentration of these elements include: Hemoglobin count, Hematocrit value (PCV), total WBC'S or total leucocytes count (TLC), mean cell volume (MCV), erythrocyte sedimentation rate(ESR) ETC

1. RBC (ERYTHROCYTES)

NORMAL VALUES: MEN 4.3 TO 5.9 MILLION/mm³ of blood
 Women 3.5 to 5.0 million/mm³ of blood

The RBC count is most useful as raw data for calculation of erythrocyte indices MCV and MCH.

(Decreased RBC is usually seen in anemia of any cause.)

Increased RBC is seen in erythrocytotic state polycythemia, dehydration etc

The main function of erythrocytes or RBC's is to carry oxygen from lungs to the tissues and transport carbon dioxide back to lungs. Anemia occurs when the hemoglobin, hemotocrit and RBC count are below normal range.

Normal sized RBCs are called as normocytes, small ones are called as microcytes and large ones are macrocytes.

- NORMOCYTIC/NORMOCHROMIC ANEMIA (NORMAL MCV, NORMAL MCHC)

- Anisocytosis: variability in the size of red blood cells.

- poikilocytosis: any variation in the normal biconcave disc shape.

- Such abnormalities are seen with iron deficiency or period of increased erythrocyte production and/or red cell damage.

○ NORMOGENERATIVE NORMOCYTIC ANEMIA:

- IMMUNOHEMOLYTIC ANEMIA
- G6pd deficiency
- Hereditary spherocytosis
- Microangiopathic hemolytic anemia
- Paroxysmal hemoglobinuria

○ HYPOGENERATIVE NORMOCYTIC ANEMIA:

- anemia in chronic diseases
- anemia of chronic renal failure
- aplastic anemia

drugs and other substances that causes aplastic anemia includes: amphotericin, sulphamide, cabamazepines, chloramphenicol, primidone, methimazole, benzene, aspirin, trimethadone, streptomycin, gold, mercury etc

➤ MICROCYTIC/HYPOCHROMIC ANEMIA (decreased MCV andMCHC)

- iron deficiency
- thalassemia
- anemia of chronic disease
- lead poisoning
- sideroblastic anemia

➤ MACROCYTIC/NORMOCHROMIC ANEMIA (increased MCV andMCHC)

- folate deficiency
- vit b12 deficiency
- myelodysplastic syndromes
- hypothyroidism

(Ht or HCT)

2. HEMOTOCRIT VALUE (PACKED CELL VOLUME)

Normal values: men 39% to 49%

Women 33% to 43%

It is the ratio of volume obtained by red cells to total blood volume. it is measured by centrifugation. PCV is usually 3 times the Hb value and is given as percent.

Low PCV indicates anemia or hydration. High PCV value indicates polycythemia or dehydration.

This test is used to evaluate:

$$\text{Blood volume} = \text{plasma volume} \times \frac{100}{(100 - \text{Hct})}$$

- anemia
- polycythemia
- response to treatment for anemia
- dehydration
- blood transfusion decision
- effectiveness of blood transfusion

3. THE HEMOGLOBIN TEST:

Hemoglobin: the part of blood that contains iron

Normal values: men - 14-18g/dl

Women - 12-16g/dl

It measures the grams of Hb contained in 1 dl of whole blood and also it estimates the oxygen carrying capacity of the RBC's.

Low value indicates anemia. Below normal Hb levels may lead to anemia that can result of:

- iron deficiencies or other deficiencies like folate etc
- hereditary: sickle cell anemia
- cirrhosis of liver
- excessive bleeding
- kidney disease
- bone marrow failure
- excessive destruction of RBC's
- cancer

Males: 0-15 mm/hr

Females: 0-20 mm/hr

4. ERYTHROCYTE SEDIMENTATION RATE (ESR)

It is the measurement of settling of RBC in the sample of anti coagulated blood over a period of time.

Commonly used method is westergren method

ESR increases in acute / chronic infections, inflammatory bowel disease, rheumatoid arthritis etc

ESR decreases in polycythemia

ESR is an easy, non expensive test and used to diagnose many diseases like cancer, acute and chronic inflammation, infections etc

5. THE RETICULOCYTE COUNT: → = immature RBCs → measures the percentage of reticulocytes in the blood

Measure of immature RBC's normal RBC's circulate in the blood for about 1-2 days in this form. It is the index of bone marrow production of matured RBC's

- Number helps to determine causes of anemia.

Normal: 1.0-2.0% / [Women and children usually have higher -]

- A normal count means that the production is adequate, a decreased count means it is not. This information

helps determine whether a lack of red cells in an anemic person is caused by a bone marrow problem, by excessive bleeding, or by red cell destruction.

bone marrow is not producing a normal number of red blood cells. Decreased reticulocyte count is seen in drug induced aplastic anemia. when the bone marrow makes more RBCs in response to blood loss or treatment of anemia

may be caused by a lack of Vit B₁₂, folic acid or iron in diet etc.

White blood cells (leucocytes)

1. WBC COUNT $5-10 \times 10^9/L$

Increased WBC is known as leukocytosis usually signals infection (usually bacterial)

Decreased WBC is known as leucopenia it indicates bone marrow depression

Sometimes some drugs also reduces the WBC COUNT such as anti cancer or anti aids drugs

2. WBC DIFFERENTIAL COUNT

It has two types of cells: granulocytes including neutrophils, basophils and eosinophils

Agranulocytes includes lymphocytes and monocytes

a. NEUTROPHILS: these are body's first line of defence

These increase in case of certain diseases like virus infection (chicken pox), inflammatory diseases (gout), metabolic disorders (diabetes) use of certain drugs like epinephrine etc

Decreased condition is known as neutropenia. It occurs in case of infection and also due to some drugs

b. BASOPHILS: an increased no is seen lung cancer, viral infection and iron deficiency

c. EOSINOPHILS: an increased no is seen in acute allergic reactions like asthma, hay fever and amebiasis.

d. LYMPHOCYTES: it plays a major role in immunological activity.

They are classified as B-LYMPHOCYTE and T-LYMPHOCYTES

LYMPHOCYTOSIS or increased no is seen in case of viral infection.

Lymphopenia or decreased no is seen in case of AIDS, uremia, acute inflammatory disorders and TB

e. MONOCYTES:

Monocytosis or increase in no is seen in case of TB, endocarditis, ulcer etc

3. PLATELETS OR THROMBOCYTES: $130-400 \times 10^9/L$

It is the smallest formed element in the blood and involved in blood clotting.

- Small amounts of enzymes circulates in the blood at all times and are released into the blood in larger quantities when tissue damage occurs.
- Creatine kinase (CK): CK levels are used primarily to aid in the diagnosis of acute myocardial, skeletal muscle damage.

→
Thrombocytopenia is seen in case of infections, pregnancy and by certain drugs like sulphonamides

An increase in platelet is seen in case of inflammatory diseases, malignancy etc

COMMON SERUM ENZYMES TESTS

> ALKALINE PHOSPHATASE (ALP)

It is done for the liver or bone disorder. High ALP means bone or liver has been damaged. Increased serum alkaline phosphatase is seen in osteoblastic activity, liver dysfunction, in sepsis, inflammatory bowel disease etc

Decreased serum alkaline phosphatase is not much significant. It is seen in hypothyroidism, scurvy etc

> Lactate dehydrogenase (LDH)

It has been used to diagnose and monitor heart attack. It is present in all tissues and they released when the cell are damaged or destroyed. Hence it can be used as a marker for cell injury.

> ALANINE AMINOTRANSFERASE (ALT /SGPT)

ALT is found mostly in liver and smaller amount in kidneys, heart and muscles. alt are present in low concentration in blood but in case of liver damage its concentration increases like hepatitis, necrosis of liver, jaundice.

> ASPARTATE AMINOTRANSFERASE (AST /SGOT)

AST is an enzyme present mostly in heart and liver, to a lesser extent in other tissues.

It is also used to detect liver damage along with AST, ALP.

Summary:

Without the ability to interpret laboratory test results accurately, knowledge of pathophysiology and therapeutics is insufficient to provide high quality clinical consultation.

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Clinical pharmacy and therapeutics by roger and walker

Clinical pharmacy and therapeutics. Herfindal, Williams & Wilkins

The isoenzymes of CK-CK-MM, found in skeletal muscle, CK-BB found in brain tissue, CK-MB found in heart muscle - can be used to differentiate the source of damage.

□ Bone marrow is a highly structured and metabolically active organ of both the hematopoietic and reticuloendothelial systems.

-It normally produces 2.5 billion RBCs, 1 billion granulocytes, and 2.5 billion platelets/kg of body weight daily.

□ Complete Blood Count (CBC):

-It supplies useful information regarding the concentration of the different cellular and noncellular elements of blood and applies to multiple disorders.

-These results traditionally include:

- 1- Leukocyte (WBC) count
- 2- RBC count
- 3- Hemoglobin (Hgb)
- 4- Hematocrit (Hct)
- 5- RBC indices
 - Mean corpuscular volume (MCV)
 - Mean corpuscular Hgb (MCH)
 - Mean corpuscular Hgb concentration (MCHC)
 - RBC distribution width (RDW)

Red blood cell indices

- Because the following laboratory test specifically assess red blood cell characteristics, they are called RBC indices.

- These indices are useful in the evaluation of anemias, polycythemia, and nutritional disorders.

i. Mean corpuscular Volume: (MCV)

Normal range: 80-96 fL/cell

→ MCV is an estimate of the average volume of RBCs and is the most clinically useful of the RBC indices.

- It can be calculated by dividing the hematocrit by the RBC count.

- Abnormally large cells have an increased MCV and are called macrocytic. Vit B₁₂ and/or folate deficiency cause the formation of macrocytic erythrocytes.

- The MCV may also be falsely increased in hyperglycemia.

- Abnormally small cells (with a decreased MCV) are called microcytic. The most common cause of microcytic erythrocytes (microcytosis) is iron deficiency.

ii - Mean Corpuscular Hemoglobin: (MCH)

Normal range: 27.5 - 33.2 pg/cell

MCH is the amount of hemoglobin per RBC.

It is calculated by dividing the Hgb by the RBC count.

- MCH can be falsely increased in patients with hyperlipidemia due to turbidity falsely elevating the Hgb, but it can be truly increased in the presence of folate deficiency due to the presence of macrocytic erythrocytes.

- A low MCH corresponds with hypochromic (pale) RBCs, as seen in iron deficiency anemia.

iii - Mean corpuscular Hemoglobin concentration:

Normal range: 33.4 - 35.5 g/dl or 334 - 355 g/L

MCHC is the hemoglobin divided by the hematocrit.

- Iron deficiency is the only anemia in which the MCHC is routinely low, although it can also be decreased in other disorders of Hgb synthesis.

- Like MCH, it can be falsely elevated in hyperlipidemia.

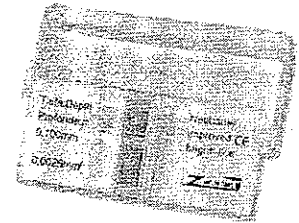
iv-Red Blood cell Distribution Width:

Normal range: 11.5% to 14.5%

The red blood cell distribution width (RDW) is an indication of the variation in red cell size, termed anisocytosis.

-This value is used primarily with other tests to differentiate iron deficiency anemia from thalassemias.

Cell Counting with Neubauer Chamber Basic Hemocytometer Usage



Introduction

Despite the fact of the recent technical development of scientific laboratories, the Neubauer chamber remains the most common method used for cell counting around the world.

This article has been written in order to help newbies and experimented researchers to perform a proper cell counting using a Neubauer chamber or Hemocytometer.

The principles described in this article apply to any cell counting chamber, although the dimensions and volumes of each chamber may differ.

First, the parts and basic principle of the Neubauer chamber are described

Second, the article describes how to perform a cell count step by step, in order to achieve reliable and reproducible results. The article describes best practices and recommendations when performing a cell count.

Materials

The necessary elements to perform a cell count with Neubauer chamber are as follows:

- cellular dilution to measure
- hemocytometer, or Neubauer chamber
- optical microscope
- cover glass
- pipette / micropipette with disposable tips
- Dilution buffer / PBS (if needed)

THE NEUBAUER CHAMBER, OR HEMOCYTOMETER

The Neubauer chamber is a thick crystal slide with the size of a glass slide. (30 x 70 mm and 4 mm thickness)

In a simple counting chamber, the central area is where cell counts are performed. The chamber has three parts.

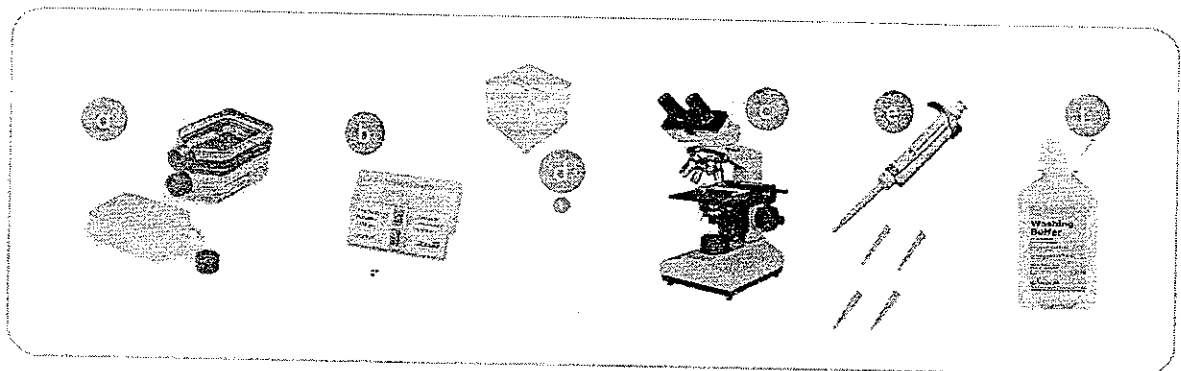


Fig 1. Necessary equipment to perform a cell count with hemocytometer.

The central part, where the counting grid has been set on the glass.

Double chambers are most common than simple chamber. In this case, the chamber has two counting areas than can be loaded independently.

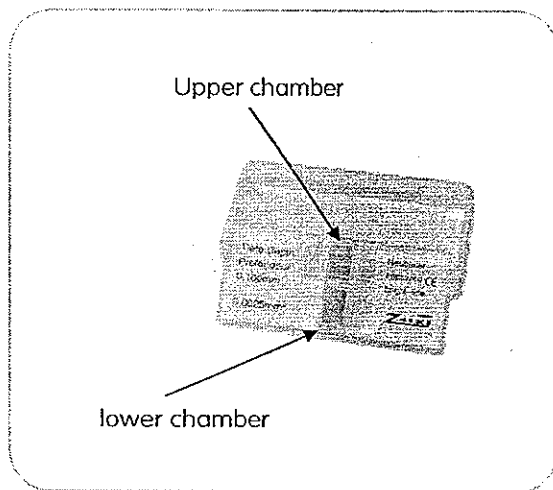


Fig 2. Neubauer comercial chamber

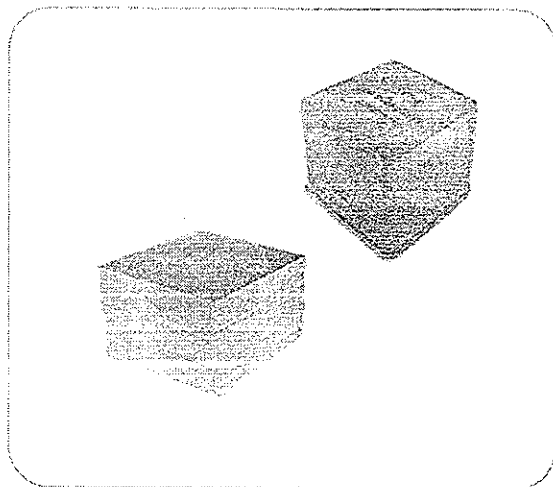


Fig 3. Pile of glass covers, and box.

Neubauer chamber's counting grid is 3 mm x 3 mm in size. The grid has 9 square subdivisions of width 1mm. (See Fig. 4-1)

In case of blood cell counting, the squares placed at the corners are used for white cell counting. Since their concentration is lower than red blood cells a larger area is required to perform the cell count.

The central square is used for platelets and red cells. This square is split in 25 squares of width 0,2 mm (200µm). See Fig. 4-2. Each one of the 25 central squares is subdivided in 16 small squares. Fig 4-3.

Therefore, the central square is made of 400 small squares.

GLASS COVER.

The glass cover is a squared glass of width 22 mm. The glass cover is placed on the top of the Neubauer chamber, covering the central area. The glass cover leaves room for the cell concentration between the bottom of the chamber and the cover itself. The chamber is designed so that the distance between the bottom of the chamber and the cover is 0,1 mm.

It is not uncommon that the glass cover remains slightly lifted when we introduce more liquid than necessary in the chamber. To avoid this, some counting chambers have two special clamps to avoid the cover glass to avoid edge-lift.

If the glass cover is lifted, the distance between the chamber and the cover will be higher than 0,1 mm, and the cell counts will not be accurate.

PIPETTE

The pipette allows for the introduction of a precise amount of liquid into the Neubauer chamber. Historically, they have been manufactured in glass. Nowadays, glass pipettes have been replaced by micropipettes, than can be calibrated with a maximum capacity of 20, 200 and 2000 µl.

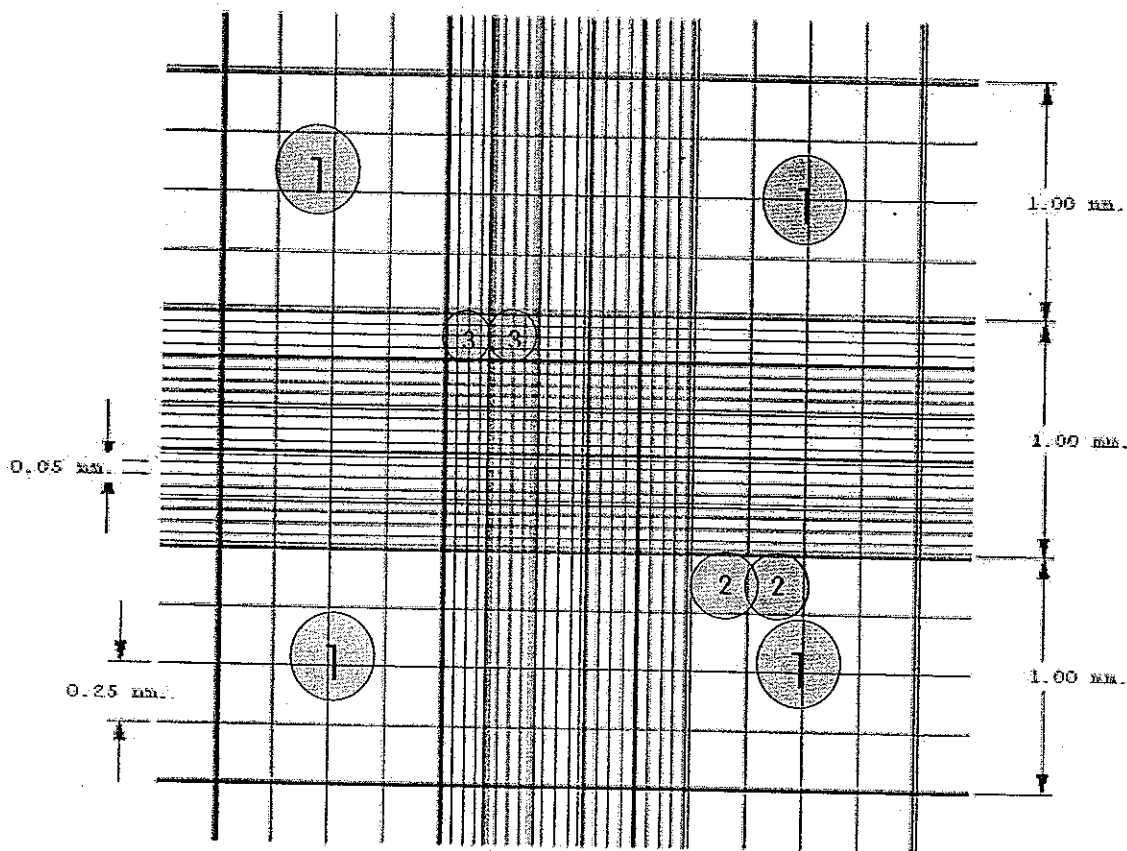


Fig 4. Neubauer-improved chamber counting grid detail.

Cell count, step by step

STEP 1. Sample preparation.

Depending on the type of sample, a preparation of a dilution with a suitable concentration should be prepared for cell counting.

Typically, the concentration range for a cell count with Neubauer chamber is between 250.000 cells / ml and 2,5 million cells / ml.

It is recommended for the dilution concentration to be around 10^6 cells / ml (1 millón cells / ml) applying the required dilutions.

With concentrations below 250.000 cells per ml, ($2,5 \times 10^5$ cells / ml) the amount of cells counted will not be enough to obtain a fair estimation of the original concentration.¹

Above 2,5 million cells / ml ($2,5 \times 10^6$), the probability of counting errors increases as well as the time and effort required to achieve a reliable cell count.

Above 2,5 million, it is preferable diluting the sample to obtain a final concentration closer to the optimum 1 million per ml. It is important to write down the dilution performed to the original sample.

¹ See:

<http://www.celeromics.com/conteo-celular-concentraciones-bajas.htm>, for an statistical explanation

STEP 2. Introducing the sample into the Neubauer chamber

Take 10 μ l of dilution prepare in STEP 1 with the micropipette.

- 1) Put the glass cover on the Neubauer chamber central area. Use a flat surface to place the chamber, like a table or a workbench.
- 2) Put a disposable tip at the end of the micropipette.
- 3) Adjust the micropipette to suck 10 μ l. You can adjust it by turning the upper plunger roulette to select the required pipetting volume.
- 4) Introduce the micropipette tip on the dilution previously prepared (STEP 1)
- 5) Push the pipette plunger slowly until you feel it has arrived to the end of its travel.
- 6) Remove the pipette tip from the dilution, and bring it to the Neubauer chamber. When the pipette is loaded, it must always be held in vertical position.
- 7) Place pipette tip close to the glass cover edge, right at the centre of the Neubauer chamber.
- 8) Release the plunger slowly watching how the liquid enters the chamber uniformly, being absorbed by capillarity. See Fig. 5
- 9) In case of the appearance of bubbles, or that the glass cover has moved, repeat the operation.

Congratulations!. The Neubauer chamber has been loaded, and it is ready to perform the cell count.

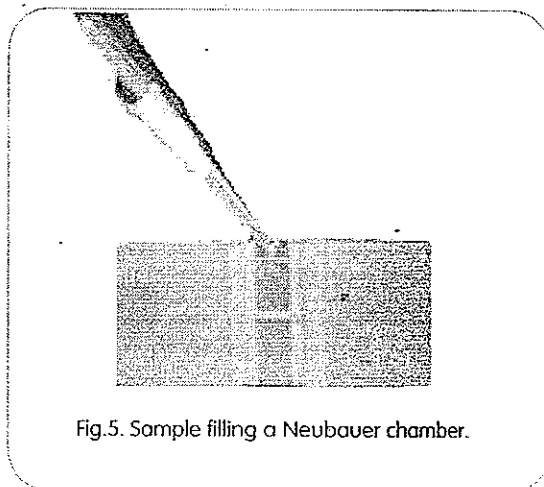


Fig.5. Sample filling a Neubauer chamber.

STEP 3. Microscope set up and focus.

1. Place the Neubauer chamber on the microscope stage. If the microscope has a fixing clamp, fix the Neubauer chamber.
2. Turn on the microscope light.
3. Focus the microscope until you can see a sharp image of the cells looking through the eyepiece and adjusting the stage.
4. Look for the first counting grid square where the cell count will start. In this example, 5 big squares from a Neubauer-Improved chamber will be counted. See Fig. 6

See <http://www.celeromics.com/easy-formula-for-manual-cell-counting.htm>, for the formulas to be applied for the most common counting chamber (Thoma, Fuchs-Rosenthal, Nageotte, etc)

5. Start counting the cells in the first square.

Different laboratories have different counting protocols, but there is a popular unwritten rule that states:

"Cells touching the upper and left limits should be counted, unlike cells touching the lower and right limits which should not be taken into account"

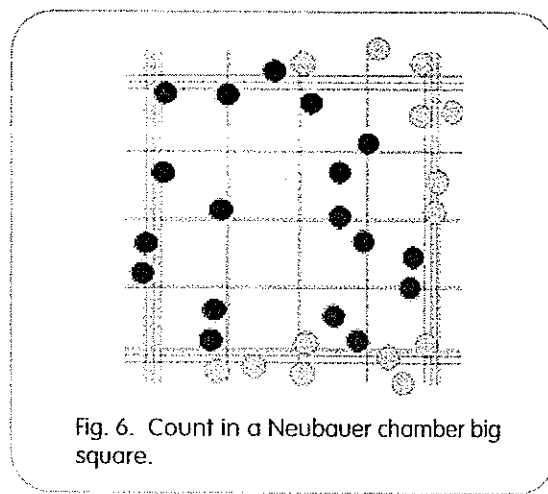


Fig. 6. Count in a Neubauer chamber big square.

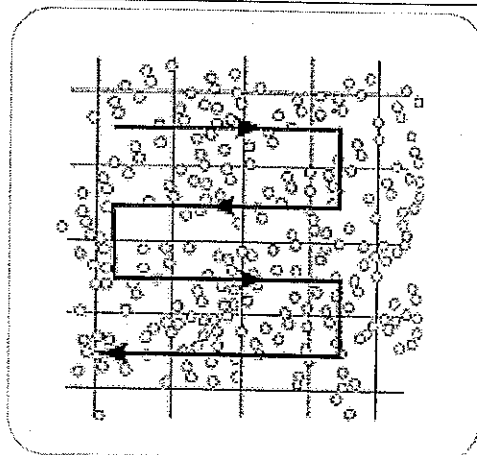


Fig. 7. High cell concentration cell count.

In case of high cell concentration, it will become very easy to get lost when counting cells. In this case, a counting technique in zig-zag is used.

6. Write down the amount of cells counted in the first square.
7. Repeat the process for the remaining squares, writing down the counting results from all of them. The higher the number of cells counted, the higher the accuracy of the measurement.

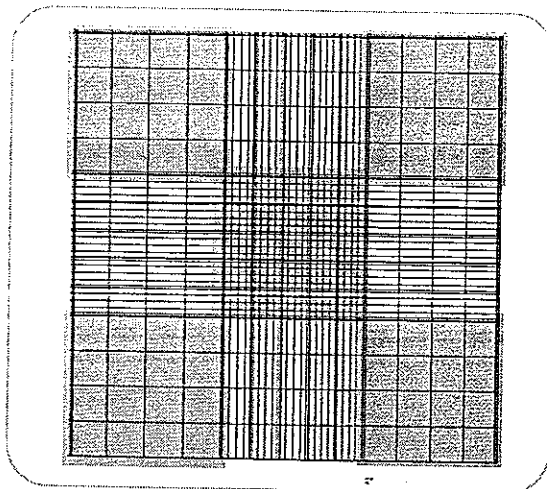


Fig. 6. Example of cell count in one of the 9 big squares of a Neubauer chamber.

STEP 4: Concentration calculation

We apply the formula for the calculation of the concentration

$$\text{Concentration (cel / ml)} = \frac{\text{Number of cells}}{\text{Volume (in ml)}}$$

The number of cells will be the sum of all the counted cells in all squares counted.

The volume will be the total volume of all the squares counted.

Since the volume of 1 big square is:

$$\begin{aligned} 0,1 \text{ cm} \times 0,1 \text{ cm} &= 0,01 \text{ cm}^2 \text{ of area counted.} \\ \text{Since the depth of the chamber is } 0,1 \text{ mm} \\ 0,1 \text{ mm} &= 0,01 \text{ cm} \\ 0,01 \text{ cm}^2 \times 0,01 \text{ cm} &= 0,0001 \text{ cm}^3 = 0,0001 \text{ ml} = 0,1 \mu\text{l} \end{aligned}$$

So, for the Neubauer chamber, the formula used when counting in the big squares.

$$\text{Concentration} = \frac{\text{Number of cells} \times 10.000}{\text{Number of squares}}$$

In case a dilution was applied, the concentration obtained should be converted to the original concentration before the dilution.

In this case, the concentration should be divided by the dilution applied.

The formula will be:

$$\text{Concentration} = \frac{\text{Number of Cells} \times 10.000}{\text{Number of square} \times \text{dilution}}$$

Example:

For a 1 : 10 dilution.

Dilution = 0,1

For a 1 : 100.

Dilution = 0,01

Error

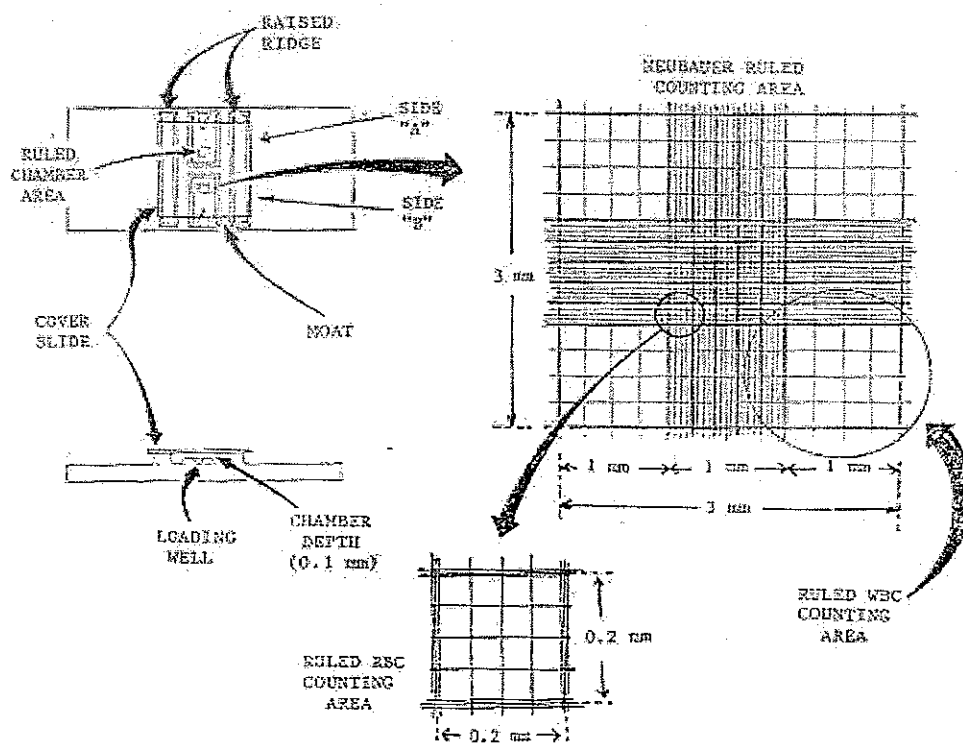
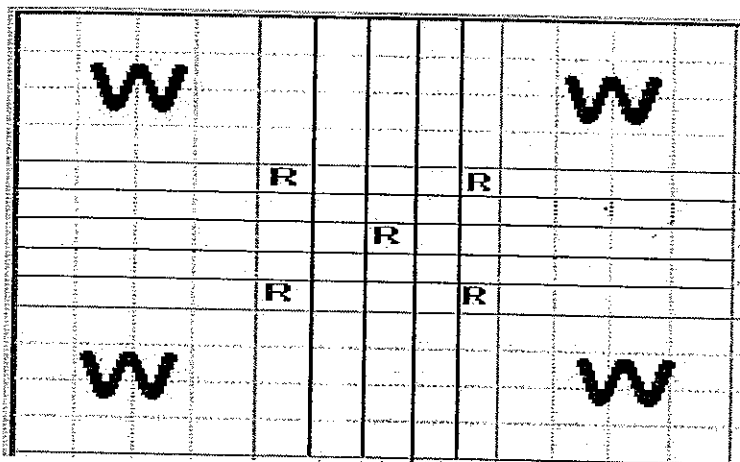
Errors in the range of 20%-30% are common in this method due to pipetting errors, statistical errors, chamber volume errors, and errors from volume of sample introduced into the chamber.

Even though, the Neubauer chamber remains the most widely used cell counting method in the world.

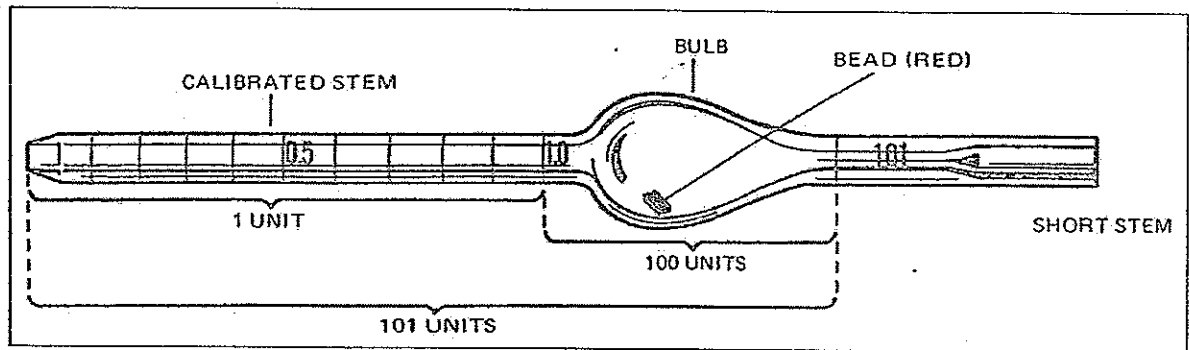
To obtain a detailed analysis of the error introduced in a cell count, go to:

<http://www.celeromics.com/cell-count-error.htm>

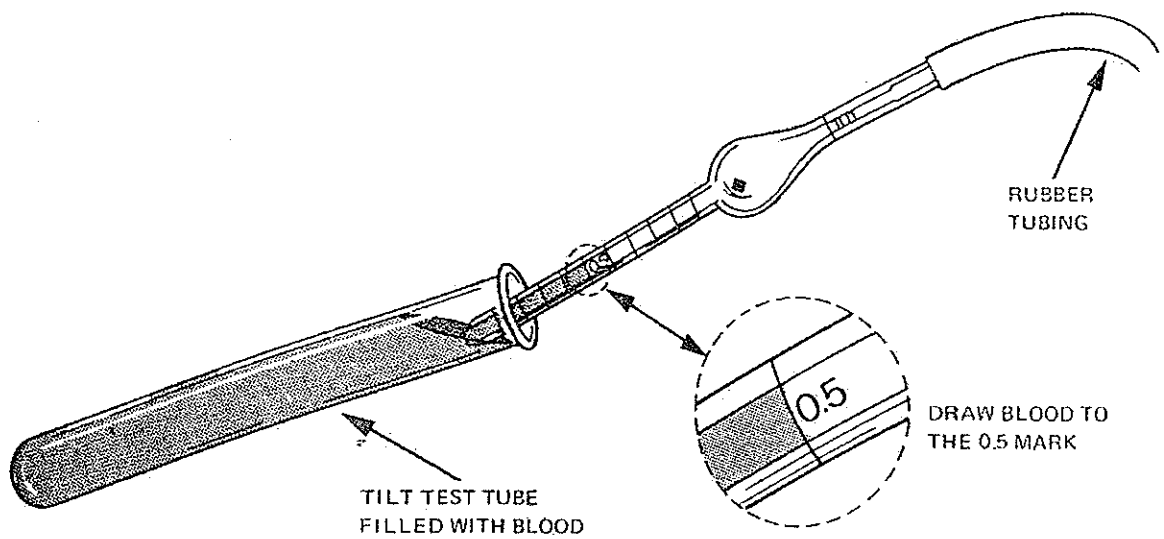
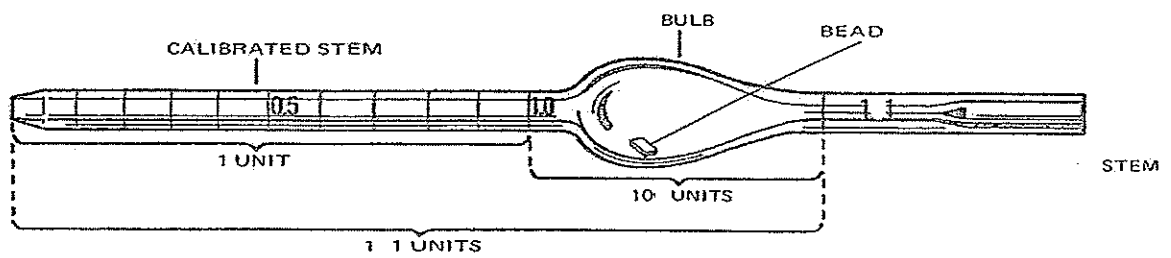




RBC PIPETTE



WBC PIPETTE



Estimation of Hemoglobin Concentration

Reem Alsolami

Hb concentration is estimated by:

Colorimetric techniques or spectrophotometer, based on light intensity principle

Methods

1. Oxyhemoglobin method
2. Hemoglobincyanide method (HICN)

Reference method

Internationally recommended

Principle

Blood (from EDTA) is diluted in a solution called (Drabkin's solution) :

It contains potassium cyanide + potassium ferricyanide.

As a result:

RBCs are hemolyzed and the hemoglobin is released.

And the released hemoglobin is oxidized as the following reaction is occurred:

Cont. Principle

- 1. Hemoglobin (Hgb) + ferricyanide $\rightarrow$ methemoglobin
- 2. methemoglobin + cyanide $\rightarrow$ cyanmethemoglobin (or also called stable) (HiCN).
- Absorbance of the HiCN solution is read in a spectrophotometer at (540 nm).
- The absorbance of the HiCN solution is compared with of a reference HiCN standard solution.
- Hemoglobin values are obtained from tables prepared from calibration graph or by using hemoglobin meter.

Objective

- Hemoglobin is measured to detect anemia and its severity and to monitor anemic patient under the treatment.
- It is also used to check the Hb level of potential donor's blood, prior of donation.

Methodology

The blood is diluted (EDTA) in Drabkin's solution by 1:201

→ 20 μ L of blood in 4000 μ L (equal to 4 mL).

The tube is then covered and inverted several times.

The tube is left to stand at R.T for 5-10 minutes to insure complete conversion.

The HiCN solution is poured into cuvette .

The spectrophotometer is set to 100% transmittance at 540nm, using Drabkin's solution as blank.

The Hgb value is then determined by using, Beers law and STD curve.

HICN is used as standard

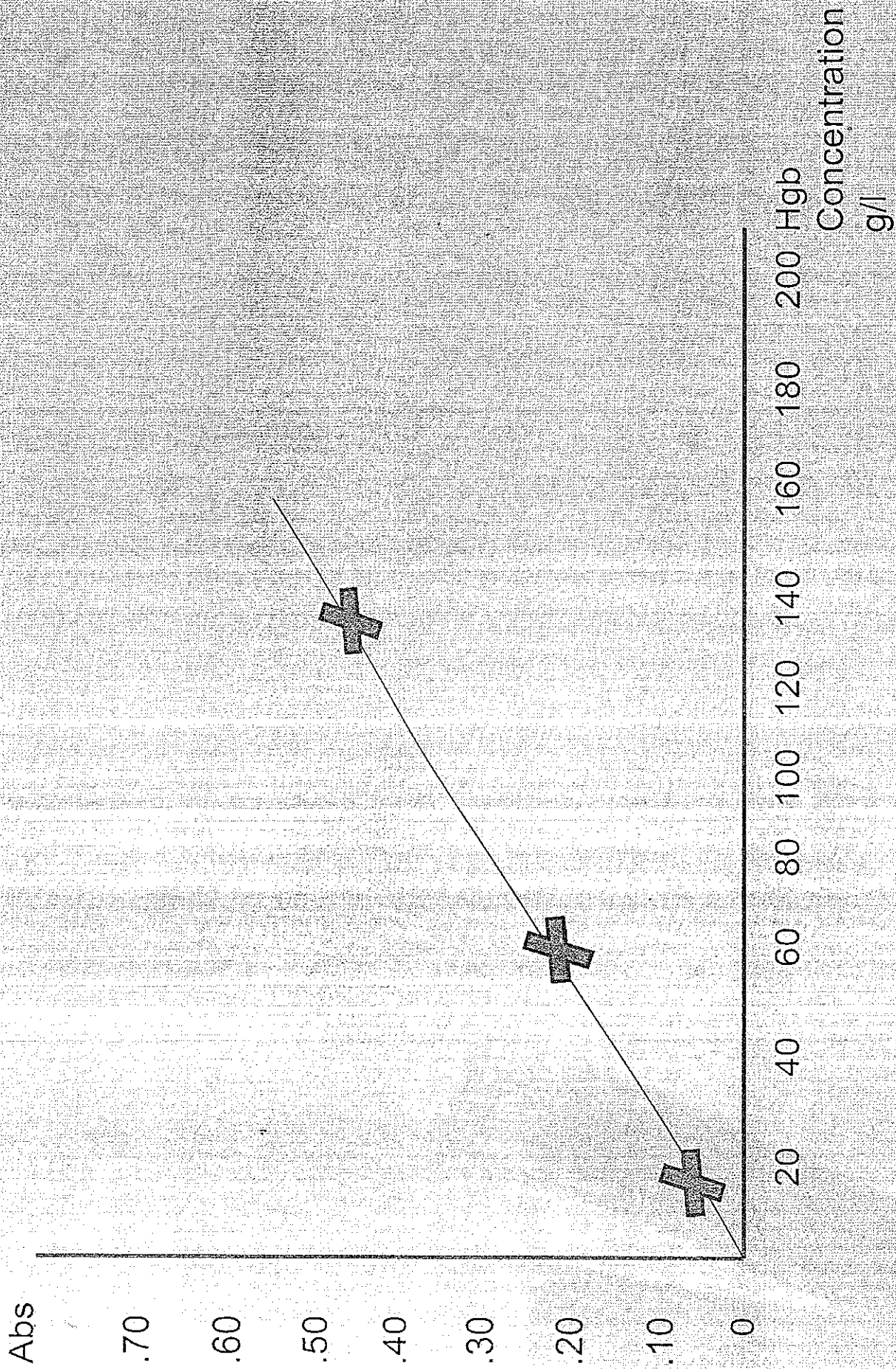
To calculate the Hgb concentration use the following equation:

Hgb concentration =

$$\frac{\text{Abs of test sample}}{\text{Abs of Standard}} \times \text{concentration of STD (in mg/l)} \times \frac{\text{dilution factor}}{1000}$$

= result g/l ----> g/dl ÷ 10

1000 = factor to convert mg/dl to gm/dl



Liver function tests

PID BA SACP

Liver function test give information about the activity or concentration enzymes/ compounds in serum. Results are useful in confirming a diagnosis of clinically suspected liver disease/ monitoring its course.

Alkaline phosphatase (ALP)

It is a protein bound in all body tissue, particularly high in liver, bile duct and bone. It is a group of isoenzymes widely distributed through the body including the liver, bone, intestine, kidney, leucocytes.

Normal range 30-120 iu/l

Higher level of alkaline phosphatase may indicate

- ✓ Intra/extra hepatic cholestasis. ^{متوقف في داخل وخارج الكبد}
- ✓ Hepatitis.
- ✓ Osteomalacia
- ✓ Rickets
- ✓ Bone tumours
- ✓ Osteomyelitis
- ✓ Healing fracture.

- bile duct obstruction
- rapid bone growth
- pregnancy

Gamma-glutamyl transpeptidase (GGT)

It is microsomal enzyme widely distributed through the body, including in the liver, pancreas, kidney, heart, brain.

It is not found in bone (useful tool to exclude bone as a source of ALP elevation)

It is a microsomal enzyme is therefore inducible by many drugs by alcohol, phenytoin, barbiturate, carbamazepine, warfarin, rifamycin.

→ In liver disease, the levels of GGT correlate well with elevations of the ALP and thus are sensitive and specific marker for biliary tract disease

Normal range 0-30 iu/l. 0-70 unit/L

Higher level of GGT of may indicate

- ✓ Hepato biliary disease
- ✓ Cholestatic disorder
- ✓ Alcoholic liver disease
- ✓ Cirrhosis
- ✓ Pancreatitis
- ✓ CCF

Aminotransferase

Aspartate transaminase/SGOT (serum glutamic-oxaloacetic transaminase)

It is found high concentration in heart, liver cells (mitochondria) skeletal muscle
Drugs - INH, rifampicin

Normal level 0-34 iu/l

Higher level indicates

- ✓ Myocardial infarction
- Cerebral ischemia
- ✓ Pancreatitis
- ✓ Liver disease - cirrhosis, necrosis, hepatitis, cancer
- Skeletal muscle trauma
- Severe deep burn
- ✓ Hemolytic anemia.

Alanine transferase/SGPT (serum glutamic-pyruvic transaminase)

It is located in high concentration in liver cells (cytoplasm)

Normal level 0-34 iu/l

Higher level indicate

- ✓ Liver damage
- ✓ Hepatic necrosis
- ✓ Alcoholic liver disease
- ✓ Liver ischemia

Lower level indicates

- Renal failure
- Vitamin K deficiency

Lactate dehydrogenase (LDH)

LDH1 and LDH2--present in the heart

LDH3-----lungs

LDH4 and LDH5--present in the liver and skeletal muscle

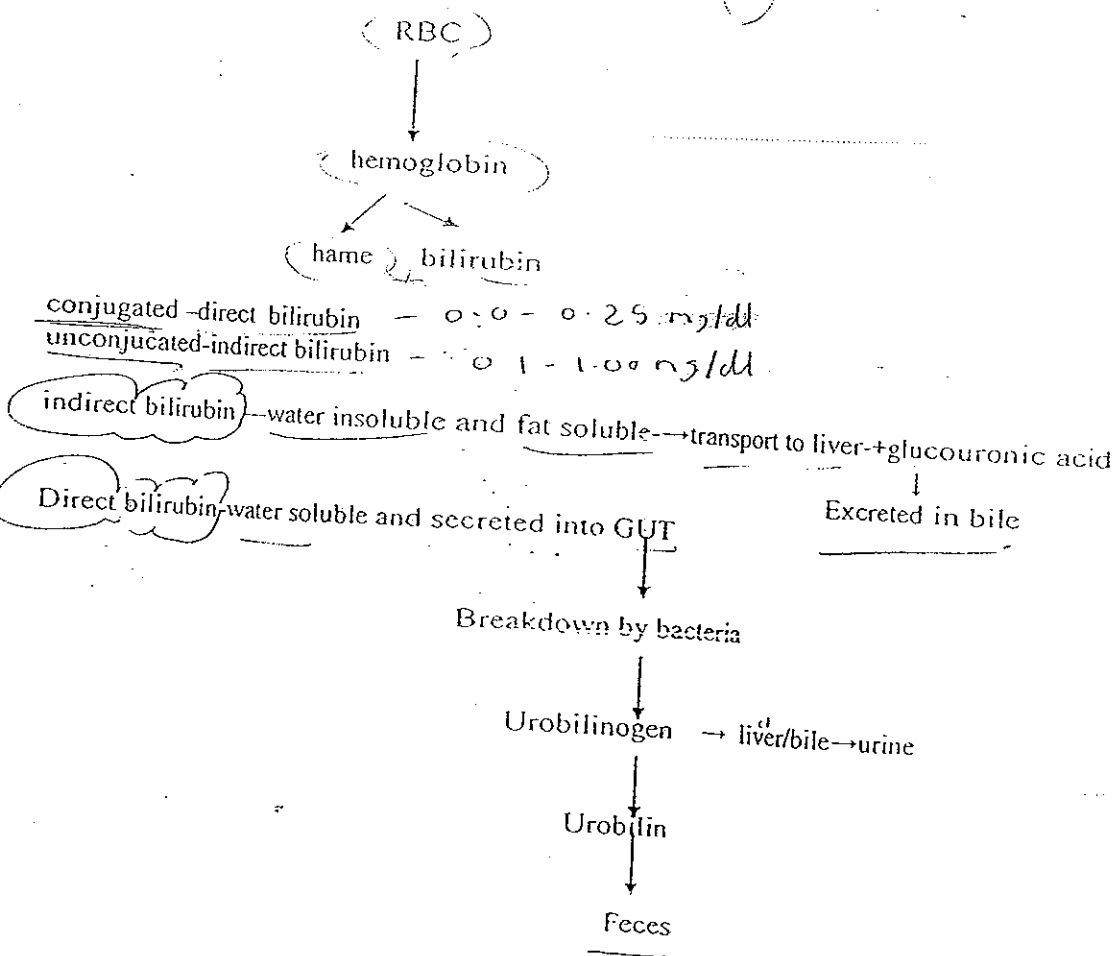
Normal level-----100-190 iu/l

Increased level may indicate

- Liver damage

Bilirubin

It is a breakdown product of hemoglobin derived from RBC



Conjugated bilirubin level may increase due to

- Hepatocellular damage
- ✓ Viral hepatitis
- ✓ Gallstones
- ✓ Malignancy
- ✓ GI bleeding
- ✓ Hemolysis
- ✓ inflammation

unconjugated bilirubin

- ✓ hemolysis
- ✓ jaundice
- ✓ gilbert's syndrome
- ✓ pulmonary infarction

Proteins

Albumin

Albumin is synthesized by the liver. Normally individual can synthesis 10-15 gm of albumin,

Albumin test represents a reliable and inexpensive lab test to assess the degree of liver damage.

Normal range-3.5-5.5 g/dl

Lower level may indicate

- ✓ Liver disease -hepatitis,cirrhosis or necrosis
- Ascites
- ✓ Burns
- Glomerulonephritis
- ✓ Nephritic

Higher level indicates

- ✓ Dehydration
- ✓ Shock

11-1-13-1

Prothrombin time

Normal time 10-14 seconds

Increased PT time may be due to ↑

- ✓ Severe liver damage
- ✓ Bile duct obstruction
- ✓ Hepatitis
- ✓ Cirrhosis
- ✓ Vitamin k deficiency
- ✓ Malabsorption of vitamin k
- ✓ Coagulation factors 1,2,5,7,10 deficiency.

Endoscopic and radiographic abnormalities

The use of imaging techniques can provide useful information regarding the presence of liver disease and portal hypertension

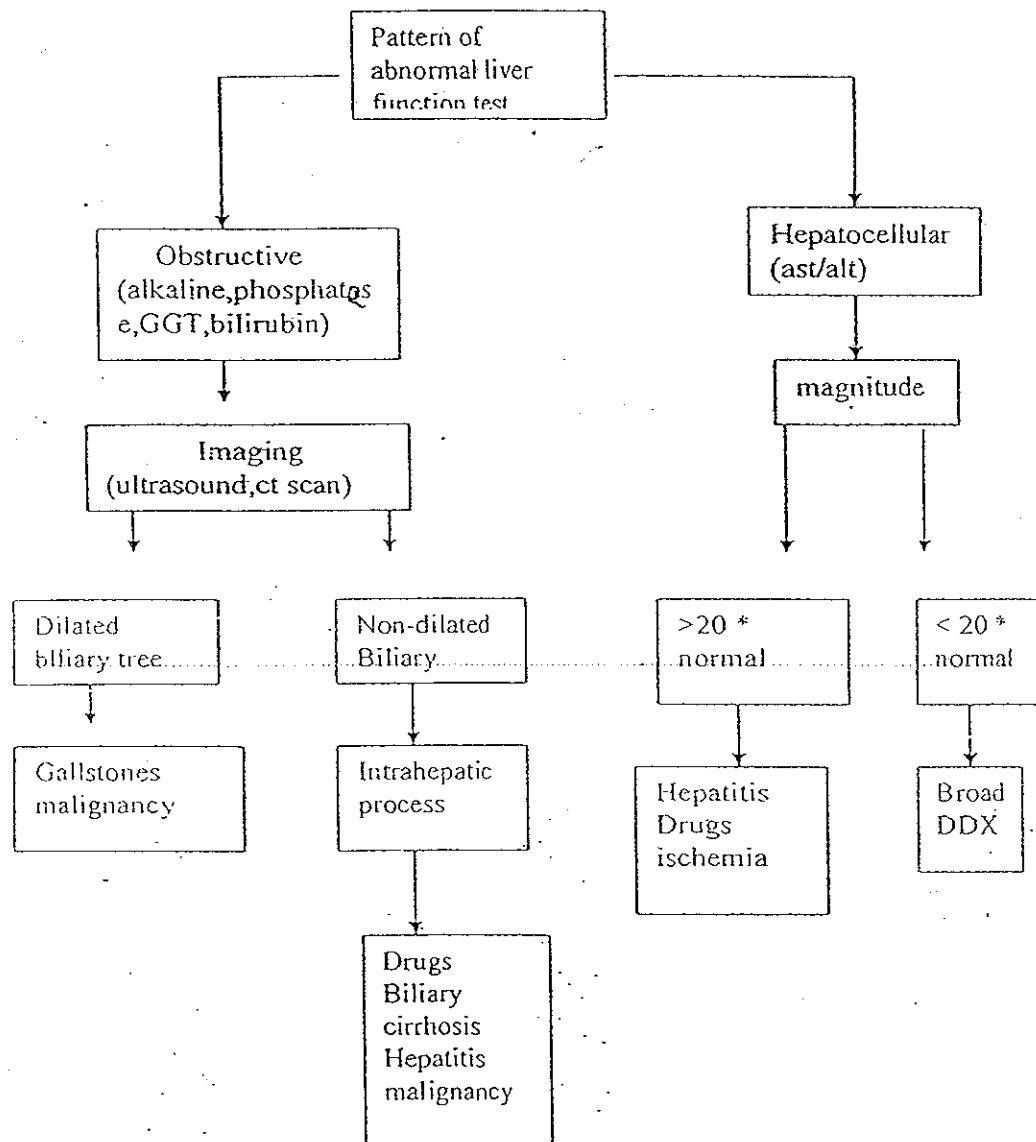
Ultrasound technique- for the detection of gallstones and biliary duct abnormalities in acute pain and jaundice

Endoscopic retrograde pancreatography (ERCP) - detection of choledocholithiasis

Computerized tomography - detection liver biopsy

Upper endoscopy - indicator of portal hypertension

Interpretation of liver function test



Reference

1. pharmacotherapeutics by joseph.t.dipirio
2. textbook of pharmacotherapeutics by roger walker, 4th edition
3. current medical diagnosis and treatment by Lawrence, 41st edition

- Exogenous Markers:

→ • Inulin clearance:

Normal range: M: 127 ml/min/m^2

F: 118 ml/min/m^2

- An inert carbohydrate, which is not bound to plasma proteins, inulin is freely filtered through the glomerulus and not metabolized, secreted or reabsorbed and can be regarded as gold standard for measuring GFR in adults and older children.

- The test is fairly invasive because inulin must be administered i.v. and it requires special analytical methods that limit the practical application in many health care facilities.

• Iothalamate and Cr-clearance:

Normal range: M: 127 ml/min/m^2

F: 118 ml/min/m^2

- This test involves injection of the radioactive exogenous marker and repeated blood sample and timed urine collecting.

- As with inulin, the need for i.v. administration and timed urine collections for both these

markers make them impractical for routine use.

Endogenous markers:

Cystatin C:

- Cystatin C is a protease inhibitor produced at a steady state by all nucleated cells that is filtered by glomerulus and neither reabsorbed or secreted by kidneys.
- Cystatin C may be more sensitive than serum creatinine.
- Serum cystatin concentrations would be expected to be inversely proportional to GFR.

- Blood urea nitrogen (BUN)

→ ⊕ - Direct measurement of GFR using marker such as inulin and iothalamate are the most accurate assessment of kidney function. Go to the last page: ↩

RENAL FUNCTION TESTS.

Renal function tests provide information on how well the kidneys are working and are useful in diagnosing and monitoring dysfunctions caused by medication, HIV-associated nephropathy, or other cause kidney disease. ⊕ → ↑

1. BLOOD UREA NITROGEN ("BUN")

This test measures the amount of urea nitrogen in the blood. (Nitrogen, in the form of ammonia) is produced in the liver when protein is broken into its component parts (amino acids) and metabolized. The nitrogen combines with other molecules in the liver to form the waste product urea. (The urea is then released into the bloodstream and carried to the kidneys, where it is filtered out of the blood and excreted in the urine). Since this is an ongoing process, there is usually a small but stable amount of urea nitrogen in the blood. Most diseases or conditions that affect the kidneys or liver have the potential to affect the amount of urea present in the blood. (If increased amounts of urea are produced by the liver or decreased amounts are excreted by the kidneys, then urea concentrations will rise.)

Urea has MW 60, of which 28 comes from the two nitrogen atoms.

Clinical chemists used to measure only the nitrogen in urea, hence the "urea nitrogen" measurement on lab reports.

→ Normal blood urea nitrogen is (11-23 mg/dL)

- When it is carried out- A blood sample is drawn from a vein in the arm. The BUN test is primarily used, along with the creatinine test, to evaluate kidney function under a wide range of circumstances and to monitor patients with acute or chronic kidney dysfunction or failure.

- Increased BUN is, by definition, azotemia. It is due either to increased protein catabolism or impaired kidney function.

Increased protein catabolism results from:

- ✓ a really big protein meal
- ✓ severe stress (myocardial infarction, high fever, etc.)
- ✓ upper GI bleeding (blood being digested and absorbed)
- ✓ Impaired kidney function may be "prerenal", "renal", or "postrenal".

(- Prerenal azotemia) results from underperfusion of the kidney:

dehydration, hemorrhage, shock, congestive heart. glomerulonephritis is likely also to be "prerenal" if mild, since it compromises renal blood flow more than tubular function

(- Renal azotemia) has several familiar causes:

acute tubular necrosis, chronic interstitial nephritis, some glomerulonephritis, etc.

(- Postrenal azotemia) results from obstruction of urinary flow: prostate trouble, stones, surgical mishaps, tumors

◦ Decreased BUN

- ✓ Lack of protein (celiac disease, some patients with nephrotic syndrome)
- ✓ Fluid excess - especially a concern with IV fluids
- ✓ trauma, surgery, opioids,
- ✓ Liver failure - urea synthesized by liver (end-stage cirrhosis, yellow atrophy, really bad hepatitis, halothane or acetaminophen toxicity, enzyme defects)
- ✓ Malnutrition
- ✓ Anabolic Steroid use
- ✓ Pregnancy - dilutional

- Both decreased and increased BUN concentrations may be seen during a normal pregnancy.)
If one kidney is fully functional, BUN concentrations may be normal even when significant dysfunction is present in the other kidney.

NOTE: The result of BUN test is measured by the doctor against a reference range for the test to determine whether the result is "normal" (it is within the range of numbers), high (it is above the high end of the range), or low (it is below the low end of the range). Because there can be many variables that affect the determination of the reference range, the reference range for this test is specific to the lab where your test sample is analyzed. For this reason, the lab is required to report your results with an accompanying reference range. Typically, the doctor will have sufficient familiarity with the lab and your medical history to interpret the results appropriately.

- While there is no such thing as a "standard" reference range for BUN, most labs will report a similar, though maybe not exactly the same, set of numbers as that included in medical textbooks or found elsewhere online.

- BUN levels can increase with the amount of protein in your diet. High-protein diets may cause abnormally high BUN levels while very low-protein diets can cause an abnormally low BUN.

2. SERUM CREATININE TEST - Definitive test of renal function

- This test measures the amount of creatinine in blood and/or urine (Creatinine is a waste product produced in your muscles from the breakdown of a compound called creatine. Creatine is part of the cycle that produces energy needed to contract your muscles and it as well as creatinine are produced at a relatively constant rate. Almost all creatinine is excreted by the kidneys, so blood levels are a good measure of how well your kidneys are working. The quantity produced depends on the size of the person and their muscle mass. For this reason, creatinine concentrations will be slightly higher in men than in women and children.

- It is filtered by the glomerulus and a small amount is also secreted into the glomerular filtrate by the proximal tubule. If the urine volume goes up, the serum creatinine does go down slightly.
- Creatinine is generally considered a somewhat more sensitive and specific test of renal function than BUN
- Normal serum creatinine is 0.6-1.2 mg/dL for men and 0.1 mg/dl in women

When it is carried out-

When the doctor suspects that patient is suffering from kidney dysfunction or if acutely or chronically ill with a condition that may affect kidneys and/or be exacerbated by kidney dysfunction; at intervals to monitor treatment for kidney disease or kidney function while on certain medications.

- A blood sample drawn from a vein in the arm and possibly a 24-hour urine sample is collected. The laboratory gives a large container and instructions for properly collecting this sample. Typically, urine is collected right after patient wakes up in the morning and empty bladder and save all of the urine produced until the same time the following day.
 - Excessive turbulence can cause false measurements
 - Prolonged delay in sending to lab can cause ammonia to form
 - Warming can cause falsely elevated results
 - Creatinine rises and falls more slowly than BUN. Preferred method for assessment of renal function.

Decreased Creatinine are Seen:

- Elderly
- Persons with small stature, decreased muscle mass
- inadequate dietary protein
- Muscle atrophy

Increased Creatinine Levels -

- due to any cause of impaired kidney function listed above, a lot of meat in the diet, or a very large muscle mass (bodybuilders, anabolic steroid users, giants and acromegaly patients). Hyperthyroidism, obstruction,
- A few drugs block the tubular secretion of creatinine, and will increase serum creatinine levels even though they have not damaged the kidney. This will be important if, and only if, the GFR is already very low.

- ✓ In massive rhabdomyolysis / crush injury, there is so much creatinine released that the creatinine will probably rise.

3. CREATININE CLEARANCE (2m)

A creatinine clearance test measures how well creatinine is removed from the blood by patients kidneys. i.e. to help evaluate the rate and efficiency of kidney filtration. (It is used to help detect kidney dysfunction and/or the presence of decreased blood flow to the kidneys) A creatinine clearance test gives better information than a blood creatinine test on how well your kidneys are working. (A creatinine clearance test is done on both a blood sample and on a sample of urine collected over 24 hours (24-hour urine sample

When it is carried out-

The creatinine clearance test may be ordered whenever a doctor wants to evaluate the filtration ability of the kidneys. It may be ordered when a patient has increased blood creatinine concentrations, a known or suspected kidney disorder, or decreased blood flow to the kidneys due to a condition such as congestive heart failure. the creatinine clearance test may be ordered to help monitor the progress of the disease and evaluate its severity.

(Any disease or condition that affects the glomeruli can decrease the kidneys' ability to clear creatinine and other wastes out of the blood. When this occurs, the blood creatinine level will be increased and the creatinine clearance will be decreased because not as much creatinine is able to be excreted in the urine.)

The value is given in units of ml/min, representing the volume of blood (in milliliters) cleared of creatinine by the kidneys per minute

(Normal values of men range from 75 ml/min to 125 ml/min)

Calculation requires knowledge of urinary creatinine excretion (usually over 24 hours) and concurrent serum creatinine levels. Creatinine clearance is calculated as follows

$$CL_{CR} = \frac{C_u \cdot V}{C_{CR}}$$

CL_{CR} is the creatinine clearance in ml/min, C_u concentration of creatinine in the urine, V is the urine volume (in ml/min of urine formed over the collection period) and C_{CR} is the serum creatinine concentration.

Incomplete bladder emptying and other problems may interfere with obtaining an accurate timed urine specimen. Thus estimations of creatinine clearance may be necessary. These estimation may require only a serum creatinine value.

Various methods have been proposed to estimate creatinine clearance based on concentration of creatinine in serum. Most of these method are essentially based on the age and/or weight of the patient, and concentration of creatinine in the serum.

• Three methods are frequently used they are:

1. Jellife's Method ✓
2. Method of Cockraft and GAult ✓
3. Siersback-Nielsen method ✓

JELLIFE'S METHOD This is based on age and serum creatinine concentration of the patient. This method is not intended for patients under 20 years of age, and should be used to calculate creatinine clearance in mature male adults only. This method is generally applicable for adult patients upto the age of 80 years.

$$\text{Males: } Cl\ cr = \frac{98-0.8(y-20)}{(C\ cr)}$$

Where y=age in years and C cr = Serum creatinine concentration in mg/100mL

$$\text{Females: } CL\ cr = (0.9) \frac{98-0.8(y-20)}{(C.\ cr)}$$

2. COCKRAFT AND GAULT'S METHOD - This method differs from Jellife's method in that it takes into account the weight of the patient also i.e this method is based upon the age, weight and serum creatinine concentration of the patient.

$$\text{Males: } Cl\ cr = \frac{(140-y)(w)}{(72)(C\ cr)}$$

Where y= age in years, C cr = serum creatinine concentration in mg/100 mL and w= weight in kg.

Lean body weight in males = $0.3281W + 0.3393H - 29.5336$

Where W= weight in kilograms and H= height in centimeters

$$\text{Females: } Cl\ cr = \frac{(0.85)(140-y)(w)}{(72)(C\ cr)}$$

The lean body weight is determined using the following equation $0.2967W + 0.4181H - 43.2933$

Where W = weight in kilograms, H = height in centimeters

3. SIERSBACK-NIELSEN NOMOGRAM METHOD - Here instead of an equation this method uses a nomogram.

④ Urinalysis:

- This provides information regarding renal function, urinary tract disease and presence of certain systemic diseases.
- Components of urine test include appearance, pH, specific gravity, protein level, glucose level, ketone level and microscopic examination.

1. Appearance: Normal urine is clear and ranges in colour from pale yellow to deep gold.

2. pH: 4.5-9 but is typically acid.

3. Protein: Normal values for urine protein are 50-80mg/hr as glomerular membrane prevents most protein molecules in the blood from entering the urine. Proteinuria occurs with many conditions like renal disease, bladder infection, fever etc.

4. URINE SPECIFIC GRAVITY TEST - 1.010 - 1.025

→ The kidneys are responsible for maintaining the blood osmolality

within a normal range.

It is a crude indicator of fluid status. A measure of the DENSITY of urine compared with the density of water

→ Specific gravity is the ratio of the weight of a given fluid to the weight of an equal volume of distilled water.

Normal Values: Adult 1.001-1.040 | Infants and children < 2 years 1.001-1.018

Increased Specific Gravity

- Dehydration
- Increased ADH - SIADH: Trauma, surgery, stress, drugs
- False high = glucose, protein, or dye in urine

Decreased Specific Gravity

- Renal failure - fixed sp grav
- Glomerulonephritis, pyelonephritis
- Decreased ADH (diabetes insipidus)

Sodium, urea, Sulphate and phosphate contribute to the specific gravity of urine

REFERENCES:

1. Leon Shargel, Comprehensive Pharmacology Review, Common Clinical Laboratory tests, Harwel Publishers, 2nd edition, pg-547,548
2. www.labtestsonline.org/understanding/creatinine clearance/BUN tests.
3. P L Madan, Biopharmaceutics and pharmacokinetic, Jaypee publishers, pgs 319-322

5. Color: Changes in color can result from drugs, diet or disease. Red colour indicate presence of blood or phenolphthalein etc.

6. Glucose: Glucose does not normally appear in urine. Glycosuria usually indicates diabetes mellitus.

6. Ketones: Ketones do not normally appear in urine. ketonuria usually indicates uncontrolled diabetes mellitus but it may also occur with starvation and with zero or low carbohydrate diets.

4. Urinalysis:

This provides information regarding renal function, urinary tract disease and presence of certain systemic disease.

Components of urine test include appearance, pH, specific gravity, protein level, glucose level, ketone level and microscopic examination.

i- Appearance:

Normal urine is clear and ranges in colour from pale yellow to deep gold.

ii- pH: 4.5-9 but is typically acid.

iii- Protein: Normal values for urine protein are $50-80 \text{ mg/}_{24\text{hr}}$ as glomerular membrane prevent most protein molecules in the blood from entering the urine.

Proteinuria occurs with many conditions like renal disease, bladder infection, fever etc.

IV. Urine Specific Gravity test:

Normal range: 1.010-1.025

- The kidneys are responsible for maintaining the blood osmolality within a normal range.
- Specific gravity is the ratio of the weight of a given fluid to the weight of an equal volume of distilled water.
- Sodium, urea, sulphate and phosphate contribute to the specific gravity of urine.

Specific gravity can be measured by:

1. Reagent strips=

The Spg can be measured by reagent strips which change colour based on the change in pK_a which is related to the ionic strength of the urine. The indicator substance on the strip changes colour, which can be calculated to Spg.

2. Urinometer (hydrometer):

It is a graduated buoy it requires sufficient urine volume to float freely. The reading is adjusted according to the urine temperature.

3. Refractometer: it uses refractive index as a basis and needs only a few mm of urine and no temperature adjustments.

Increased Specific Gravity:

Dehydration

Increased ADH

Trauma, surgery, stress, drugs

False high = glucose, protein or dye in urine

decreased Specific Gravity:

renal failure

decreased ADH

Glomerulonephritis

5. Colour:

Changes in colour can result from drugs, diet or disease.

Red colour indicate presence of blood or phenolphthalein etc.

6. Glucose:

Glucose does not normally appear in urine. Glycosuria usually indicates diabetes mellitus.

7. Ketones:

Ketones do not normally appear in urine. Ketonuria usually indicates uncontrolled diabetes mellitus but it may also occur with starvation and with zero or low carbohydrate diets.

THYROID FUNCTION TEST

Definition

Thyroid function tests are blood tests used to evaluate how effectively the thyroid gland is working

These tests are used to

1. diagnose an underactive thyroid (hypothyroidism) and an overactive thyroid (hyperthyroidism)
2. evaluate thyroid gland activity
3. monitor response to thyroid therapy

The thyroid gland synthesizes, stores & secretes hormones that are important to growth & development and the metabolic rate. ①

These hormones are thyroxine (T₄) & triiodothyronine (T₃)

Thyroid gland also secretes calcitonin, which reduces blood calcium ion concentration

Secretion and transport of thyroid hormone are controlled by TSH (thyrotropin)

This TSH is released by the anterior pituitary gland which is triggered by thyrotropin releasing hormone (TRH) ②

This TRH is secreted from hypothalamus

Most thyroid hormones transported by thyroxine binding globulin (TBG)

Pre albumin & albumin also serves as carriers

Thyroid hormones affect the following

1. growth and development
2. calorigenics by increasing the rate of basal metabolism
3. cardiovascular system- an increased metabolic rate increases blood flow and in turn cardiac output & heart rate this may be related in part to an increased tissue sensitivity to catecholamines
4. the CNS by increasing or diminishing cerebration
5. musculature- a fine tremor characterizes hyperthyroidism
6. lipid metabolism- lipid mobilization & degradation are stimulated

Precautions

Thyroid treatment must be stopped one month before blood is drawn for a thyroxine (T₄) test.

Steroids, propranolol (Inderal), cholestyramine (Questran), and other medications that may influence thyroid activity are usually stopped before a triiodothyronine (T₃) test.

Estrogens, anabolic steroids, phenytoin, and thyroid medications may be discontinued prior to a thyroxine-binding globulin (TBG) test. The laboratory analyzing the blood sample must be told if the patient cannot stop taking any of these medications. Some patients will be told to take these medications as usual so that the doctor can determine how they affect thyroxine-binding globulin.

Patients are asked not to take estrogens, androgens, phenytoin (Dilantin), salicylates, and thyroid medications before having a triiodothyronine resin uptake (T_3 RU) test.

Prior to taking a long-acting thyroid stimulant (LATS) test, the patient will probably be told to stop taking all drugs that could affect test results.

Description

TSH "tells" the thyroid gland to secrete the hormones thyroxine (T_4) and triiodothyronine (T_3). Before TSH tests were used, standard blood tests measured levels of T_4 and T_3 to determine if the thyroid gland was working properly. The triiodothyronine (T_3) test measures the amount of this hormone in the blood. T_3 is normally present in very small amounts, but has a significant impact on metabolism. It is the active component of thyroid hormone.

The thyroxine-binding globulin (TBG) test measures blood levels of this substance, which is manufactured in the liver. TBG binds to T_3 and T_4 , prevents the kidneys from flushing the hormones from the blood, and releases them when and where they are needed to regulate body functions.

The triiodothyronine resin uptake (T_3 RU) test measures blood T_4 levels. Laboratory analysis of this test takes several days, and it is used less often than tests whose results are available more quickly.

The long-acting thyroid stimulator (LATS) test shows whether blood contains long-acting thyroid stimulator. Not normally present in blood, LATS causes the thyroid to produce and secrete abnormally high amounts of hormones.

It takes only minutes for a nurse or medical technician to collect the blood needed for these blood tests. A needle is inserted into a vein, usually in the forearm, and a small amount of blood is collected and sent to a laboratory for testing. The patient will usually feel minor discomfort from the "stick" of the needle.

Normal levels

Total T_4 → 5-11 micro g/dl

Free T_4 → 0.8- 2.0 ng/dl

Total T_3 → 70- 132 ng/dl

Free T_3 → 2.5- 5 pg/dl

TSH → 0.5 - 4.7 micro unit/ml

Thyroid function studies.

1. serum total thyroxine (TT4)

- * This test provides the most direct reflection of thyroid function through indicating hormone availability to tissues. Total (free & bound) T_4 is determined by radio immuno assay, which is sensitive and rapid.

- Changes in TBG concentration, which increases during pregnancy, alter the total concentration of T4 & may produce a misleading high or low test result
- These changes in TBG do not affect the concentration of free T4, therefore to clarify thyroid function, either protein binding (T3 up take test) or free T4 must be measured
- Elevated TT4 level indicates hyperthyroidism & decreased TT4 level indicates hypothyroidism
- The TT4 level in euthyroid patient can be altered by other factors, such as pregnancy or febrile illnesses (which elevate TT4), nephrotic syndrome or cirrhosis (which lowers TT4) and various drugs

2. serum total tri iodo thyronine(TT3)

- This test measures total (free & bound) T3
- Serum T3 & T4 usually raise and fall together / Hyperthyroidism commonly causes a disproportionate raise in T3 & TT3 can rise before the TT4 level does
- Therefore TT3 is useful for early detection or to rule out hyperthyroidism. Many of the symptoms associated with hyperthyroidism are due to elevated TT3
- This test may not be diagnostically significant for hypothyroidism, in which TT3 levels may fall but stay within the normal range
- The TT3 may be low in only 50% of patients with hypothyroidism

3. resin tri iodo thyronine up take(RT3U)

- This test clarifies whether abnormal T4 levels are due to a thyroid disorder or to abnormalities in the binding proteins because it evaluates the binding capacity of TBG
- If an abnormal amount (high or low) of thyroid hormone is present in the blood, the (RT3U) results change in the same direction as the altered level elevated in hyperthyroidism & decreased in hypothyroidism
- If abnormalities in binding proteins underlie the abnormal levels of TT4, TT3 or both, the RT3U results change in the opposite direction, decreasing as TBG increases, increasing as TBG decreases
- Normal (25 to 35%)

→ thyroid stimulating hormone

4. serum thyrotropin(TSH) & sensitive TSH assays

a. serum TSH assay

- This test is the most sensitive test for detecting the hypothyroid state because the hypothalamic-pituitary axis compensates very quickly for even slight decreases in circulating free hormone by releasing more TSH. The TSH levels may be elevated even before low circulating levels of TT4 are detectable by diagnostic testing

- Serum TSH is not a reliable test for hyperthyroidism (in which TSH is suppressed) because low levels & low normal levels of TSH may be indistinguishable with the current technology

b. sensitive TSH assay

- The sensitive TSH assay uses immuno radiometric methodology or other new methods of analysis instead of the older radio immuno assay techniques and demonstrates greater sensitivity in the detection of the thyroid disease than older tests
- This assay is more expensive and more commonly used to monitor patients receiving replacement therapy to control over treatment

5. free thyroxine index

- This is not a separate test but rather an estimation of the free T4 level through a mathematical interpretation of the relationship between RT3U & serum T4 levels

$$FTI = TT4 \times RT3U$$

Mean serum RT3U

FTI values are elevated in hyper thyroidism or when TBG is low & decreased in hypothyroidism or when TBG is elevated

Thyroid function test	Hypo thyroidism	Hyper. thyroidism
1. serum resin tri iodo thyronine uptake(RT3U)	↓ (<35%)	↑ (>45%)
2. serum total thyroxine (TT4)	↓ (<5mg/dl)	↑ (>12mg/dl)
3. serum total tri iodothyronine(TT3)	↓ (<80ng/dl)	↑ (>180ng/dl)
4. free thyroxine index	↓ (<5.5)	↑ (>10.5)
5. serum thyrotropin (TSH)	↑ (>6μu/ml)	↓ (<0.5μu/ml)
6. sensitive thyrotropin (TSH) assay	↑ (>5μu/ml)	↓ (<0.2μu/ml)

Thyroid function tests:

1. Tests that directly or indirectly measure the concentration of T_3 and T_4 :

- free T_4
- Total serum T_4
- Serum T_3 resin uptake
- Free T_4 index
- Total serum T_3

2. Tests that evaluate integrity of the hypothalamic pituitary-thyroid axis:

- TSH
- TRH

3. Test that assess intrinsic thyroid gland function:

- Radioactive iodine uptake

4. Test that detects antibodies to thyroid tissue: Anti thyroid antibodies

- Free thyroxine (T_4):

Normal range: 0.8-1.5 ng/dL

- The test measures the unbound T_4 in the serum.
- It is the most accurate reflection of thyrometabolic status.
- A decreased direct equilibrium dialysis free T_4 with an elevated TSH is diagnostic of primary hypothyroidism.
- A decreased direct ^{method} equilibrium dialysis free T_4 with an elevated TSH is diagnostic of primary hypothyroidism.
- An increased direct equilibrium dialysis free T_4 with a TSH of less than 0.10 mIU/L is consistent with nonpituitary hyperthyroidism.

- TRH: (Thyroid releasing hormone):

- TRH is a hormone secreted by the hypothalamus.
- It regulate TSH secretion from the pituitary.
- TRH test measures the ability of injected

TRH to stimulate the pituitary to release TSH.

- This test is performed by drawing a baseline serum TSH concentration and then administering approximately 200-400 mcg of TRH intravenously over 30-60 seconds.

TSH concentrations are drawn at 30-60 min.

- Normal response is a TSH rise of 5 microunits/ml over baseline.

- Significant increase rule out hyperthyroidism.

Radioactive iodine uptake test:

- This test is used to detect the ability of thyroid gland to trap and concentrate iodine and produce thyroid hormone.

- This test assesses intrinsic function of thyroid gland.

- A low test result occurs in hypothyroidism.

- Antithyroid antibodies:

- Normal range: varies with antibodies.

- Antibodies that attack various thyroid tissue components. Can be detected in serum of patients with autoimmune disorders such as Graves disease

Anatomy of the heart:

Heart is about 12 cm long, 9 cm wide at its broadest point and 6 cm thick with an average mass of 250 g in adult females and 300 g in adult males.

.The heart rests on the diaphragm, near the midline of the thoracic cavity.

.It lies in the mediastinum.

.The membrane that surrounds and protects the heart is the pericardium.

.Layers of heart walls:

1.The epicardium

2.The myocardium

3.Endocardium

The heart has four chambers:

The two superior receiving chambers are Atria.

The two inferior pumping chambers are the ventricles.

Cardiac function tests:

The heart has two basic properties electrical and mechanical.

They work in harmony to propel blood, delivering oxygen and nutrients to all tissues.

Electrocardiography : it is the recording of electrical activity of the heart on an electrocardiogram.(ECG).

<https://www.facebook.com/Pharmacy-Notes-1593423834279694/>

Normal conduction system and electrocardiogram recording :

Conduction system is composed of specialized , non contractile cells that serve to Originate and conduct action potentials in the appropriate rate from the atria to the ventricles.

At the rest the cardiac cells are more negatively charged intracellularly Than extra cellularly or polarized , with a voltage difference of 60-90 mV.

When excited , ionic currents across cell membranes lead to charge shifting where the interior of the cells become more positive or depolarized, and action potential is generated.

Calcium influx leads to the excitation – contraction coupling of the cells.

-Subsequently , the action potential is propagated and cells return to normal resting State repolarization.

-Depolarization leads to myocardial contraction.

-Repolarization leads to myocardial relaxation.

-ECG provides presentation of depolarization and repolarization of atrial and ventricular

Cells that can be assessed by reviewing a number of waves and intervals.

Each cardiac cycle is presented on ECG by P wave reflecting atrial depolarization .

QRS complex reflecting ventricular depolarization.

T wave reflecting ventricular repolarization .

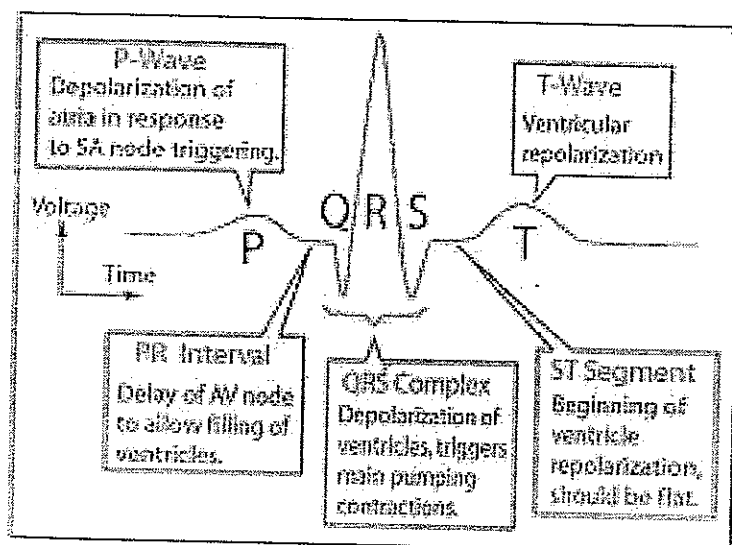
By placing multiple leads on the patient , the electrical impulses of the heart

are recorded .

Standard ECG is composed of 12 leads : six limb leads and six chest leads .

ECG provides information on the presence of myocardial ischemia , injury or infarction,

Location of the infarction , and the site of occlusion in coronary artery involved.



Classic ECG pattern of myocardial infarction is reflected by three changes :

1-T wave inversion , 2. ST-segment elevation ,3. appearance of Q waves.

T wave inversion or ST segment depression suggest acute ischemia.

ST-segment elevation or Q waves suggest acute infarction.

ST- segment elevation is the earliest sign of myocardial infarction.

As the infarction evolves , changes to QRS complex include loss of R-wave height ,And development of pathologic Q waves.

Biochemical cardiac markers :

Infarction of the myocardial cells disrupt membrane integrity , leaking intra cellular macromolecules in to the peripheral circulation where they are detected.

Cardiac – specific Troponin I : diagnostic level: <1.5ng /ml (assay dependent)

Cardiac –specific Troponin T: diagnostic level:<0.1ng/ml(assay dependent)

Troponin is a protein complex consisting of three subunits:

Troponin C(TnC), troponin I(TnI), troponin T(TnT).

These three sub units are located along thin filaments of myofibrils.

They regulate calcium mediated interaction of actin and myosin necessary for the contraction of cardiac muscles.

TnC binds Ca^{+2} , Tn I inhibits actomyosin ATPase, TnT attaches to tropomyosin on the thin Filaments.

Monoclonal antibody –based immunoassay is used to detect cardiac specific

TnI and cardiac Specific TnT. cardiac –specific TnT & TnI are highly specific and sensitive for myocardial Infarction.

Following Myocardial injury , serum cTnI & cTnT begin to rise.

The initial rise of troponin is due to release of cytoplasmic troponin .

Later it is due to release of complexed troponin from disintegrating myofilaments.

Troponins are most beneficial in identifying AMI 6 hours or more after symptom onset. The prolonged time course of elevation of cTnI and c TnT is useful for late diagnosis of AMI.

First –generation troponin assay T Elisa was limited by lack of specificity to cardiac troponin And long turn around time

(90 min at 20 degree C).

Second generation troponin assay T Elisa was improved by changing the antibody detected To the cardiac specific antibody, resulting in Enhanced specificity.

Third generation assay uses recombinant human cardiac

troponin T enabling reproducibility And standardization of c Tn T assay

Because c TnT and cTnI are not detected in the peripheral circulation of healthy individuals and high sensitivity of available assay , micro-infarction of myocytes may be detected.

Elevated Troponin levels are strong predictor of mortality and serious adverse outcome 30-42 days after ACSs.

Troponin plays a role in risk stratification of patients presenting with chest pain , identifying high risk groups and leading to early utilization of aggressive medical regimens and invasive treatment.

Creatine Kinase :

Normal range : male ,40-200 international units/L or 667-3334nmol sec/L

Female ,35-150 international units/L or 583-2501nmol sec/L

Creatine kinase is an enzyme that stimulates the transfer of high energy Phosphate groups.

CK is found in skeletal muscle ,myocardium ,and the brain.

Circulating serum CK is directly related to the individuals muscle mass.

Serum CK concentration rise sharply 4-8 hours after the onset of chest pain associated with AMI. Serial CK measurements following AMI provide excellent sensitivity but poor specificity.

Other causes for increased serum CK concentrations include any musculoskeletal -injury or disease , intra muscular injection ,and some medications like:

-Clofibrate, ethanol , lithium , halothane .

Creatine kinase isoenzymes :

Normal range : CK_MB < 12 international unit /L or 0-5.9ng/ml

Enzyme CK is a dimer of two B monomers (CK-BB), two M monomers (CK-MM) or hybrid of two (CK-MB).

Three isoenzymes are found in different sources :

CK-BB found in the brain ,lung and intestinal tract.

CK-MM found in skeletal muscle and cardiac muscle.

CK-MB found predominantly in myocardium but also in skeletal muscle.

Later is most specific for myocardial tissue and is used for diagnosis of AMI.

Other causes for elevated CK -MB is trauma , skeletal muscle injury , surgical procedures Involving small intestine , tongue , diaphragm , uterus .

Electrophoretic separation followed by fluorometric analysis of isoenzyme bands is used to determine the actual CK_MB concentration

Diagnosis of AMI is strongly suggested when CK-MB concentration is greater than 10 international units /L.

When interpreting serum CK-MB levels, the timing of blood specimen collection in relation to the onset of symptoms must be assessed .

Lack of absolute cardiac specificity limits CK_MB interpretation.

CK-MB Isoforms:

CK-MB in myocardial tissue is released in to circulation following AMI ,and then undergoes metabolism by lysine carboxypeptidase producing more negatively Charged isoform CK_MB.

Normal level is 0.5-1 international units/L. for each isoform .

CK-MB isoforms were most specific and sensitive when measured 6 hours after Onset of chest pain in patient with myocardial infarction presenting to the emergency department.

Myoglobin:

It is a low molecular weight heme protein found in cardiac and skeletal muscle.

This protein is one of two preferred markers for the early detection of AMI due to Early rise of myoglobin after onset of symptoms of AMI.

Myoglobin is cleared rapidly by renal glomerular filtration and level return to reference Value 24 hours following AMI.

The fast rise and fall of myoglobin level make it an appropriate marker to detect reinfarction if occurring 24 hours after initial insult.

It is highly sensitive to myocardial ischemia and is most useful in ruling out AMI.

Lack of specificity to cardiac muscle limits the interpretation of myoglobin level.

Condition leading to false –positive results include skeletal muscle injury of any Causes ,trauma ,and renal failure.

Lactate dehydrogenase :

Normal range : 100-210 international units/L or 1667-3501nmol sec/L.

Lactate dehydrogenase is an enzyme that catalyze the reversible formation of Lactate from pyruvate.

Following AMI,serum LDH rise in 24-48 hours ,return to normal in 8-14 days after The onset of chest pain.

Major limitation to LDH is the lack of specificity as it is found in numerous organs And tissues including the heart, liver , kidney , skeletal muscle ,red blood cells ,And lymphocytes.

Electrophoretic fractionation of LDH to its five major isoenzyme (LDH1-LDH5) better distinguishes the site of origin, but these tests are not specific for AMI.

Heart contain mainly LDH1 and to a lesser extent LDH2.

Elevation of LDH1 or ratio of LDH1:LDH2 greater than one was used in diagnosis of AMI.

Aspartate amino transferase :

Normal range : male ,0-37 international unit /L or 0-617 nmol sec/L

Female ,0-31 international unit /L or 0-517 nmol sec /L.

Aspartate aminotransferase (AST) is an enzyme involved in amino acid synthesis.

AST is widely distributed in liver ,heart , skeletal muscle ,red blood cell , kidney and pancreas.

Serum level of AST rise within 12 hours of AMI ,peak in 24-48 hours,and return to baseline in 3-4 days .

It has poor specificity for myocardial cells damage.

Recommendation for measurement of biochemical markers :

Early rising biochemical markers (myoglobin or CK_MB) are most appropriate For patient presenting within 6 hours of onset of symptoms.

Troponins are better markers for patients presenting 6 hours or

later after AMI.

Combination of an early markers with troponin is an acceptable practice .

Troponins are more sensitive to the presence of myocardial damage than myoglobin and CK.

Specific c TnI and cTnT have emerged as the preferred cardiac biochemical markers for the evaluation of patient with ACS.

B-type natriuretic peptide (BNP):

It is a neurohormone released by ventricular myocardium in response to volume overload.

Its primary use is for evaluation of patient with heart failure.

C-reactive protein (CRP):

is a non specific acute -phase reactant that is released

In the presence of inflammatory processes caused by various etiologies

Eg : infection , malignancy , trauma , rheumatoid arthritis .

CRP is synthesized in liver and is normally present in trace amount in peripheral circulation .

In presence of inflammation CRP production is stimulated by systemic Cytokines .

Serum level of CRP is elevated in patients with CAD and ACS.

Echocardiography is based on sound transmitted to and through the heart .

Different tissues present different acoustical impedance (resistance to Transmitting sound) .

Transthoracic echocardiography involves sound waves from a transducer positioned on the anterior chest directed across cardiac tissues .

The sound is reflected back in different frequencies and images of cardiac anatomy are displayed on an oscilloscope or an electronic monitor .

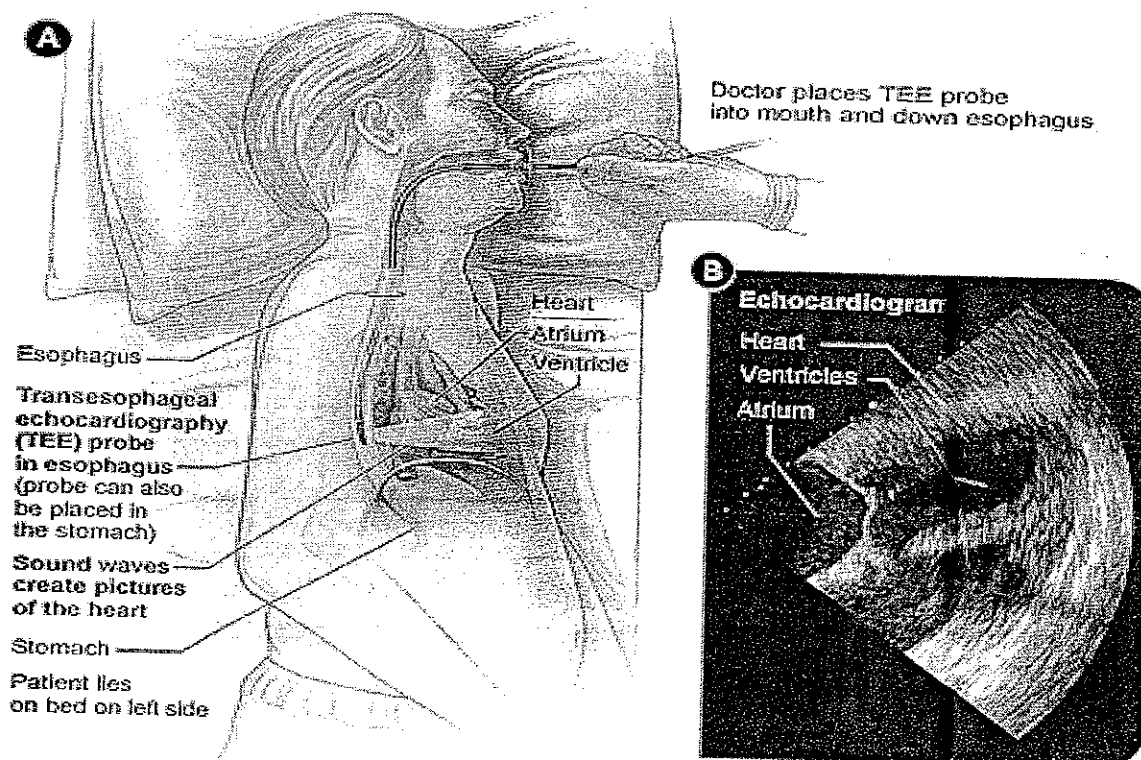
Clinical uses include anatomic assessment of heart and functional assessment Of cardiac chambers and valves .

Contrast agents may be injected for better visualization of endocardial borders .

Doppler echocardiography uses sound or frequency ultrasound to record the velocity And direction of blood and wall motion .

This method permits the assessment of valvular and wall motion abnormalities.

-Transducer: *جهاز*



TEE plays an important role in assessing patient with ACS presenting with apparent large infarct and hemodynamic instability .

Information provided includes wall motion abnormalities to assess the extent of the Infarct or the level of function of remaining myocardium, recognition of complications such as postinfarction ventricular septal defect and presence of left ventricular thrombi .

Transesophageal echocardiography involves mounting the transducer at the end of A flexible endoscope and passing it through the esophagus to position it closer To the heart .

TEE provides higher resolution of the posterior cardiac structures making it ideal For viewing the atria , cardiac valves , and aorta .

Clinical indication include detection of atrial appendage thrombi , native and Prosthetic valvular function and morphology , cardiac mass , thoracic aortic dissection .

Non invasive stress testing :

exercise stress testing :

Physical exercise is performed using a graded exercise protocol on a treadmill Or upright bicycle .

The most widely used protocol is Bruce protocol .

Non imaging end points include reproduction of anginal symptoms , exhaustion Hypertention or 20 mmHg decrease in systolic blood pressure , ventricular arrhythmias,or Severe ST-segment depression on ECG .

Exercise allows for several useful measurement including the duration of exercise ,Total workload , maximum heart rate , exercise-induced symptoms ,ECG changes ,And blood pressure response.

Limitation includes patients with orthopedic , neurological , peripheral vascular problem.

Computed tomography (CT):

It involves an intense , focused electron beam that is swept along target rings by Electromagnets .

When the electron beam strikes the target ring, a fan of X-rays is produced and moves around the patient.

Ultra fast CT allows scanning in real time without gating.

Main advantage of CT is enhanced resolution and special definition of structures.

Cardiac CT is useful in the assessment of cardiac structure including cardiac masses, Pericardial condition, and evaluation of aortic and pulmonary disease

Magnetic resonance imaging (MRI):

It is a noninvasive imaging technique capable of detailed tissue characterization, And blood flow measurements.

The procedure involves placing patients in a device generating a powerful magnetic field and aligning the protons of the body's hydrogen atoms relative to the magnetic field.

Radio waves pulsed through the field force the protons to shift their orientation.

When the radio waves stop, the protons return to their previous orientation, Releasing energy in the form of radio waves.

The waves are detected by a scanner and converted into images.

Images are physiologically gated to an ECG.

During the procedure, the patients are required to remain motionless.

Patients with metal prostheses should not undergo MRI.

Clinical uses include assessment of congenital , aortic , pericardial diseases ,tumors , and intravascular thrombus .

Reference :

Basic skill of interpreting of laboratory data

By Mary lee

Exercise Stress Testing

Testing the heart during exercise can help identify coronary artery disease. In coronary artery disease, blood flow through the coronary arteries (which supply blood to the heart muscle) is partly or completely blocked. If the coronary arteries are only partly blocked, the heart may have an adequate blood supply when the person is resting but not when the person exercises. Thus, testing the heart during exercise can help identify coronary artery disease.

-To stress the heart, most people walk on a treadmill or pedal an exercise bicycle.

Gradually, the pace of the exercise and the force required to do it (workload) are increased.

The ECG is monitored continuously, and blood pressure is measured at intervals....

If symptoms, such as shortness of breath or chest pain, become too uncomfortable or if significant abnormalities appear on the

ECG or blood pressure recordings, the test is stopped sooner. Testing takes about 30 min.

- People who cannot exercise can be evaluated using pharmacologic stress testing. For this procedure, a drug such as dipyridamole, dobutamine or adenosine is injected to stimulate the effects of exercise on blood flow.

Computed tomography (CT):

- A computed tomography (CT) scan is an imaging method that uses X-rays to create pictures of cross-sections of the body.

- You will be asked to lie on a narrow table that slides into the center of the CT scanner. Once you are inside the scanner, the machine's X-ray beam rotates around you.

- A computer creates separate images of the

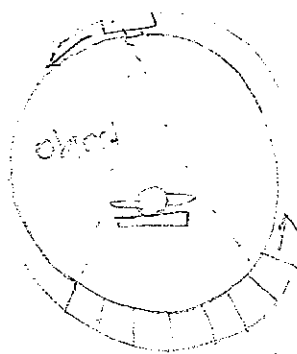
body area, called slices. These images can be stored, viewed on a monitor, or printed on film.

- You must stay still during the exam, because movement cause blurred images.

- A CT scan creates detailed pictures of the body, including the brain, chest, spine etc the test may be used:

1. Diagnose an infection
2. Guide a surgeon to the right area during a biopsy
3. identify masses and tumors
4. Study blood vessels.

X-ray 3D CT



□MRI

-An MRI (magnetic resonance imaging) scan is an imaging test that uses powerful magnets and radio waves to create pictures of the body. It does not use radiation (x-rays).

-Single MRI images are called slices. The images can be stored on a computer or printed on film.

-You may be asked to wear a hospital gown or clothing without zippers or snaps. Certain types of metal can cause blurry images.

You will lie on a narrow table, which slides into a large tunnel-shaped scanner.

Some exams require a special dye (contrast). Most of the time, the dye will be given through a vein (IV) in your hand or forearm before the test. The dye helps the radiologist see certain areas more clearly.

-MRI images taken after a special dye (contrast) is delivered into your body may provide extra

information about the blood vessels.

- An MRA, or magnetic resonance angiogram, is a form of magnetic resonance imaging, that creates three-dimensional pictures of blood vessels. It is often used when traditional angiography cannot be done.

Arteriogram:

An arteriogram is an imaging test that uses X-rays and a special dye to see inside the arteries. It can be used to view arteries in the heart, brain, kidney, and other parts of the body.

Endomyocardial biopsy:

Removal of a small sample of heart tissue to check it for signs of damage caused by organ rejection.

FLUID AND ELECTROLYTE BALANCE

INTRODUCTION

- Electrolytes are minerals in our body that have an electric charge.
- They are in blood, urine and body fluids.
- Maintaining the right balance of electrolytes helps our body's blood chemistry, muscle action and other processes.
- Sodium, calcium, potassium, chlorine, phosphate and magnesium are all electrolytes.
- Levels of electrolytes in your body can become too low or too high.
- That can happen when the amount of water in the body changes. Causes include some medicines, vomiting, diarrhoea, sweating or kidney problems.

Role of lungs in maintaining acid-base balance

A normal adult produces about 300 liters of CO_2 daily from the metabolism of foodstuffs. In the blood, CO_2 reacts with water to form carbonic acid, which dissociates to H^+ and HCO_3^- . In the lung capillaries they are converted back to CO_2 and water and the CO_2 is expired.

As a secondary respiratory compensation, the lungs react to metabolic acidosis and alkalosis. Metabolic acidosis stimulates breathing causing hyperventilation while metabolic alkalosis suppresses it. These are attempts to correct pH by changing the concentration of carbon dioxide and carbonic acid in the blood.

Role of lungs in gas exchange

In the alveoli (lungs air bags) "fresh" air enters that has approx 80% Nitrogen 19% oxygen and a little carbon dioxide and other gases.

In our blood there is high carbon dioxide levels but in the air a low carbon dioxide levels and vice versa for oxygen.

Effectively the respiratory gases diffuse to equalize in concentration in both the blood and in alveoli. Basically in blood (deoxygenated) CO_2 concentration is 50 mmHg in the air sacs it is 45 mmHg so they try to equalize.

This results in carbon dioxide leaving the blood and entering the alveoli.

The same thing happens to the oxygen. It's higher in air than in blood so the oxygen moves from high concentration (in air) to low concentration (in blood).

The end result is carbon dioxide leaving blood and oxygen entering blood.

-
- Human Homeostasis: is a process by which the body manages a assembly of highly complex interactions to maintain balance or return systems to functioning within a normal range.
 - The inability to maintain homeostasis may lead to death or disease, a condition known as homeostatic imbalance like Gout etc.
 - The liver, kidney and brain helps to maintain homeostasis.

Role of kidneys in maintaining acid-base balance

The kidneys have two important roles in the maintaining of the acid-base balance:

to reabsorb bicarbonate from and to excrete hydrogen ions into urine. 4500 mmol of bicarbonate are filtered into the primary filtrate of urine daily, but only 2 mmol of it are finally excreted. 70-80% of bicarbonate is reabsorbed in the first part of proximal tubule, 10-20% in the loop of Henles and 5-10% in the distal tubule and collecting ducts.

Carbonic anhydrase plays an important role in the reabsorption in the proximal tubule. Disturbance in the reabsorption of bicarbonate in the proximal tubule leads to metabolic acidosis, hyperchloremia and alkalotic urine. This disease is named as "type II renal tubular acidosis".

Renal tubules actively secrete hydrogen ions. Most of this takes place in the distal part of the nephron, but active transport of hydrogen ions occurs in the proximal tubule, too. The H-ATPase of the apical cell membrane secretes hydrogen ions into urine. For each hydrogen ion secreted, one bicarbonate molecule is transported to the interstitial fluid, from there it diffuses into the bloodstream. Fifty mmol of hydrogen ions are normally excreted daily.

If the hydrogen ions are not properly secreted into the collecting ducts, the result is metabolic acidosis, hypokalemia, hypocalcaemia, nephrocalcinosis and alkalotic urine. This disease is called "type I renal tubular acidosis".

The maximal hydrogen ion gradient, against which the transport mechanism can secrete H^+ ions, corresponds to a urine pH of 4.5 in humans. However, three important molecules remove free hydrogen ions from the tubular fluid permitting more acid to be secreted: H^+ is bound to ammonia, phosphate and bicarbonate to form NH_4^+ , $H_2PO_4^-$, CO_2 and H_2O .

The renal acid secretion is mainly regulated by the changes in the intracellular pCO_2 , potassium concentration, carbonic anhydrase activity and adrenocortical hormone concentration.

Haemostatic mechanism involved in plasma sodium and water balance:

The principle role of sodium is the regulation of serum osmolality as well as fluid and acid base balance. Sodium is needed for appropriate trans membrane electric potential for neuro muscular functioning.

Water intake is determined by thirst. Thirst is the most important haemostatic mechanism controlling body water.

When sodium is in the GIT, its actively absorbed and water passively along the osmotic gradient.

kidney are primary organ controlling sodium and water.

Sodium

Normal range: 136-145 mmol/L

• Sodium is most abundant cation in extracellular fluid, which is important in the control of water movement between extra-cellular and intra-cellular fluid spaces.

Physiology:

The principal role of sodium is the regulation of serum osmolality as well as fluid and acid-base balance. It is also needed for maintaining the appropriate trans-membrane electric potential for neuromuscular functioning.

- The kidney are the primary organs responsible for controlling body sodium and water.

Hyponatremia:

- It is defined as a serum sodium concentration less than 135 mmol/L.

- May be related to dilution of serum sodium

or total body depletion of sodium.

- Causes:

- Clinical condition such as cirrhosis, CHF etc.
- Administration of osmotically active solutes such as albumin or mannitol.
- Diuretic therapy.

- Signs and Symptoms:

Hypothermia

Seizures

agitation

lethargy

nausea

- muscle cramp

1. Hyponatremia associated with low total body sodium:

Which reflects reduction in total body water and larger reduction in total body sodium.

Caused due to: Vomiting, diarrhoea, etc.

2. Hyponatremia associated with normal total body sodium:

-This condition is also called as Euvolemic/Dilutional hyponatremia, this condition refers to impair water excretion without any alteration in sodium excretion.

-Caused due to:

oAny mechanism that enhances ADH secretion or potentiates its action at the collecting tubules.

3. Hyponatremia associated with high total body sodium:

which involves an increase in total body sodium with a larger increase in total body water.

Most frequently observed in edematous states such as CHF, cirrhosis, CRF, in these conditions water and sodium excretion from kidneys is impaired.

Edema is the most common sign of hyponatremia with increased total body sodium.

Hypernatremia:

Hypernatremia is defined as a serum sodium concentration greater than 175 mmol/L . less common than hyponatremia.

-It is a state of relative water deficiency and hence excessive concentrations of sodium in all body fluids.

Causes:

- loss of free water
- loss of hypotonic fluids
- excessive sodium intake
- osmotic diuretics
- Acute renal failure
- Drugs therapy with agents such as lithium

Signs and Symptoms:

-thirst	-Seizures
-restlessness	-elevated urine specific gravity
-hyperreflexia	-muscle twitching
-coma	

1. Hypernatremia associated with low total body sodium:

- Hypernatremia reflects when both sodium and water losses occur, but water is lost to a greater extent the thirst mechanism generally increases water intake, but this adjustment is not always possible. This condition may also be iatrogenic when hypotonic fluid loss (profuse sweating and diarrhea) are replaced with an inadequate quantity of water and salt. In these circumstances, fluid loss should be replaced with dextrose 5% in water, or sodium chloride 0.45%.

2. Hypernatremia associated with normal total body sodium:

- It is also known as euvolemic hypernatremia. This condition ~~redress~~ ^{results} to a general water loss without sodium loss because of water redistribution b/w the intracellular and extra-

cellular fluids.

- caused due to:

increased insensible water loss (fever, extensive burns, mechanical ventilation).

3. Hypernatremia associated with high total body sodium:

- This form of hypernatremia usually is due to exogenous administration of high sodium containing solutions such as: sea water near drowning.

Potassium

Normal range: 3.5-5 mmol/L

Functions:

- impulse transmission
- protein synthesis
- Carbohydrate metabolism
- Cardiac contractility
- aldosterone secretion

Hyperkalemia:

It is a condition where serum potassium concentration level > 5.0 mmol/L

Causes:

renal failure

Acidosis

potassium sparing diuretics
increase intake of potassium

Signs and Symptoms:

Cardiac rhythm disturbance

Bradycardia, Hypotension.

Muscle Weakness

Hypokalemia:

It is defined as a serum potassium concentration less than 3.5 mmol/L .

Causes:

- diuretics
- Diarrhea
- Vomiting
- hypotension
- Arrhythmia

Chloride

Normal range: 96-106 mmol/L

Physiology:

Chloride is influenced by the extracellular fluid balance and acid-base balance. The role of chloride is primarily passive. It balances out positive charges in the extracellular fluid and, by passively following sodium, helps to maintain extracellular osmolarity.

Causes (Hyperchloremia)

Kidney disease

Metabolic acidosis

respiratory alkalosis

Hypochloremia:

metabolic alkalosis

respiratory acidosis

- Hypochloremia occurs with prolonged vomiting etc.

Bicarbonate test

-The bicarbonate test is performed when an acid-base imbalance is identified, to determine whether it is primarily respiratory or metabolic in nature.

low bicarbonate level:

Chronic diarrhoea

Metabolic acidosis

Kidney diseases

Methanol poisoning

High bicarbonate level:

Severe vomiting

Lung disease

Metabolic alkalosis

-When bicarbonate levels are higher or lower than the normal, it suggests that our body is having trouble in maintaining the acid base

balance perhaps by loss or retention of fluid.

Normal level: 22-30 mmol/L

Maintenance of electrolyte balance. (2M)

- Kidney increase or decrease their fluid and electrolyte output by the action of ADH and aldosterone.

- If osmolality of ECF is higher than normal or blood volume low, ADH is released and water is reabsorbed and vice versa.

- Aldosterone increases Na reabsorption and release of this hormone is stimulated by low total body Na.

Test to evaluate fluid and electrolyte balance:

- Electrolytes are minerals in our body that have an electric charge.

- They are in blood, urine and body fluids.

-levels of electrolytes in our body can become too low or too high due to changes in body water. due to: Vomiting

diarrhea

Sweating

Kidney problem

medicines

Tests:

1. Bicarbonate test	22-30 mmol/L
2. Chloride test	98-105 mmol/L
3. Potassium test	3.5-5 mmol/L
4. Sodium test	135-145 mmol/L
5. Calcium test	2.2-2.6 mmol/L
6. Magnesium test	0.8-1.2 mmol/L
7. Phosphate test	0.8-1.6 mmol/L

Microbiological Culture Sensitivity Tests

Microbiological tests are one of the diagnostic tests used to diagnose a disease condition, especially the infections caused from bacteria, virus, fungi or any other micro organisms.

Infectious diseases are one of the leading causes of death all over the world. The term infectious disease covers all the diseases caused by bacteria, fungi, viruses and parasites.

As a clinical pharmacist, having thorough knowledge about the causative organism and choice of appropriate antibiotic for treatment is very essential. Also development of resistance to micro organisms is a reason for concern as the older antibiotics are getting resistant to traditional microorganisms. Also, the clinical pharmacist can contribute to the management of patients with infectious disease by ensuring the appropriate choice of anti-infective agent, correct dose and route of administration is used and appropriate patient monitoring is performed.

The parameters considered to go on for choosing an antibiotic and helping in the interpretation of the lab data are as follows:

1. Body temperature
2. Blood pressure
3. Heart rate
4. Renal function tests
5. Liver function tests

Confirmation of an Infection:

To confirm any infection, understanding the definitions of colonisation and infection are very important.

Colonisation: Colonisation may be defined as invasiveness of an organism without disease condition in the host.

Infection: Infection implies the presence of an organism within the tissues that evokes a response in the hosts' defense mechanism.

Colonizing organisms may also contribute to diagnostic problems as specimen contamination may result in 'False Positive Result'.

Non-Specific Tests supporting Microbiological Data:

1. White Blood Cell Count and Differential Count
 - (a) Neutrophils - Neutrophilia, Neutropenia.

Microbiological Culture Sensitivity Tests

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- (b) Lymphocytes – Lymphocytosis, Lymphopenia.
- (c) Monocytes
- (d) Eosinophils – Eosinophilia
- (e) Basophils.
- 2. Erythrocyte Sedimentation Rate (ESR)
- 3. C3 Component
- 4. C-reactive protein
- 5. Rheumatoid factor

Definition:

Microbiological Culture Sensitivity Tests are defined as the tests that provide final identification of the pathogen as well as information regarding the possible effectiveness of various antimicrobials.

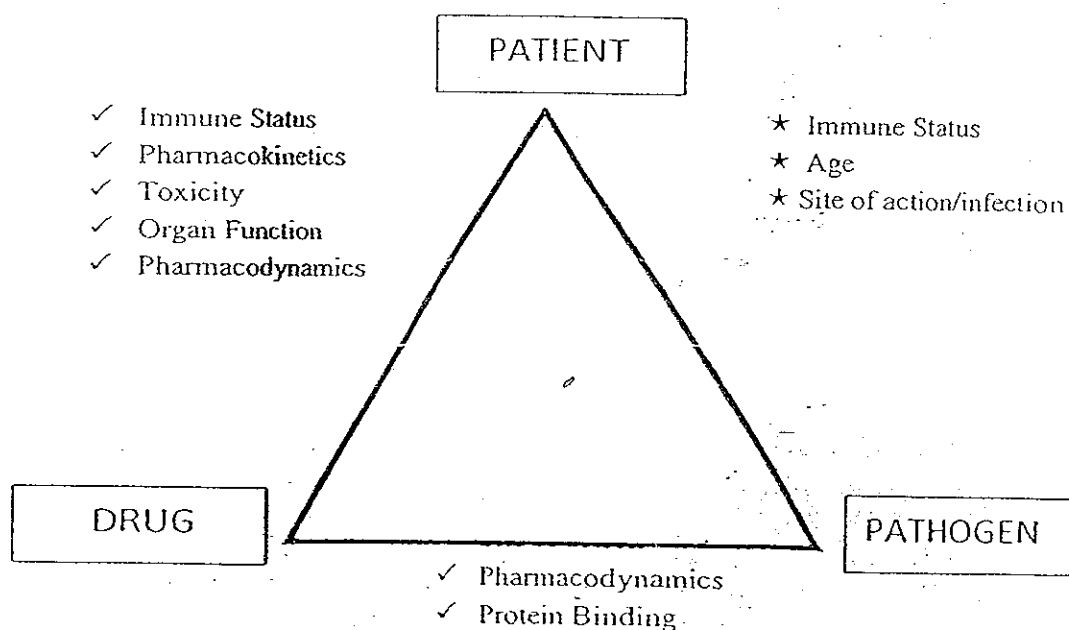


Figure 1. Interpretation of patient, microbiological and pharmacological factors

Identification of Pathogens:

1. Obtain culture specimens from the suspected site of infection like throat swab for upper respiratory tract infection, sputum examination for lower respiratory tract infection.
2. Type of specimen depends on the site of infection and patient characteristics.
Eg: Pneumonia – Sputum examination,
Cystitis – Urine culture (From Bladder).

Pyelonephritis – Kidney infection,
Meningitis – Cerebro Spinal Fluid (CSF)

3. Staining techniques:

(a) Grams' Stain identifies either Gram Positive Bacteria or Gram Negative Bacteria.

(b) Acid Fast Stain

4. Oxygen tolerance: Aerobic or Anaerobic bacteria.

5. Morphology: Cocci, bacilli, etc.,

6. Cell wall structure: Gram Positive Bacteria or Gram Negative Bacteria

7. Once the staining and morphology of the organism is identified, the culture test for sensitivity is performed for the resistance and dose calculation of the antibiotic.

8. The time required ranges from 4 hours to 48 hours depending upon the type of test and organism involved.

Minimum Inhibitory Concentration: (MIC)

The minimum inhibitory concentration is defined as the minimum concentration required to inhibit the growth of a micro organism is used to assess the sensitivity of that micro organism to a particular anti microbial agent.

Uses:

1. Quantitative determination of antimicrobial activity.
2. Assess the sensitivity of a microorganism to a particular antimicrobial.
3. Classifies organism sensitiveness either as sensitive, resistant, etc.,

Minimum Bactericidal Concentration:

Minimum bactericidal concentration is defined as the lowest concentration of a drug that results in a 99.9% reduction in the initial bacterial density.

Uses:

1. Presence of an organism, those inhibited by drugs but not killed.
2. When MBC: MIC ratio is > 32 , development of tolerance to microorganisms.
Eg: Streptococci, Staphylococci, etc.

Grams Staining			
Positive		Negative	
Cocci	Bacilli	Cocci	Bacilli
Clusters - Staphylococci	Small - Listeria - Corynebacterium - Gardnerella	Neisseria Sps. (Gonorrhoeac meningitides) Veillonella	Lactose Fermenter (Oxidase +ve)
Coagulase +VE - Staphylococcus	Large - Spore Forming		Aeromonas Pasteurella

Microbiological Culture Sensitivity Tests

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aureus	- Non Spore Forming		Vibrio
Coagulase -VE - Stap. Epidermidis - Stap. saprophyticus	Spore Forming Bacteria: ★ Clostridium ★ Bacilli		Oxidase -ve E.coli Klebsiella Sps. Enterobacter Sps.
Pairs - Pneumococci	Non Spore Forming ★ Lactobacillus	Gram Negative Coccobacilli	
Chains - Streptococci	Branching/filamentous - Nocardia - Actinomyces	H. Influenzae Moraxella	

Antibacterial Susceptibility Tests:

1. Diffusion methods
2. Disk diffusion method
3. Epislomer or E-test
4. Dilution test
5. Automated test
6. Timed-kill curve test

Methods of antimicrobial concentration determination in clinical samples:

1. Fluorescence polarization immunoassay
2. Radio Immuno Assay
3. HPLC
4. Serum inhibitory or Bactericidal Titers
5. Microbiological Assay
6. TDM Methods

References:

1. A textbook of Clinical Pharmacy Practice by G. Parthasarathi.
2. A textbook of applied therapeutics, The Clinical use of drugs by Koda Kimble.
3. A textbook of therapeutics by Herfinal
4. A textbook of pharmacotherapy, a pathophysiologic approach by Joseph T Dipiro.

Disk diffusion method:

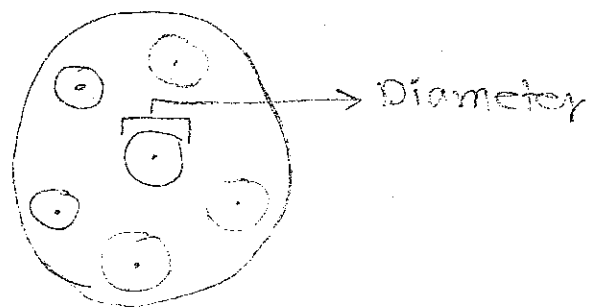
This method utilize an agar plate on which an inoculum of the organism is placed.

After inoculation several antimicrobial landen disks are placed on the plate and evidence for bacterial growth is observed after 18-24 hrs

→ If antimicrobial is active against the pathogen: A zone of growth inhibition is observed around the disk.

The diameter of inhibition is reported as:

- Susceptible
- Intermediate
- or - resistant



Application:

Enterobacteria

Staphylococcus

Broth dilution method:

- It involves placement of bacterial inoculum into several tubes or wells filled with broth.

Several dilutions of antimicrobials are placed in the respective wells.

→ Bacteria are allowed to incubate for 18-24 hrs

→ After $\subseteq$ the wells are examined for bacteria growth:

If the well is cloudy → Bacteria growth has taken place

Suggesting resistance to antimicrobial in that concentration

→ After incubation the MIC of bacteria to various antimicrobial agents can be read directly from wells by measuring the turbidity.

→ Based on this, bacteria are reported to Susceptible (S)

Intermediate (I) to antimicrobial agents
or - Resistant (R)

Applications:

Can be used to detect most organisms except H-influenza, N-gonorrhoea and S.pneumonia.

E-test (epsilometer):

This method is based on a combination of dilution and diffusion tests.

- In this test a plastic ^{strip} impregnated with a known, prefixed concentration gradient of antibiotic is placed on an agar plate streaked with a suspension of known bacteria inoculum.

- The drug instantly diffuses from the plastic strip to form an effective concentration gradient within the agar.

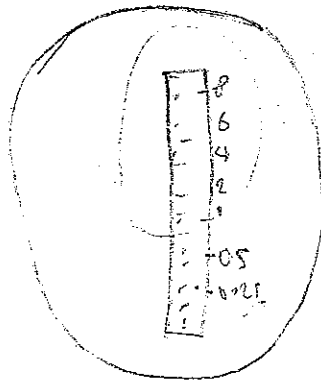
- After overnight incubating, elliptical zones of inhibition are formed.

- The point where the bottom of the ellipse crosses the plastic strip is correlated to a printed MIC value the strip.

Applications:

H. influenza

S. pneumonia



B-lactamase test:

- Many bacteria produce B-lactamase enzyme that can inactivate numerous B-lactam containing antibiotics.

→ While MIC tests often require overnight incubation B-lactamase test can be performed in minutes.

→ In this test, penicillin is used as a substrate along with an indicator system (nitrocefin). Detection of B-lactam ring by bacterial enzymes, nitrocefin changes color when its B-lactam ring is hydrolyzed.

- A +ve B-lactamase test predicts resistance to penicillin, ampicillin, amoxicillin etc.

Application:

to detect most organism containing β -lactam ring except - enteric G^{-ve} bacilli or pne -

□ Tests to diagnose specific infectious disease:

1. Meningitis → Gram's stain
2. latex Agglutination (LA)
3. Viruses → viral culture
Antigen detection
Serological testing
4. HIV → ELISA Test
Western Blot
5. Lyme disease → ELISA test
Western Blot
6. Fungal infection → Blood culture technique

Pulmonary Function Test:

Purpose of pulmonary Function Test:

- Pulmonary function testing has been a major step forward in assessing the functional status of the lungs.

Pulmonary function test are used for the following:

1. Screening for the presence of obstructive and restrictive diseases.
2. Evaluating the patient prior to surgery especially those who:
 - Are older than 60-65 years of age
 - Have history of smoking, cough or wheezing
- 3 Documenting the effectiveness of therapeutic intervention

Normal values change with:

i-Age: As a person ages, the natural elasticity of the lungs decrease. This result in smaller lungs volume and capacities as we age.

2. Gender: Male have large lung volume and capacities than females.

3. Body height and size: A small man will have smaller PFT result than a man of same age who is much larger.

4. Race: Affects PFT values.

□ Terminology And Definitions:

① Lungs volumetests: routinely measure the:

1-Tidal volume: The tidal volume is the volume of air breathed in and out during normal quiet breathing. (about 500ml)

- Only about 350ml of the tidal volume actually reaches the alveoli, the remaining 150 ml remains in the air spaces of nose, pharynx, trachea and bronchi and is called Dead air volume.

2. Minute volume of respiration: The total air taken in during 1 min.

- It is approximately 6000 ml/min . Tidal volume $\times$ respiratory rate per minute (12)

3. Inspiratory Reserve volume: The air that can be breathed in by maximum inspiratory effort after an ordinary inspiration.

- This is approximately 3100 ml above 500 ml of tidal volume, thus inspiratory system can fill in 3600 ml of air.

4. Expiratory Reserve volume: The air that can be breathed out by maximum expiratory effort after an ordinary expiration.

- This is about 1200 ml .

5. Residual volume (RV): The volume of air which remains in the lungs after maximal expiration

- This is about 1200 ml of air.

Lungs Capacities:

1. Inspiratory capacity: it is the maximum volume of air that can be inspired i.e. the sum of the tidal volume + inspiratory reserve volume = 3600ml

2. Vital capacity: It is the maximal volume of air that can be exhaled after a maximum inspiration.

- It is the sum of inspiratory reserve volume + tidal volume + expiratory reserve volume.

It is approx equal to 4800ml.

TLC

3. Total lungs capacity: It is the sum of all the lungs volumes (6000ml).

Forced Vital Capacity (FVC):

- The maximum volume of air exhaled with maximally forced effort from a position of maximal inspiration.

Blowing Flow Tests: routinely assess the lungs
↳ By Spirometry:

① Forced Expiratory Volume (FEV): The amount of air measured after forceful and completely exhaling after maximal inspiration.

Forced Expiratory Volume (FEV₁): The measure of forced expiratory volume in the first second of exhalation is FEV₁.

FEV₁% = ratio of FEV₁/FEV.

② Peak Expiratory Flow Rate (PEFR):

This is the maximum flow rate achieved by the patient during the FVC measured from the beginning after full inspiration and ending with maximum expiration.

③ Forced Expiratory Flow Rate (FEF):

It is mean forced expiratory flow during the middle half of the FVC and is measured as the slope of the line b/w 25 and 75% of the FVC on the flow-volume curve i.e. the FVC curve is divided into

3 quartiles which are FEF 25%, FEF 50%, FEF 75%.
FEF 25% - This measurement describes the amount of air that was forcibly expelled in the 1st 25% of FVC test.

Slow vital Capacity (SVC): The amount of air you can slowly exhale after you inhale as deeply as possible.

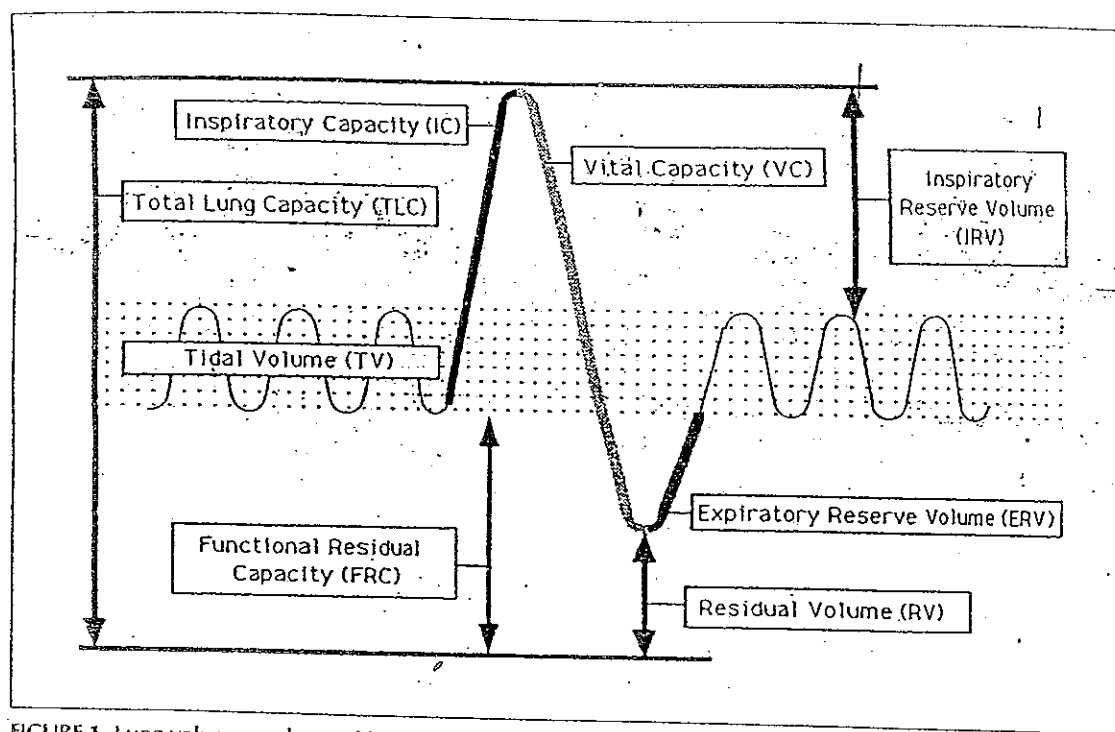


FIGURE 1. Lung volumes and capacities—a schematic representation of various lung compartments based on a typical spirogram. (Graphic artwork by Michele Betterton)

Spirometry:

- Spirometer is the primary instrument used in pulmonary function testing.

It is designed to measure changes in volume and can measure lungs volume compartments that change gas with the atmosphere.

- As the patient breathes in and out from the air enclosed on the surface of the water below the bell jar. As the patient breathes, the bell of the spirometer is displaced and the pen deflection reflects the volume of air entering or exiting the lungs.

The device usually attached to the spirometer, which measures the movement of gas in and out of the chest, is referred as spiograph.

Sometimes, the spiograph is replaced by a printer like unit used in laboratory. The resulting tracing is called spiogram.

A visual record of respiratory movements made by a spirometer.

□ Pulmonary function can be grouped into main categories:

- i. Obstructive Airway Disease
- ii. Restrictive Airway Disease

Obstructive Air Flow:

Obstructive disease limits airflow during expiration.

The potency (dilation or openness) is estimated by measuring the flow of air as the patient exhales as hard and as fast as possible. Flow through the tubular passage ways can be decreased because:

1. Narrowing of the airways due to bronchial smooth muscle contraction (asthma).
2. Narrowing of airways due to inflammation and swelling of bronchial mucosa as in bronchitis.
3. Material inside the bronchial passageways physically obstructing the flow of air as in the case of excessive mucous plugging, inhalation of foreign objects or presence of tumors.

4. Destruction of lungs tissue with loss of elasticity and hence the loss of external support of airways as in emphysema.

- In obstructive lung condition, the airways are narrowed, create air turbulence and increased resistance to airflow.

LUNGS FUNCTION TEST

- 1) Forced vital capacity (FVC)
- 2) Forced expiratory volume (FEV1)
- 3) FEV1/FVC
- 4) Forced expiratory flow 25%-75%
- 5) Peak expiratory flow
- 6) Residual volume
- 7) Total lungs capacity

RESULT

N or decreased
Lower with higher FEV1 and FEV2
Decreased
Decreased
Lower
Higher
Normal or Lower

Restrictive Airflow:

Restrictive disease limits airflow during inspiration. This is seen in patients whose total lung capacity is significantly reduced. Restrictive disease results from loss elasticity (e.g. fibrosis, pneumonia) or physical deformities of the chest e.g. (kyphoscoliosis) with a consequent inability to expand the lungs and reduced TLC.

There are varieties of restrictive disorders which are:

1. Intrinsic restrictive lungs disorders: TB, pneumonia
2. Extrinsic restrictive lungs disorders: Obesity, Pregnancy
3. Neuromuscular restrictive lungs disorders:
Generalized weakness, paralysis of the diaphragm, myasthenia gravis, muscular dystrophy.

In restrictive lung condition there is loss of lungs tissue, a decrease in the lungs ability to expand or decrease in the lungs ability to transfer oxygen to the blood.

<u>LUNG FUNCTION TEST</u>	<u>RESULT</u>
1) Forced vital capacity (FVC)	Lower
2) FEV1	Normal or Lower
3) FEV1/FVC	Normal or Higher
4) FEF (25%-75%)	Normal or Higher
5) Residual volume	Normal or Higher
6) Total Lungs Capacity	Lower
7) Peak Expiratory Flow	Normal or Lower

Effects of pulmonary Disease on PFTs:

Disease	Vital Capacity	Residual Volume	FEV: FVC
1. Chronic obstructive Pulmonary Disease	Normal or ↓	Normal or ↑	↓
2. reversible obstructive (asthma)	Normal or ↓	↑	↓
3. Restrictive [Extra and Intra pulmonary]	↓	↓	N or ↑
4. Combined obstructive and restrictive	↓	↓	↓

(C)

Flow Volume Curves:

- Graphical representation of inspiration and Expiration.
- The shape of the curve indicates both the type of disease and severity of disease.

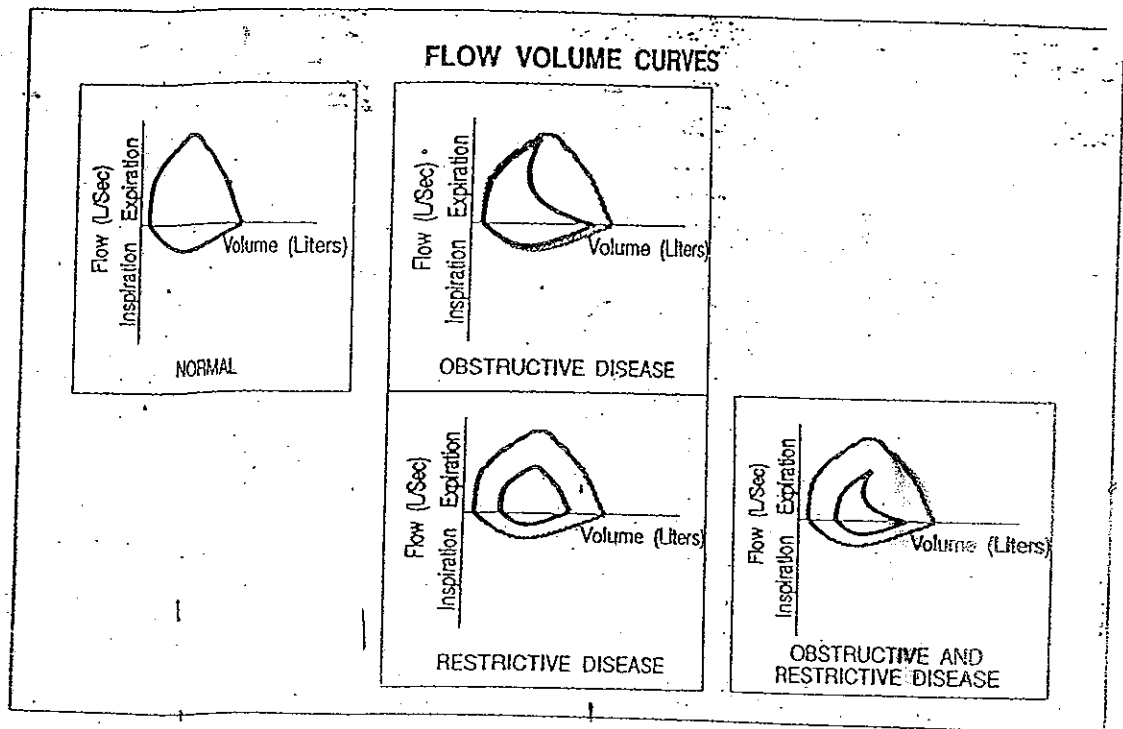


FIGURE 2. Flow-volume loops seen with common obstructive and restrictive pulmonary diseases. (Graphic artwork by Michele Betterton)

① - Diffusion Capacity tests:

- Tests of gas exchange measure the ability of gases to cross (diffuse) the alveolar-capillary membrane and are useful in assessing interstitial lung disease. Typically, these tests measure the per minute transfer of a gas, usually carbon monoxide from the alveoli to the blood. The diffusion capacity may be lessened following losses in the surface area

of the alveoli or thickening of the alveolar-capillary membrane. Thickening may be due to fibrotic changes.

-These test results can be confounded by a loss of diffusion capacity due to poor ventilation.

-The diffusion capacity of the lungs to carbon monoxide (DL_{CO}) can be measured by either a single-breath or steady-state test.

(E)

Airway Reactivity Tests:

① Bronchoprovocational testing:
-Inhaled histamine or methacholine is used to provoke bronchospasms in susceptible individuals.
-Typical protocols begin by nebulizing low concentrations of either agent followed by spirometry (FEV_1 and/or FVC). The concentration is doubled at specific time intervals (about 5 min) until a set decrease (usually 20% from baseline) in the FEV_1 or FVC is attained.

If the maximal concentration of the agent used is less than or equal to 8 mg/ml, the

patient has increased airway reactivity -
- If the concentration is greater than 8 mg/mL,
the patient has normally sensitive airways.

6

-Definition:

PV or PhV, also known as Drug Safety, is the pharmacological science relating to the collection, detection, assessment, monitoring and ^{Prevention of} adverse effects with pharmaceutical products.

- Pharmacovigilance heavily focuses on adverse drug reactions or ADRs.

-Aims:

- 1- Early detection of hitherto unknown adverse reactions and interactions
- 2- Improve patient care and safety in relation to the use of medicines and all medical and paramedical intervention.
- 3- Improve public health and safety in relation to the use of medicines.
4. Promote understanding, education, and clinical training of pharmacovigilance and its effective communications to the public.
- 5- Detection of increases in frequency of (known) adverse reactions.

Pharmacovigilance

مراقبة الأدوية

6. Identification of risk factors and possible mechanisms underlying adverse reactions.

Ultimate goals:

- the rational and safe use of medical drug
- the assessment and communication of the risks and benefits of drugs on the market
- educating and informing of patients

PHARMACOVIGILANCE

BY:

ZEINAB BAGHERI

PHARM.D 4TH YEAR

DEFINITION AND AIMS:

Pharmacovigilance, also known as drug safety, is the pharmacological science relating to the detection, assessment and prevention of adverse reactions of drugs.

Major AIMS of pharmacovigilance are;

- >Early detection of hitherto unknown adverse reactions and interactions
- >Detection of increases in frequency of (known) adverse reactions
- >Identification of risk factors and possible mechanisms underlying adverse reactions
- >Estimation of quantitative aspects of benefit/risk analysis and dissemination of information needed to improve drug prescribing and regulation.

THE ULTIMATE GOALS ;

- >The rational and safe use of medical drugs
- >The assessment and communication of the risks and benefits of drugs on the market
- >Educating and informing of patients

ADVERSE DRUG REACTIONS(ADR);

World Health Organization (WHO) defines an adverse drug reaction(ADR) AS "A response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function.

CLASSIFICATION OF ADRs;

- Type A: Augmented pharmacological effect
- Type B: Bizarre effects (or bugs or idiosyncratic)
- Type C: (chemical) chronic reactions
- Type D: Delayed/delivery reactions
- Type E: End-of-treatment (Exit) reactions
- F: Failure of therapy/familial reactions
- Type G: Genotoxicity reactions
- Type H: Hypersensitivity reactions
- Type U: Unclassified reactions

TYPE A(Augmented) reaction:

>These reactions are usually exacerbation of the pharmacological effects of a drug and are thus dose _dependent.

>these reactions are usually predictable due to known pharmacology of a drug and are thus preventable

>These are generally associated with less morbidity,mortality.

>An example is ; insulin _ induced hypoglucemia

MECHANISM;

Type A --reactions may results from the following causes:

>Pharmaceutical: changes in formulation resulting in enhanced bioavailability

>Pharmacokinetics: changes in absorption,distribution,metabolism,eliminatin of drugs commonly due to Drug-disease or drug-drug interactions

>Pharmacodynamics:

changes in drug receptor sensitivity or homeostatic mechanisms.

TYPE B (Bizarre) reactions:

>These are hypersensitivity reactions and are not dose-dependent and are not predictable and preventable in individual case(unless the patient has known history of this type of reaction)

>This type is associated with morbidity and mortality.

EXAMPLE; penicillin induced hypersensitivity reaction.

MECHANISM;

Type B reactions may result from the following causes:

>Pharmaceutical:

Use of wrong excipients in a drug formulation

>Pharmacokinetics:

Formulation of toxic metabolites or electrophilic compounds

>pharmacodynamics:

Altered target organ sensitivity

TYPE C(chronic) reactions:

>An irritant reaction

>Associated with long_term use

>Involves in dose accumulation

>Related to drug concentrations

Example:

Antimalarials causing ocular toxicity

TYPE D(delayed) reaction:

>Delayed effect(dose independent)

>Caused by method of administration or nature of formulation

- >Improves if medicine withdrawn or method of delivery changed
- >Carcinogenicity(eg;immunosuppressants)
- >Teratogenicity

TYPE E(end off treatment) reactions:

- >Pharmacologically predictable
- >Begins only when medicine is stopped or dose reduced
- >Improve if medicine reintroduced

TYPE F (failure of therapy)reactions;

- >Only occurs in those genetically predisposed
- >Improves if medicine withdrawn

TYPE G(genotoxicity)reactions:

- >Causes irreversible genetic damage

TYPE H (hypersensitivity) reactions:

- >Requires activation of immune system
- >Improves if medicine withdrawn

TYPE U(unclassified) reactions:

- >Mechanism not understood

>>RISK FACTORS/PREDISPOSE FACTORS OF ADRs:

- .Age
- .Gender
- .Prior history of ADRs
- .Multiple drug therapy(polypharmacy)
- .Current disease
- .Pharmacokinetic differences
- .Pharmaceutical factors
- .Intercurrent disease
- .Multiple co-morbid condition
- .Ethnic differences
- .Others(Genetic polymorphism,race,etc..)

AGE(children and elderly):

The very young and very old are more susceptible to having adverse reactions.
This reflects age related differences in body

GENDER:

Women appear to be at greater risk of ADRs than men (pregnancy itself affects the absorption, distribution, metabolism and elimination of a drug)

Prior History of ADRs:

Previous history of ADRs can be the highest risk for reappearing the ADRs

Multiple drug therapy (polypharmacy)

Incidence of ADRs from drug interactions increase sharply with the number of drugs taken.

CURRENT DISEASES:

> Drug handling may be altered in patients with impaired metabolism such as renal or liver impairment.

> Disease in which multiple drug treatment occurs are also associated with greater likelihood of ADRs.

PHARMACOKINETIC DIFFERENCES:

There may be increased toxicity from a drug because of :

> genetic factors (eg. difference in enzyme activity)

> or environmental influences (eg. high alcohol intake)

PHARMACEUTICAL factors:

Example include difference in pharmacokinetics (processes by which a drug is absorbed, distributed, metabolized, and eliminated by the body) resulting from different delivery systems and reactions to drug excipients (eg. Binding agents, solvents, antibacterial agents)

INADEQUATE PATIENT KNOWLEDGE

Patient's knowledge about ADRs play an important role in the reduction of ADR's in the population

MULTIPLE CO-MORBID CONDITIONS:

More than two/multiple co-morbid conditions with primary disease may lead to multiple drug with prescription which may be risk for ADR's.

INCOMPLETE MEDICINE RECONCILIATION:

Medicine reconciliation refers to the checking of medicines patients are taking, either prescribed, over the counter, folk medicines, or from other sources.

High risk settings where medicines reconciliation is a problem include acute presentation to the accident and Emergency department and New interactions which may currently hold separate clinical records, e.g. HIV services.

ETHNIC DIFFERENCES:

Ethnic genetic or dietary differences may increase the risk of ADR's.

Example

> interaction of diet with glucose 6-phosphate dehydrogenase deficiency

Example;

>Iron overload resulting from giving iron supplements to sickle cell patients when they do not need it.

>>DETECTING and MONITORING of ADR's:

Following types of methods can be used for detecting type A- ADR's :

- >spontaneous reporting by doctors , pharmacists , nurses , patients , etc.
- >clinical trials(all phases including post-marketing surveillance)
- >Follow up studies
- >prescription event monitoring
- >Experimental studies

Following types of methods can be used for detecting type B-ADR's:

- >spontaneous reporting by doctor ,dentists,pharmacists,nurses,patients,etc.
- >prescription event monitoring
- >case control studies and case control surveillance
- >Diagnosis (episode) registration
- >Vital statistics (mortality , morbidity , birth registers for congenital defects)
- >Drug use record linkage

Monitoring of ADR's:

The following systems can be used for monitoring ADR's:

1.Retrospective Systems

2.Prospective (or) concurrent monitoring System

1.Retrospective Systems:

- >Patient's case charts can reviewed retrospectively by a random or selective process.
 - >Chart screening can be performed by supporting personnel and may be able to generate more reports than voluntary methods.
 - >However retrospective system dose not give any benefit to the patient who experienced the reaction;because the Patient has already been discharged
 - >This system may helpful in generating the data for ADR's ; like high risk drug or high risk patient
 - >This can provide the information on types of ADR's that may be encountered
- So that prospective programs can be developed.

2.Prospective (or) concurrent monitoring System:

- >It offers many benefits;
- because patients can be identified and treated readily .
- >The most commonly used method is the voluntary system , because it is easy to implement and inexpensive

This method is based on the voluntary cooperation of healthcare providers who come into contact with the patient

>Anyone suspecting an ADR voluntarily fills out an ADR report form; which can be forwarded to pharmacy for documentation.

The number of ADR's reported voluntarily may be small.

>This limitation can be overcome by the pharmacist

The pharmacist can follow up the ADR management by ensuring the report form is completed.

>The prospective system benefits the patients who experience a reaction because they are recognized earlier and future patients benefit from information learned from past patients

>Other benefits include the economic impact of reduced hospitalization, efficient and economical drug use and minimized organizational liability.

> Assessment and Management of ADR's:

CAUSALITY assessment scales for ADR's;

Causality assessment is the method by which the extent of relationship between a drug and a suspected

Reaction is established

These scales include:

>karch and lasagna scale

>naranjo's scale

>WHO probability scale (common)

>spanish quantitative imputation scale

>kramer's scale

WHO SCALE :

1.Certain:

>A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration,

>and which cannot be explained by concurrent disease or other drugs or chemicals

>Response to withdrawal plausible

>Rechallenge (If necessary)

2.PROBABLE :

>Event or laboratory test abnormality, with reasonable time to administration of drug

>Unlikely to be attributed to disease or other drugs

>Response to withdrawal clinically reasonable

>Rechallenge not necessary

3.POSSIBLE:

>Event or laboratory test abnormality, with reasonable time relationship to drug intake.

>Could also be explained by disease or other drugs

>Information on withdrawal of drug lacking or unclear

4.UNLIKELY:

>Event or laboratory test abnormality with time to drug intake makes a relationship

improbable(but not impossible)

>Diseases or other drugs provide plausible explanations

5.Unassessable/Unclassified:

>A report suggesting an adverse reaction

>cannot be judged because of insufficient or contradictory information

>Report can not be supplemented or verified

6.CONDITIONAL/UNCLASSIFIED:

>Event or laboratory test abnormality

>More data for proper assessment needed

>Additional data under examination

>>MANAGEMENT OF ADR's:

Discontinue the offending agent if:

>It can be safely stopped

>The event is life -treating or intolerable

>There is reasonable alternative

>Continuing the medication will further exacerbates the patient's condition

CONTINUE the medication if :

>It is medically necessary

>There is no reasonable alternative

>The problem is mild and will resolve with time

>>DIS.continue non-essential medications

>>ADMINISTER appropriate treatment

eg;atropine,glucagon,dextrose,antihistamines

>>PROVIDE supportive or palliative care:

eg; hydration, warm/cold compression ,glucocorticoids,anagesics

>>CONSIDER rechallenge or desensitization

>>Role of pharmacist in the management of ADR's:

>Monitoring patients who are at greater risk of developing ADR's

> Monitoring patient who are prescribed with drugs highly likely to cause ADR's

>Assessing and documenting the patients previous allergic status

>Assessing the patient's drug therapy for its appropriateness

>Assessing possible drug interactions in multiple therapies

>Assisting healthcare professionals in the detection and assessment of ADR's

>Encouraging/stimulating healthcare professionals in reporting an ADR

> Documetation of suspected reported reactions for further reference

>Follow - up of patient s to assess the outcome of the reaction and management

- >Obtained feedback about the reported reaction
- >Educating healthcare professional about the importance of reporting an ADR
- >Educating patient
- >creating awareness about ADR's among healthcare professionals,patients and the public.

- >Preparation and utilisation of promotional materials
- >Communication with other healthcare professionals such as nurses an community pharmacists
- >Presentation of reports in meeting and conferences

- >Conducting workshops/conferences/seminars on ADRs for healthcare professionals
- >Dissemination of signals generated through publication through publication of reports in bulletins or journals

Reference:

A textbook of clinical pharmacy practice by G PARTHASARATHI



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National Pharmacovigilance Programme

(Source: National Pharmacovigilance Protocol, Ministry of Health & Family Welfare, Govt. of India)

India has more than half a million qualified Doctors and 15,000 hospitals having bed strength of 6,24,000. It is the fourth largest producer of pharmaceuticals in the world. It is emerging as an important Clinical trial hub in the world. Many new drugs are being introduced in our country. Therefore, there is a need for a vibrant pharmacovigilance system in the country to protect the population from the potential harm that may be caused by some of these new drugs.

Clearly aware of the enormity of task the Central Drugs Standard Control Organization (CDSCO) has initiated a well structured and highly participative National Pharmacovigilance Programme. It is largely based on the recommendations made in the WHO document titled "Safety Monitoring of Medicinal Products – Guidelines for Setting up and Running a Pharmacovigilance Centre".

The National Pharmacovigilance Programme was officially inaugurated by the Honorable Health Minister Dr. Anbumani Ramadoss on 23 November, 2004 at New Delhi.

The specific aims of the Pharmacovigilance Programme are to:

- contribute to the regulatory assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost effective) use.
- improve patient care and safety in relation to use of medicines and all medical and paramedical interventions.
- improve public health and safety in relation to use of medicines.
- promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

The Programme aims to foster the culture of ADR notification in its first year of operation and subsequently aims to generate broad based ADR data on the Indian population and share the information with global health-care community through WHO-UMC.

Under the program 26 peripheral centers, 5 Regional Centers and 2 Zonal Centers were established. The Peripheral centers will record the Adverse Events (AE) and send to the Regional Centers. They in turn collate and scrutinize the data received from the Peripheral Centers and submit

to the National Pharmacovigilance Centre. The Zonal Centre will also provide training, general support and coordinate the functioning of the Regional Centers.

The National Pharmacovigilance Advisory Committee (NPAC) oversee the performance of various Zonal, Regional and Peripheral Pharmacovigilance centers as well as recommend possible regulatory measures based on the data received from various centers. It also oversees data collection and assessment, interpretation of data as well as publication of ADR monitoring data. The Committee also periodically evaluates their protocol compliance levels to ensure that the data received is homogenous and can be scientifically pooled for informed regulatory decisions. Wherever necessary, NPAC also seeks the opinion of experts in various specializations.

NATIONAL PHARMACOVIGILANCE POLICY

Since there are considerable social and economic consequences of adverse drug reactions and the positive benefit/cost ratio of implementing appropriate risk management – there is a need to engage health-care professionals and the public at large, in a well structured programme to build synergies for monitoring adverse drug reactions.

The purpose of the programme is to collate data, analyze it and use the inferences to recommend informed regulatory interventions, besides communicating risks to healthcare professionals and the public.

The National Pharmacovigilance Programme will have the following milestones:

- **Short-term objectives:** To foster a culture of notification
- **Medium-term objectives:** To engage several healthcare professionals and NGOs in the drug monitoring and information dissemination processes.
- **Long-term objectives:** To achieve such operational efficiencies that would make Indian National Pharmacovigilance Programme a benchmark for global drug monitoring endeavors.

NATIONAL PHARMACOVIGILANCE PROGRAMME

Before a product is marketed, experience of its safety and efficacy is limited to its use in clinical trials, which are not reflective of practice conditions as they are limited by the patient numbers and duration of trial as well as by the highly controlled conditions in which Clinical Trials are conducted.

The conditions under which patients are studied during the pre-marketing phase do not necessarily reflect the way the medicine will be used in the hospital or in general practice once it is marketed. Information about rare but serious adverse drug reactions, chronic toxicity, use in special groups (e.g. pregnant women, children, elderly) and drug interactions are often incomplete or not available. Certain adverse drug reactions may not be detected until a very large number of people have received the medicine. Pharmacovigilance is therefore one of the important post-marketing tools in ensuring the safety of pharmaceutical and related health products.

Pharmacovigilance is defined as the detection, assessment and prevention of adverse drug reactions in humans. It is the process of:

- Monitoring medicines as used in everyday practice to identify previously unrecognized adverse effects or changes in the patterns of their adverse effects
- Assessing the risks and benefits of medicines in order to determine what action,

- if any, is necessary to improve their safe use
- Providing information to users to optimize safe and effective use of medicines
- Monitoring the impact of any action taken

FRAMEWORK FOR PHARMACOVIGILANCE IN INDIA

The Central Drugs Standard Control Organization (CDSCO) has initiated a country-wide Pharmacovigilance programme under the aegis of DGHS, Ministry of Health & Family Welfare, Government of India.

Directorate General of Health Services

The programme is coordinated by the National Pharmacovigilance Centre at CDSCO. The National Centre is operating under the supervision of the National Pharmacovigilance Advisory Committee to recommend procedures and guidelines for regulatory interventions.

THE NATIONAL PHARMACOVIGILANCE CENTRE AT CDSCO

The National Pharmacovigilance Centre is based at CDSCO and shall:

1. monitor the adverse drug reactions of medicines in order to identify previously unexpected adverse drug reactions or indicate that certain reactions occur more commonly than previously believed. This will include the collation, review and evaluation of all spontaneous ADR reports received by the unit on a nation-wide basis. This information will then be keyed into the ADR database for use in aggregate analysis. These reports shall also be submitted to the WHO International Drug Monitoring Programme for international collaboration on drug safety.
2. review Periodic Safety Update Reports (PSURs) submitted by pharmaceutical companies. Pharmaceutical companies are required to submit the PSURs of all new chemical drugs. PSURs shall be expected to be submitted every 6 monthly for the first 2 years of marketing in India, and annually for the subsequent 2 years.
3. maintain contacts with international regulatory bodies working in pharmacovigilance and exchange information on drug safety.
4. assess the regulatory information relating to safety in order to determine what action, if necessary, needs to be taken to improve safe use. Based on the available data, the Advisory Committee shall make recommendations on product label amendments, product withdrawals and suspension.
5. provide information to end-users through adverse drug reaction news, bulletins, drug alerts and seminars.

For further information please contact:

The National Pharmacovigilance Centre
Office of Drugs Controller General of India,
Central Drugs Standard Control Organization,
Room No. 347-A,
D.G.H.S., Ministry of Health & Family Welfare,
Nirman Bhawan, New Delhi 110 011.
Tel: (11) 23018806 Fax: (11) 23012648
Email: dci@nb.nic.in www.cdscn.nic.in

Glossary of terms

National Pharmacovigilance Programme (NPPI)

The nation wide programme, sponsored and coordinated by the country's central drug regulatory agency – Central Drugs Standard Control Organization (CDSCO) – to establish and manage a data base of Adverse Drug Reactions (ADR) for making informed regulatory decisions regarding marketing authorization of drugs in India for ensuring safety of drugs.

Peripheral Pharmacovigilance Centers (PPC)

Primary pharmacovigilance centers. Relatively smaller medical institutions including individual medical practitioners' clinics, private hospitals, nursing homes, pharmacies etc. First contact ADR data collection unit at a health care facility. They would be identified and coordinated by RPCs / ZPCs in consultation with CDSCO.

Regional Pharmacovigilance Centers (RPC)

Secondary pharmacovigilance centers. Relatively larger healthcare facilities attached with medical colleges. They would act as second level centers in the administrative structure of the NPPI. They will function as first contact ADR data collection units also. They would be identified and coordinated by ZPCs in consultation with the CDSCO.

Zonal Pharmacovigilance Centre (ZPCs)

Tertiary pharmacovigilance centers. Large healthcare facilities attached with medical colleges in metro cities identified by the CDSCO for the purpose. They would act as third level centers in the administrative structure of the NPPI. They will function as First contact ADE data collection units also.

Coordinator

Designated in-charge of a particular participating PVig centre

Investigator

A healthcare professional involved in investigation of drug related adverse events.

Notifier

Any person who suspects to have experienced / observed an ADR and informs any participating Pharmacovigilance centre about it.

Reporter

A healthcare professional reporting ADR on the ADR form.

Monitoring

The process of overseeing drug related adverse events at the PVigC participating in the PVig Programme.

Reporting

The process of providing ADR information by filling in the ADR form appropriately and forwarding

the same to the appropriate level.

Notification

Process of informing by a notifier to any participating pharmacovigilance centre about the occurrence of a suspected ADR. The process may involve informing over telephone, in person, email, fax or any other means of communication-verbal or written. All notifiers must give their contact details. Appropriate and adequate measures must be taken to keep track of the notifier. Any follow up action will be initiated on a notification only after the due verification of the notifier. If the notifier cannot be traced back, it will be recorded on the notification slip before closing the case.

Notification slip

A pre-designed structured form made available by the NPPI for written communication of a suspected ADR by the notifier duly signed by him/her wherever feasible.

National pharmacovigilance programme India

ADR Form

It's the pre-designed structured form issued by NPPI to record ADR.

Archiving

This is to be done at the Regional / Zonal Centers for a period of 5 years

Audit

A systematic and independent examination (conducted by personnel, independent of the centre) of center's activities and documents to determine whether center's activities were conducted and the data were recorded, analysed and accurately reported according to the protocol

Confidentiality

In a confidential / secretive manner.

Side Effect

Any unintended effect of a pharmaceutical product occurring at doses normally used in man which is related to the pharmacological properties of the drug.

Comment: This is an old term and is broad enough to include both positive and negative effects of a drug apart from its main properties or indications. Some use the term as synonymous with 'adverse reaction', but the proposed definition will improve clarity of use of this term.

Adverse Event / Adverse Experience

Any untoward medical occurrence that may present during treatment with a pharmaceutical product at the same time, does not necessarily have a causal relationship with this treatment.

Comment: This is a more recent term which some use interchangeably with 'adverse reaction', but, as indicated, it is better reserved for clinical phenomena occurring during drug treatment where causality cannot be or is not ascertained.

Signal

Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incomplete.

Comment: This describes the first alert of a problem with a drug. By its nature a signal cannot be regarded as definitive but indicates the need for further enquiry or action. On the other hand it is prudent to avoid a multiplicity of signals based on single case reports since follow up of all such would be impractical and time consuming. The definition allows for some flexibility in approach to signal based on the characteristics of individual problems. Some would like a 'signal' to include new information on positive drug effects, but this is outside the scope of a drug safety Programme.

Adverse Reaction

WHO Technical Report No 498 (1972); 'A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.'

Comment: This basic definition includes all doses prescribed clinically, but is intended to exclude accidental or deliberate overdose. The sub classification of 'unexpected' was included to facilitate understanding of the type of adverse reaction which is most important to report to drug monitoring agencies.

Unexpected Adverse Reaction

An adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from characteristics of the drug.

Serious Adverse Event or Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- results in death
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- is life-threatening

To avoid any confusion or misunderstanding of the difference between the terms 'serious' and 'severe', the following note of clarification is provided: The term 'severe' is not synonymous with serious. 'Severe' is used to describe the intensity (severity) of a specific event (as in mild, moderate or severe); the event itself, however, may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient/event outcome or action criteria serves as guide for defining regulatory reporting obligations.

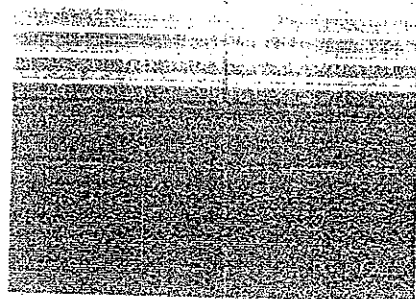




World Health Organization

SAFETY MONITORING of MEDICINAL PRODUCTS

Guidelines for setting up and running
a Pharmacovigilance Centre



SAFETY MONITORING of MEDICINAL PRODUCTS

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a Pharmacovigilance Centre



World Health Organization



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INTRODUCTION

This booklet aims to provide practical guidelines and information for the setting up of new Pharmacovigilance Centres.

The history of international pharmacovigilance goes back as much as thirty years, when the twentieth World Health Assembly adopted a resolution to start a project on the feasibility of an international system of monitoring adverse reactions to drugs. This resolution was the basis of WHO's Programme on International Drug Monitoring.

At this moment more than fifty countries participate in this Programme. The world of today no longer is as it was at the time the Programme was established. New developments challenge our attention, require adequate reaction, and raise new questions in adverse drug reaction monitoring.

A few examples may illustrate this: The current financial climate forces national authorities to find ways to contain the cost of pharmaceutical care. In some countries a strong tendency to self-medication can be seen, and many pharmaceuticals that used to be prescription only are now available over the counter. The question arises: Does this have consequences for the safety of the patients?

Traditional medication is increasing in the Western world, but the use of herbal medicines risks escaping control. Nonetheless several herbal medicines are quite active, and may be associated with adverse effects. Continuing vigilance is needed.

A phenomenon that has received the attention it deserves in only the last few years, is the prevalence of counterfeit drugs on the market. Instances of calamities, claiming the lives of numerous children due to the use of a toxic solvent have been documented. Drug monitoring programmes may well be instrumental in detecting such products.

The way drugs are being monitored has changed, both internationally as well as on the national level. The WHO Programme was established with ten countries, all of them highly developed. Gradually more countries showed interest and eventually joined the Programme, once they felt that their national systems were sufficiently developed.

Criteria for this development are not only the functioning of the centre in question itself, but also the presence of an effective drug regulatory body in the country that has the will and the potential to react to signals emanating from the centre and to take proper regulatory measures. WHO considers this point as vital: *a pharmacovigilance system must be backed up by the regulatory body.*

In particular the last five years have seen an increasing number of countries expressing the wish to participate in the Programme, and several countries are in contact with WHO and the WHO Collaborating Centre the Uppsala Monitoring Centre in Sweden, to receive support with the development of their national programmes. Practically all industrialised countries already participate; new countries now are all coming from the developing world. In several cases new countries have requested WHO's collaboration and assistance in setting up a monitoring system.

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At national level also many changes have been taking place. In the original model a pharmacovigilance system is strongly centralised, and consists of one national centre collecting reports from health professionals in the country. Many countries, however, now prefer a more decentralised system, with a national centre functioning as a focal point for some regional or local centres. Several countries are in the process of starting their systems (conforming to this model), and countries with a long-standing experience in drug monitoring are changing their programmes into a decentralised organisation. Both schemes are similar in many aspects.

Monitoring Centres always start on a very small scale, often with only one enthusiastic (part-time) professional. These pioneers in their field need help and guidance. There is a need to provide such emerging centres with some information:

- the materials and resources required
- how to operate
- what kind of support is needed
- where to find adequate literature sources
- what kind of assistance can be expected
- what is the relationship to be sought with drug information centres and poison information systems, and so on.

WHO has reacted to this perceived need by holding a consultative meeting that was asked to share experience and competence through discussion of a draft guideline, prepared by Dr Ronald Meyboom. On the basis of this discussion this document has been produced, that is intended to be used by new monitoring centres, in order to prevent them from losing time and money as a consequence of the lack of experience. It discusses practical aspects of how to run a pharmacovigilance centre at the technical level, with down-to-earth recommendations. We hope that this guideline booklet helps people on the way to a well-organised and well-run pharmacovigilance centre.

This guideline booklet is based on the proceedings of a Consultation on Setting up and Running of a Pharmacovigilance Centre, World Health Organization, Geneva, 26-27 June 1996.

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1. WHY PHARMACOVIGILANCE?

The information collected during the pre-marketing phase of a medical drug is inevitably incomplete with regard to possible adverse reactions (for definition see Glossary):

- tests in animals are insufficiently predictive of human safety
- in clinical trials patients are selected and limited in number, the conditions of use differ from those in clinical practice and the duration of trials is limited
- information about rare but serious adverse reactions, chronic toxicity, use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available.

Pharmacovigilance is needed in every country, because there are differences between countries (and even regions within countries) in the occurrence of adverse drug reactions and other drug-related problems. This may be because of differences in:

- drug production
- distribution and use (e.g. indications, dose, availability)
- genetics, diet, traditions of the people
- pharmaceutical quality and composition (excipients) of locally produced pharmaceutical products
- the use of non orthodox drugs (e.g. herbal remedies) which may pose special toxicological problems, when used alone or in combination with other drugs.

Data derived from within the country or region may have greater relevance and educational value and may encourage national regulatory decision-making. Information obtained in a certain country (e.g. the country of origin of the drug) may not be relevant to other parts of the world, where circumstances may be different. When information from a region itself is not available, it may take longer before a problem becomes known to drug regulatory authorities, physicians, pharmacists, patients and pharmaceutical companies.

On the other hand, international monitoring such as the WHO International Drug Monitoring Programme may provide information on possible safety issues which may not yet have emerged within the country's data. Pharmacovigilance is needed for the prevention of drug-induced human suffering and to avoid financial risks associated with unexpected adverse effects. In conclusion, medicines on the market need continuous monitoring in every country.

2. DEFINITION AND AIMS

Pharmacovigilance is concerned with the detection, assessment and prevention of adverse reactions to drugs. Major aims of pharmacovigilance are:

1. Early detection of hitherto unknown adverse reactions and interactions
2. Detection of increases in frequency of (known) adverse reactions
3. Identification of risk factors and possible mechanisms underlying adverse reactions
4. Estimation of quantitative aspects of benefit/risk analysis and dissemination of information needed to improve drug prescribing and regulation.

The ultimate goals of pharmacovigilance are:

- the rational and safe use of medical drugs
- the assessment and communication of the risks and benefits of drugs on the market
- educating and informing of patients.

Spontaneous reporting – a regional or country-wide system for the reporting of suspected adverse drug reactions – is the primary method in pharmacovigilance. In addition, other methods of data-collection exist or are under development (see § 8.5 and 10).

3. HOW TO START A PHARMACOVIGILANCE CENTRE

A new pharmacovigilance centre can start operating very quickly. The development of a pharmacovigilance system, however, from the first and uncertain stage to becoming an established and effective organisation, is a process that needs time, vision, dedication, expertise and continuity. The most promising location for a new pharmacovigilance centre may depend on the organisation and development of the healthcare system in the country and other local issues.

A governmental department (health authority, drug regulatory agency) can be a good host for a pharmacovigilance centre. However, any department in a hospital or academic environment, working in clinical pharmacology, clinical pharmacy, clinical toxicology or epidemiology, may be a suitable starting point for pharmacovigilance. The reporting of adverse drug reactions may start locally, perhaps in one hospital, then extend to other hospitals and family practices in the region, and progress step by step into a national activity. In some countries professional bodies such as the national medical association may be a good home for the centre.

When the centre is a country-wide organisation from the start, it should be remembered that much effort, especially in effective communications, will be needed before a substantial proportion of practitioners are contributing.

When a centre is part of a larger organisation (for example, a poison control unit, a

clinical pharmacology department, or a hospital pharmacy) providing administrative continuity, it can get going as long as there is one professional (e.g. a physician or pharmacist) available who is primarily responsible for pharmacovigilance.

Whatever the location of the centre, pharmacovigilance is closely linked to drug regulation. Governmental support is needed for national co-ordination. Pharmacovigilance is nobody's individual privilege. Good collaboration, co-ordination, communications and public relations are needed for coherent development and for the prevention of unnecessary competition or duplication.

3.1 Basic steps in setting up a Pharmacovigilance Centre

Prepare a plan according to the points below for the establishment of the pharmacovigilance system.

1. Make contacts with the health authorities and with local, regional or national institutions and groups, working in clinical medicine, pharmacology and toxicology outlining the importance of the project and its purposes.
2. Design a reporting form (see § 4.1) and start collecting data by distributing it to hospital departments, family practitioners, etc.
3. Produce printed material to inform health professionals about definitions, aims and methods of the pharmacovigilance system.
4. Create the centre: staff, accommodation, phone, word processor, database management capability, bibliography etc.
5. Take care of the education of pharmacovigilance staff with regard, for example, to:
 - data collection and verification
 - interpreting and coding of adverse reaction descriptions
 - coding of drugs
 - case causality assessment
 - signal detection
 - risk management.
6. Establish a database (administrative system for the storage and retrieval of data; see also § 7.1).
7. Organise meetings in hospitals, academia and professional associations, explaining the principles and demands of pharmacovigilance and the importance of reporting.
8. Promote the importance of reporting adverse drug reactions through medical journals, other professional publications, and communications activities.

9. Maintain contacts with international institutions working in pharmacovigilance, e.g. the WHO Department of Essential Drugs and Medicines Policy (Geneva) and the Uppsala Monitoring Centre, Sweden (see page 24 for all contact details).

4. REPORTING OF ADVERSE DRUG REACTIONS

Spontaneous reporting – a regional or country-wide system for the reporting of suspected adverse drug reactions – is currently the major source of information in pharmacovigilance.

4.1 Reporting form

A case report in pharmacovigilance can be defined as: *A notification relating to a patient with an adverse medical event (or laboratory test abnormality) suspected to be induced by a medicine.*

A case report should (as a minimum to aim at) contain information on the following elements:

1. The patient: age, sex and brief medical history (when relevant). In some countries ethnic origin may need to be specified.
2. Adverse event: description (nature, localisation, severity, characteristics), results of investigations and tests, start date, course and outcome.
3. Suspected drug(s): name (brand or ingredient name + manufacturer), dose, route, start/stop dates, indication for use (with particular drugs, e.g. vaccines, a batch number is important).
4. All other drugs used (including self-medication): names, doses, routes, start/stop dates.
5. Risk factors (e.g. impaired renal function, previous exposure to suspected drug, previous allergies, social drug use).
6. Name and address of reporter (to be considered confidential and to be used only for data verification, completion and case follow-up).

Reporting should be as easy and cheap as possible. Special free-post or business reply reporting forms, containing questions 1-6 mentioned above, can be distributed throughout the target area to healthcare professionals at regular intervals (for example, four times a year).

It may take the yearly distribution of hundreds of thousands of forms to harvest only some hundreds of case reports. It may be effective to include reply-paid reporting forms in the

national formulary, drug bulletin or professional journals. Also telephone, fax and electronic mail or internet may be easy means of reporting where reliable technology is available and accessible.

4.2 Reporting by whom?

Professionals working in healthcare are the preferred source of information in pharmacovigilance, for example family practitioners, medical specialists and pharmacists. Dentists, midwives, nurses and other health workers may also administer or prescribe drugs and should report relevant experiences.

In addition pharmacists and nurses can play an important role in the stimulation of reporting and in the provision of additional information (for example, on co-medication and previous drug use).

Pharmaceutical manufacturers, being primarily responsible for the safety of their products, have to ensure that suspected adverse reactions to their products are reported to the competent authority. If adverse reactions are reported directly by patients to the national or local centre, it is useful to consider the possibility of communication with their physicians for additional information and data verification.

4.3 What to report?

In the early stages of any pharmacovigilance system, reports on all suspected adverse reactions - known or not, serious or not - are welcome and useful, because it is necessary to create a *notification culture* in which the instinctive response to any suspected adverse drug reaction is to report it. Healthcare professionals need to learn how and what to notify, and the staff of the pharmacovigilance centre need to gain experience in assessment, coding and interpretation.

In established pharmacovigilance systems it is common practice to request the reporting of all suspected reactions, including minor ones for new drugs. For established drugs the reporting of serious or unusual suspected adverse reactions is of particular importance, whereas known and minor reactions are of less interest (see Glossary for the definition of a *serious reaction*). If an increased frequency of a given reaction is suspected this is also a reason for reporting.

Although pharmacovigilance is primarily concerned with pharmaceutical medicines (including radiologic contrast media, vaccines and diagnostics), adverse reactions associated with drugs used in traditional medicine (e.g. herbal remedies) should also be considered. Special fields of interest are drug abuse and drug use in pregnancy (teratogenicity) and lactation.

In addition, the reporting of lack of efficacy and suspected pharmaceutical defects is

recommended, especially when there is the possibility of manufacturing problems, counterfeit pharmaceuticals or of the development of resistance (e.g. antibiotics). Pharmacovigilance and poison control are closely related activities, since the problems encountered with accidental or intentional overdose may cast doubt on the safety of a medical drug.

Also, adverse reactions to cosmetics may need to be reported, especially when cosmetics contain obsolete or toxic ingredients (e.g. mercury compounds or corticoids in bleaching creams). If there is no other organisation in the country dealing with the issues, a pharmacovigilance centre may also cover problems related to medical devices and equipment, although different expertise may be needed.

The reporting of adverse events occurring during clinical trials are not covered by these guidelines. Recommendations on how to record and report such events are included in guidelines on good clinical practice for trials on pharmaceutical products (GCP).

4.4 Mandatory or voluntary reporting?

In many countries the reporting of adverse drug reactions is voluntary, but in an increasing number of countries some legal reporting obligations on healthcare professionals have been established (although a penalty is not usually associated with failure to report). Little information is available regarding the advantages and disadvantages of such obligations. In addition, in many countries it is mandatory for pharmaceutical companies to report suspected adverse drug reactions to the health authorities.

5. SPECIAL ISSUES IN REPORTING

5.1 Central or decentralised reporting?

As a rule spontaneous monitoring aims at country-wide reporting and the use of one central pharmacovigilance database to obtain a national overview. The collection of data may nevertheless be more successful in number and quality if reporting is organised regionally, especially when countries are large or have regional cultural differences. Regional centres with short lines of communication to healthcare professionals may improve communications and feedback. When regional centres are used, good collaboration and data-exchange with the national centre needs to be ensured. Regionalisation requires more staff and facilities and can therefore be more expensive.

5.2 Stimulation of reporting

The reporting of adverse reactions needs continuous stimulation. It is important to achieve the development of a positive attitude towards pharmacovigilance among healthcare professionals so that adverse reaction reporting becomes an accepted and understood routine. In summary, the following may stimulate reporting:

- easy access to pre-paid reporting forms and other means of reporting
- acknowledging the receipt of adverse drug reaction reports by personal letter or phone call
- providing feedback to reporters in the form of articles in journals, adverse drug reaction bulletins or newsletters
- participation of the centres staff in pre- and postgraduate education and scientific meetings
- collaboration with local drug or pharmacovigilance committees
- collaboration with professional associations
- integration of pharmacovigilance in the (further) development of clinical pharmacy and clinical pharmacology in a country.

5.3 Under-reporting

Under-reporting is a common phenomenon in all countries. Correcting for under-reporting is difficult, however, because its extent is unknown and very variable. Even at established centres the reported proportion of serious reactions may not be more than 10%. Several of the countries participating for many years in the WHO Drug Monitoring Programme receive 200 or more adverse reactions per million inhabitants annually from about 10% of physicians. In many other countries, however, the reporting rates are much lower.

Under-reporting may delay signal detection and cause underestimation of the size of a problem. However, in signal detection not only the quantity but also the relevance of case reports and the quality of data are important.

There are also a number of more elusive issues which require attention. Sometimes healthcare professionals fear that the acknowledgement of adverse reactions may reflect negatively on their competence or put them at risk of litigation. Some are reluctant to report adverse reactions because of doubts regarding the causal role of the drug (although, of course, it is essential that suspected reactions are reported). Under-reporting is both a technical and a psychological issue. Clarity of criteria for reporting, simple procedures and good motivational practice are all influential in addressing the problem.

6. PRACTICALITIES IN THE ORGANISATION OF A PHARMACOVIGILANCE CENTRE

6.1 Staff

The expertise desirable in the routines of a pharmacovigilance centre includes (see also § 7):

- clinical medicine
- pharmacology
- toxicology, and
- epidemiology.

However, a new pharmacovigilance centre often starts with only a part-time expert - usually a physician or a pharmacist - and some secretarial support. It may soon become necessary to have one expert who is responsible for pharmacovigilance for most of his/her time and for secretarial assistance to be expanded (see § 6.3, Continuity). When the reporting of adverse reactions increases, staff resource requirements may be calculated by assuming that the average assessment time per case report is about one hour.

6.2 Useful equipment (includes)

- multi-connection telephone
- computer (database, see § 7.1; word processor)
- printer (computer linked)
- fax
- e-mail
- photocopier.

6.3 Continuity

Continuity in accessibility and service is a basic feature of a successful pharmacovigilance centre. The centre therefore needs a permanent secretariat, for phone calls, mail, maintenance of the database, literature documentation, co-ordination of activities, etc. Secretarial continuity may be achieved through collaboration with related departments, provided there is sufficient capacity.

6.4 Advisory Committees

A multi disciplinary advisory committee is desirable, to support the pharmacovigilance centre with regard to the quality of the procedures in:

- data collection and assessment
- the interpretation of the data
- the publication of information.

An advisory committee may represent the following disciplines:

- general medicine
- pharmaceuticals
- clinical pharmacology
- toxicology
- epidemiology
- pathology
- drug regulation and quality assurance
- drug information
- phytotherapy.

In addition a network of experienced advisors in various specialisations is helpful. When the centre is located in a hospital, specialised expertise is usually within easy reach.

6.5 Information service

The provision of a high quality information service to healthcare professionals is a basic task of a pharmacovigilance centre and a major instrument in the stimulation of reporting. For this purpose and for the assessment of case reports the centre should have access to a comprehensive and up-to-date literature information database (a list of relevant literature references may be obtained from *the Uppsala Monitoring Centre*).

Location of the centre in a large hospital usually has the advantage of a library within reach. National pharmacovigilance centres can have on-line access to the database of *the UMC* and be on the mailing lists of adverse drug reaction and drug bulletins produced by the World Health Organization and many national or regional centres throughout the world (ask *the UMC* for addresses or see WHO contacts on page 24).

6.6 Communications

A bulletin or newsletter distributed to all healthcare professionals or a regular column in reputed (medical and pharmaceutical) journals are good means for the dissemination of information. Prompt data-sheet amendments are important, but data-sheets may be printed infrequently and their educational impact may not be large. In urgent cases of sufficient importance 'Dear Doctor' letters may alert the profession.

6.7 Poison Control and Drug Information Centres

Poison control and drug information centres have much in common with pharmacovigilance centres, both in organisation and from a scientific point of view. If pharmacovigilance is started in a country where a poison control or drug information centre is already in place it may be efficient to develop the pharmacovigilance system in conjunction with it. Expensive facilities such as secretariat, computer resources and library services can be shared.

In any case close collaboration between these organisations is desirable.

7 ASSESSMENT OF CASE REPORTS

The assessment of adverse reaction case reports needs combined expertise in clinical medicine, pharmacology and toxicology, and epidemiology. This expertise can be developed by training the centre's staff and by the use of specialised consultants. In the assessment of case reports the following elements can be recognised:

1. **Quality of documentation** (e.g. completeness and integrity of data, quality of diagnosis, follow-up). The basic elements of a case report are listed in § 4.1.
2. **Coding.** Drug names should be registered in a systematic way, for example by using the WHO Drug Dictionary (which is based on the INN nomenclature and the ATC classification). For the coding of the adverse events the WHO Adverse Reaction Terminology (WHOART), or another internationally recognised terminology (e.g. MedDRA) should be used.
3. **Relevance** with regard to the detection of new reactions, drug regulation, or scientific or educational value. The following questions especially may be asked:
 - **New drug?** Products on the market less than five years are usually considered new drugs
 - **Unknown reaction?** (i.e. not included in the approved Summary of Product Characteristics or 'unlabelled'). Also important is whether the reaction is described in the literature, e.g. national drug formulary, Martindale, Meyler's

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Side Effects of Drugs. (Ask *the* Uppsala Monitoring Centre for books and other information sources)

■ **Serious reaction?** (See Glossary).

4. **Identification of duplicate reports.** Certain characteristics of a case (sex, age or date of birth, dates of drug exposure, etc.) may be used to identify duplicate reporting.

5. **Causality assessment or imputation.** With few exceptions, case reports describe *suspected* adverse drug reactions. Various approaches have been developed for the structured determination of the likelihood of a causal relationship between drug exposure and adverse events, for example by the WHO Drug Monitoring Programme (see Glossary), the European Commission, and the French national pharmacovigilance programme. These systems are largely based on four considerations:

- the association in time (or place) between drug administration and event
- pharmacology (including current knowledge of nature and frequency of adverse reactions)
- medical or pharmacological plausibility (signs and symptoms, laboratory tests, pathological findings, mechanism)
- likelihood or exclusion of other causes.

The WHO causality categories have the advantages of being internationally agreed and easy to use. Definitions for selected adverse reactions have been worked out and reached by international agreement. For some of these reactions special causality algorithms have also been developed (Bénichou, 1994).

7.1 Data-processing

In the early stages case-reports can be managed manually. When reporting increases, a computer system enabling the processing and retrieval of cases according to suspected drugs and adverse reactions is generally advisable.

The computer system used should include a hierarchical drug file allowing drugs to be recorded according to product name, generic name and therapeutic category. Similarly a hierarchical adverse reaction terminology should be employed. Hierarchical systems for the recording of drugs and adverse reactions are necessary to allow for specific recording of detailed case information while still permitting retrieval of information at higher levels.

As far as possible internationally recognised terminologies and classifications of drugs (ATC, INN) and adverse reactions (e.g. WHOART, MedDRA) should be used, to facilitate international comparisons of results and international transfer of data. Special care should be taken to attain compatibility with the reporting requirements of the WHO Drug Monitoring Programme. Detailed instructions on how to organise computerised data for submission to the WHO database are obtainable from *the* Uppsala Monitoring Centre. It may not be cost-effective to design a computer system for the management of adverse

reaction reports from scratch. Commercial programmes are available which have been appropriately tested and can be customised according to local needs including local languages.

8. USE OF THE DATA

Data collected in pharmacovigilance can be used in a variety of ways.

8.1 Hypothesis generation and strengthening

A major aim of pharmacovigilance is the early detection of hypotheses or signals (see Glossary) with regard to possible adverse reactions. Early signals may be too uncertain, however, to justify firm conclusions and regulatory action, and may need further study (see § 8.5). A signal may be strengthened by combining the experiences reported in various countries. Therefore international collaboration is important.

8.2 Drug regulation

After approval of a medicinal product, all available domestic and international safety information is continuously monitored by the drug regulatory authority and the pharmaceutical company concerned. Often problems can be solved by adaptation of the approved product information (inclusion of new adverse effects, warnings, or indication changes). Sometimes stronger restrictive actions are needed, with withdrawal of the marketing authorisation as the extreme. For the approval of a given drug in a given country, it may be very helpful to have information on the experiences with the drug in countries where it is already in use (e.g. through collaboration with the Uppsala Monitoring Centre).

8.3 Information

For the dissemination of information of current importance or interest to healthcare practitioners, an adverse drug reactions bulletin or a column in medical and pharmaceutical journals may be very helpful. In the case of an emergency, a letter directly to all doctors and pharmacists may be needed. Usually such actions take place in collaboration with the regulatory authority and the pharmaceutical company's experts.

8.4 Education and feedback

Continuous pre- and postgraduate education of healthcare professionals is an important aspect of pharmacovigilance. Appropriate educational activities will improve knowledge and awareness of adverse drug reactions and stimulate reporting. Drug information officers and local or national Formulary Committees may benefit from close collaboration with the pharmacovigilance centre.

8.5 Limitations regarding the use of the data

Usually case reports of suspected adverse reactions may be influenced by all sorts of bias. The interpretation of pharmacovigilance data may be difficult. Often signals are unsubstantiated and require further study for confirmation or refutation (hypothesis testing) and for the assessment of the reaction frequency, for example, as needed for drug regulatory decision-making.

On the one hand a pharmacovigilance centre has the task to stimulate the use of the collected data by healthcare professionals, and on the other hand to ensure that the heterogeneous and largely unproven data are used in a careful and scientifically (and socially) responsible way.

The spontaneous reporting system is especially helpful in the detection of adverse reactions that are specific or occur in a suggestive time-relationship with drug use (e.g. anaphylactic shock), but may be less effective in studying other sorts of adverse reactions (e.g. cancer development). The potential of the spontaneous reporting system to determine the true frequency of adverse reactions is limited.

The detailed reporting of histories of patients with iatrogenic injury and the subsequent use of the reports are to a variable extent subject to rules regarding privacy and medical secrecy. Confidentiality of personal data is needed. The complex of details in a patient history may be as personal as a finger print and therefore a potential identifier. It is advisable for a pharmacovigilance centre to establish data-management protocols, identifying legitimate data-users and describing which data elements are available to whom and for which purpose and which uses are excluded. Confidentiality primarily concerns the secrecy of the identity of all individuals (patient, reporter, doctor) and institutions (hospital) involved. In many countries case report summaries are not considered confidential.

Besides legal obligations, the basis of spontaneous monitoring is the commitment of healthcare practitioners and patients together to make information available. If pharmacovigilance data were used against the wish of reporters, the system as a whole might collapse.

9. RELATIONS WITH OTHER PARTIES

- 9.1 *The Drug Regulatory Authority* in the country needs to be informed about suspected adverse reactions without delay, especially when unusual (e.g. reactions not included in the approved Summary of Product Characteristics) or serious. In addition, a pharmacovigilance centre should inform the regulatory authority about any cluster of case reports that is of possible interest, or when an adverse reaction is reported in high or increasing frequency.
- 9.2 *Pharmaceutical companies* need the same information as the regulatory authority. It will depend on the local situation whether companies are to be informed directly or via the regulatory authority.
- 9.3 A pharmacovigilance centre should seek the support of *professional medical and pharmaceutical associations*. In the case of an emergency, these associations should be informed in good time.
- 9.4 A new pharmacovigilance centre should make contact with the **World Health Organization** in Geneva and the **WHO Collaborating Centre for International Drug Monitoring (the UMC)** in Uppsala, Sweden.
- 9.5 In addition it may be helpful to make contacts with *national pharmacovigilance centres* in nearby countries. When more experienced, such centres may be helpful with staff training.
- 9.6 *Academia*: The need for pharmacovigilance and the nature of its procedures are a natural part of the curriculum of pre-graduate training. In addition a pharmacovigilance centre may contribute to and participate in postgraduate educational programs. Findings or hypotheses from the pharmacovigilance system may be of potential interest for further study with regard to mechanisms, reaction frequency, and so on, to academic pharmacological or epidemiological institutions and departments.
- 9.7 *Media and consumer organisations*: Support from national associations of consumers and patients may add to the general acceptance of pharmacovigilance. Good relations with leading journalists may be helpful, e.g. for general public relations and as part of the *risk management* strategy whenever an acute drug problem arises. Special attention may be needed to explain to journalists the limitations of pharmacovigilance data (see § 8.5).

10. OTHER SOURCES OF INFORMATION

Spontaneous Reporting is especially useful in picking up signals of relatively rare, serious and unexpected adverse reactions. For less rare adverse reactions several other methods may be used, e.g. clinical trials or cohort studies. In addition to spontaneous reporting several other methods have become available to provide data relevant to pharmacovigilance. Examples are: Prescription Event Monitoring, Case-Control

Surveillance and linkage of records from multipurpose databases. In addition, drug utilisation data is of value in safety assessment.

11. FUNDING

An estimation of the amount of money needed for pharmacovigilance can be calculated as a function of the rate of reporting required and the size of the population (see § 5.3 and 6.1). The collection of quantitatively and qualitatively good data and the careful assessment and distribution of such information obviously have a price. A pharmacovigilance centre should have some basic, regular source of funding in order to ensure continuity in its work. Such funding may be obtained as part of the drug registration fee, or through a special mandatory pharmacovigilance contribution. Both can be included in the budget of the drug regulatory authority.

Apart from the basic resources, the centre may try to get additional funding from various parties with an interest in pharmacovigilance. Institutions that may be approached include:

- health insurance companies and health insurance funds
- university departments
- professional associations
- governmental departments with an interest in drug safety.

In view of the great commercial and public health consequences of adverse reactions, the continuity of the funding of pharmacovigilance should be guaranteed and not be susceptible to possible pressure groups, political changes or economic factors.

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GLOSSARY

A *drug* or *medicine* is 'a pharmaceutical product, used in or on the human body for the prevention, diagnosis or treatment of disease, or for the modification of physiological function'.

An *unexpected adverse reaction* is 'an adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorisation, or expected from characteristics of the drug'. Here the predominant element is that the phenomenon is unknown.

A *side effect* is 'any unintended effect of a pharmaceutical product occurring at doses normally used in man, which is related to the pharmacological properties of the drug'. Essential elements in this definition are the pharmacological nature of the effect, that the phenomenon is unintended, and that there is no overt overdose.

An *adverse reaction* is 'a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man'. In this description it is of importance that it concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).

A *signal* refers to 'reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously'. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information.

In these definitions drug or drug food interactions are also included. It should be added that many patients have only *suspected* adverse reactions in which the causal role of the drug is unproven and may be doubtful, and that pharmacovigilance data usually refer to only suspected adverse reactions and side effects.

An *adverse event* or *experience* is defined as 'any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment'. The basic point here is the coincidence in time without any suspicion of a causal relationship.

Serious adverse events can be defined as those that:

- a. are life-threatening or fatal
- b. cause or prolong hospital admission
- c. cause persistent incapacity or disability; or
- d. concern misuse or dependence.

Type A effects ('drug actions') are those which are due to (exaggerated) pharmacological effects. Type A effects tend to be fairly common, dose related (i.e. more frequent or severe with higher doses) and may often be avoided by using doses which are appropriate to the individual patient. Such effects can usually be reproduced and studied experimentally and are often already identified before marketing.

Interactions between drugs, especially pharmacokinetic interactions, may often be classified as Type A effects, although they are restricted to a defined sub population of patients (i.e. the users of the interacting drug).

Type B effects ('patient reactions') characteristically occur in only a minority of patients and display little or no dose relationship. They are generally rare and unpredictable, and may be serious and are notoriously difficult to study. Type B effects are either immunological or non-immunological and occur only in patients, with - often unknown - predisposing conditions. Immunological reactions may range from rashes, anaphylaxis, vasculitis, inflammatory organ injury, to highly specific autoimmune syndromes. Also non-immunological Type B effects occur in a minority of predisposed, *intolerant*, patients, e.g. because of an inborn error of metabolism or acquired deficiency in a certain enzyme, resulting in an abnormal metabolic pathway or accumulation of a toxic metabolite. Examples are chloramphenicol aplastic anaemia and isoniazid hepatitis.

Type C effects refer to situations where the use of a drug, often for unknown reasons, increases the frequency of a 'spontaneous' disease. Type C effects may be both serious and common (and include malignant tumours) and may have pronounced effects on public health. Type C effects may be coincidental and often concern long term effects; there is often no suggestive time relationship, and the connection may be very difficult to prove.

Confidentiality: Maintenance of the privacy of patients, healthcare providers and institutes, including personal identities and all personal medical information.

Verification: The procedures carried out in pharmacovigilance to ensure that the data contained in a final report matches the original observations. These procedures may apply to medical records, data in case-report forms (in hard copy or electronic form), computer printouts, and statistical analyses and tables.

Validation: The action of proving that any procedure, process, equipment (including the software or hardware used), material, activity or system used in pharmacovigilance actually leads to the expected results.

CAUSALITY CATEGORIES

The causality categories described by the Uppsala Monitoring Centre are as follows:

1. **Certain:** a clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration, and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary.
2. **Probable/Likely:** a clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfil this definition.
3. **Possible:** a clinical event, including laboratory test abnormality, with a reasonable time sequence to administrations of the drug, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.
4. **Unlikely:** a clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.
5. **Conditional/Unclassified:** a clinical event, including laboratory test abnormality, reported as an adverse reaction, about which more data is essential for a proper assessment, or the additional data is under examination.
6. **Unassessable/Unclassifiable:** a report suggesting an adverse reaction which cannot be judged because information is insufficient or contradictory, and which cannot be supplemented or verified.

As a step towards harmonisation in drug regulation in the countries of the European Union, the EU pharmacovigilance working parties proposed the following three causality categories:

- **Category A:** 'Reports including good reasons and sufficient documentation to assume a causal relationship, in the sense of plausible, conceivable, likely, but not necessarily highly probable'.
- **Category B:** 'Reports containing sufficient information to accept the possibility of a causal relationship, in the sense of not impossible and not unlikely, although the connection is uncertain and may be even doubtful, e.g. because of missing data, insufficient evidence or the possibility of another explanation'.
- **Category O:** 'Reports where causality is, for one or another reason, not assessable, e.g. because of missing or conflicting data'.

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Case presentation Format

- A case presentation is a formal communication b/w health care professionals (doctor, pharmacists, nurses, etc) regarding a patient's clinical information.

include:

1. Patient identity:

- Name
- Age
- Sex
- Occupation

2. History of presenting complaint (HPC):

- Date of presentation to hospital or clinic
- Mode of admission, for example acute emergency or referral
- Presenting symptoms and time scale of their occurrence.

3. Past Medical History (PMH):

- Past medical problems listed, emphasizing those relevant to the case and with admissions to accurate sequence and timing of events including previous admissions to hospital and specialist referrals.

4. Social History: (SH)

- Smoking and alcohol habits.
- Social circumstances including social and family support.
- Unusual living condition, travel or habits where these may be relevant to the patient's medical condition.

5. Family History: (FH)

- Relevant familial illnesses.
- Especially premature death of parents or siblings

6. Drug History: (DH)

- Present drugs dose and frequency
- OTCs
- Any known allergies and explain reaction
- Past Rx and OTC drugs

7. Examination details:

- A physical examination or medical examination is the process by which a medical professional investigates the body of a patient for signs of disease.
- May include ^{checking} vital signs: temperature examination, Blood pressure, pulse and respiratory rate.

8. Investigations:

- Normal laboratory studies
- Other investigations (imaging, biopsy etc).

9. Diagnosis:

The working diagnosis or list of possible diagnoses.

10 Management plan:

- The therapeutic plan in context with the medical management of the patient's condition including multidisciplinary co-operation.

Further investigation.

11 Clinical progress:

- Progress note: A brief summary of a hospitalized Pt's current clinical status, written sequentially in the chart, reflecting information provided by physical exam, lab tests and imaging modalities.

12. Pharmaceutical care issues:

- The medical history is interpreted in term of the issues of particular relevance to the pharmacist. The care issues and accordingly the action of the pharmacist constitute pharmaceutical care plan.

SOAP Format:

- Full patient profiles are intended to give you a chance to analyze in more depth a particular pt, critically appraise the treatment choices and provide your own suggestions for how that pt's drug related problems might be managed.

Method:

- Identify the problems for each pt profile and you will "SOAP" each of the pharmaceutical problems identified.

Often any medical problem identified will have a corresponding pharmaceutical title (e.g. the medical problem 'heart failure failure'). By "SOAPing" only pharmaceutical problems students should concentrate on optimizing and monitoring drug treatment rather than on the medical work-up.

SOAP stand for

Subjective data

Objective data

Analysis (including medical and therapeutic references) [Assessment]

Plan

□ Subjective data:

- Subjective data includes patient complaints or symptoms.

In addition, it can include observations of the medical team, which may be subjective nature.

- Subjective data is obtained by talking to the pt (e.g. patient complaints of shortness breath).

The subjective data required by pharmacist may be different from that required the doctors, who use the information for different purposes.

The pharmacist must select the data that is necessary to assess drug therapy.

□ Objective data:

- Objective data includes clinical signs, results of lab tests, the findings from an examination and the results of various procedures (e.g. X-rays, ECG's and ECG).

□ Analysis:

- You should ^{والموضوع} interpret the subjective and objective data for each problem so as to develop therapeutic plan, follow the response to therapy or document an adverse drug reaction.

Discussion should include the evidence available which justifies how the patient will be clinically managed.

The following list is guide and is adapted from Hart, Gourley and Hertindal 1988:

1. A pharmacist should always consider ^{والموضوع} whether a problem is drug induced.
2. The pharmacist should consider whether drug therapy is required or not
3. If the patient is already receiving drug therapy, the pharmacist should assess the current therapy for appropriateness.

- Pharmacist considers the following:

- a. Are all the drugs necessary?
- b. Is this the drug of choice for this patient?
- c. Is this the correct dose?
- d. Is this correct dosage form? etc.
- e.

4. If the patient is receiving drug therapy, the pharmacist should assess the response to therapy and decide whether the response is adequate and/or the response is that which was expected.

□ Plan:

- The plan should include:
 - Treatment
 - Monitoring parameters for drug therapy
 - Clinical endpoints.
 - Patient education including patient counseling point that pharmacist will give to the patient and/or relatives.
 - Supply of further medication.

→ Discharge planning needs

Any specific tests required to assess toxicity should be identified in the plan.

PICCLE or PENCIL

Pallor: paleness especially of the face that is caused by illness.

[is the result of a reduced amount of oxyhaemoglobin in skin or mucous membrane]

Icterus: yellowish of the skin and the whites of the eyes caused by an accumulation of bile pigment (bilirubin) in the blood; can be a symptom of gallstones or liver infection or anemia.

Cyanosis:

-A bluish color of the skin and the mucous membranes due to insufficient oxygen in the blood.

Clubbing [or nail clubbing]:

- A condition affecting the fingers and toes in which the extremities are broadened and the nails are shiny and abnormally curved.



Normal angle of
nail bed



Distorted angle
of nail bed

clubbed
finger.

lymphadenopathy:

a swelling of the lymph nodes.

Edema:

- is a condition of abnormally large fluid volume in the circulatory system or in tissue b/w the body's cells (interstitial spaces).



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Serial No. :

Name :

Date :

PATIENT PROFILE FORM

Patient name : IP/OP No. :

Admission Date : Discharge Date :

Department : Unit :

Age: years Sex:

Weight : Kgs Occupation :

Education : Income :

DIAGNOSIS:

CURRENT COMPLAINT AND HISTORY OF PRESENT ILLNESS:

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PAST MEDICAL HISTORY:

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PAST MEDICATION HISTORY / ALLERGY:

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SOCIAL HISTORY:

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Diet : Appetite :

Sleep : Exercise :

Bowel & Bladder :

HABITS:

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FAMILY HISTORY:

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PHYSICAL EXAMINATION: General

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VITAL SIGNS:

BP:mmHg; PR:bpm ; RR:cpm; Temperature:.....

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SYSTEMS:

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[illegible]

TREATMENT DETAILS:

Sl. No.	Brand Name	Generic Name	Dose	Frequency	Date Begun	Date Ended
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
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19						
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CLINICAL PROGRESS:

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PHARMACEUTICAL CARE ISSUES (ADR, DI, Rationality, Patient Intervention, etc):

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.....
Signature of the Student

.....
Signature of the Supervisor

Pharmaceutical Care

Definition:

The pharmaceutical care is the ^{مسئول} responsible provision of drug therapy for the purpose of achieving definite therapeutic outcomes that improve the patient quality of life.

These outcomes are: ٢٠

1. Cure of disease
2. Elimination or reducing patients symptoms
3. Arresting or slowing of a disease process
4. Preventing a disease or symptoms

-The term pharmaceutical care also defined as specific activities and services through which an individual pharmacist co operates with a patient and other professionals in designing, implementing and monitoring a therapeutic plan that will produce specific therapeutic outcome for the patient.

→ This involve major three functions:

1. Identifying potential and actual drug related problems.

2. Resolving actual drug related problems
3. Preventing potential actual drug related problems.

□ Focused Area of Practice:

1. Drug monitoring for a specific drug or for therapy for a specific disease state
2. Disease monitoring for a specific disease state
3. Drug / disease management by protocol.

- PC is an important element of health care and should be integrated with other elements of health care.

The pharmacist must process the following:

- Knowledge and skill in pharmaceuticals and clinical pharmacology.
- Able to mobilize the drug distribution system by which drug use decisions are implemented.
- Able to develop relationships with the patients and other health care professionals needed to provide PC.

برای خدمت یاک، آماده شدن یا کسی/چیز را
به این منظور آماده کردن

→ mobilize, -ise:

• Available in the society / community for the patients in the time.

• تعهد ، تفكر Commitment to quality improvement and assessment procedure.

□ Scope of Practice within the Pharmaceutical Care:

1. Role:

- Prevention of drug related problems
- Drug management
- Treatment of routine acute illness
- Management of chronic disease
- Primary disease prevention

□ Essential component of pharmaceutical care:

A. Pharmacist-patient relationship

The importance of putting a face and personality with the clinical picture is a key component of pharmaceutical care. A pharmacist can have a caring relationship with a patient but not with a chart or drug profile.

B. Pharmacist's workup of drug therapy:

-It contains the thought processes necessary pharmaceutical care.

PWDT component:

- i- Finding
- ii- Desired outcomes
- iii- Desired end points
- iv- Drug related problems
- v- Therapeutic selection
- vi- Monitoring parameters
- vii- Follow up

1. Data Collection:

-The pharmacist must collect and generate subjective and objective data regarding the patient's general health and status, past medical history, medication history, social history, diet, exercise, study, history of present illness and economic situation. source of information may include, but not necessarily to, the past medical charts (MC) and reports

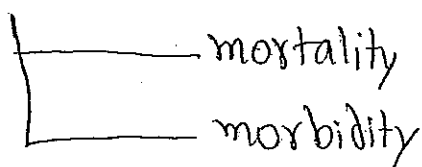
pharmacist - conducted health or physical assessment

- Patient demographic data: Age, sex, race
- Pertinent medical information
 1. Current and past medical history
 2. Family history
 3. Social history
 4. Dietary history
 5. Medication history (prescription, OTC, social drugs)
 6. Physical findings (weight, height, BP, edema)
 7. Special considerations like pregnancy, lactation
 8. Laboratory or other test results
- Patient complaints, symptoms, signs

2. Develop or identify core pharmacotherapy plan:

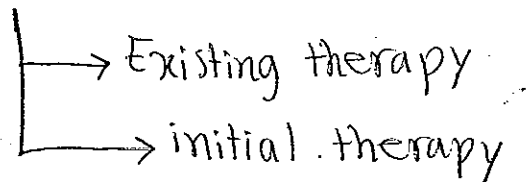
- a. C = condition / patient need
- b. O = outcome desired for that condition

↳ i - Patient outcomes



ii-therapeutic end point:

c. R=regimen to achieve the desired outcomes



d. E=evaluation

Parameter to assess outcomes achievement

1. Efficacy parameter

2. Toxicity parameter.

□ Evaluating Treatment alternative by monitoring and modifying Plan:

Some Factors are:

- Efficacy and safety, availability and cost of treatment and suitability of the treatment to the patient.
- Seriousness of the disease / condition
- Consequences of not treating the disease
- The efficacy of the drug
- Adverse drug reactions associated with the drug therapy

- Efficacy of alternative drug or non-drug therapy
- Side effect profile of alternative drug.

INDIVIDUALISING TREATMENT REGIMENS; Where more than one therapeutic alternative exists the patient's therapy should be tailored according to considering the following factors.

PATIENT FACTORS	DRUG FACTORS
▪ Diagnosis ▪ Treatment goals ▪ Physiological & pathological factors ▪ Past medical history ▪ Past medicines received ▪ Contraindications ▪ Allergies & adverse effects ▪ Patient compliance ▪ Patient's cooperation & convenience ▪ Special considerations	▪ Efficacy ▪ Adverse effects ▪ Prevalence, ability to minimize ▪ Ability to monitor for efficacy & avoid ADR ▪ Drug-drug interactions ▪ Pharmacokinetics & pharmacodynamics ▪ Dosage form ▪ Route & method of administration ▪ Cost to the patient ▪ Government or insurance company payments, presentation of bills in their formats

Monitoring outcomes:

The goals of any therapeutic treatments are obviously, the following:

1. To cure the disease
2. To eliminate or reduce patient's symptoms
3. To arrest or slow down disease process
4. To prevent the disease or symptoms

But often, sub optimal out comes (less than desirable) result due to the following broad reasons, some of which are circumstantial like the following:

- i - inappropriate prescribing
- ii - inappropriate or unnecessary drug regimen
- iii - inappropriate delivery
- iv - Drugs not available, dispensing error
- v - inappropriate behaviour of the patient
- vi - Patient idiosyncrasy (allergy or the reaction)
- vii - Inappropriate monitoring (especially with drugs having narrow therapeutic range).

Inappropriate monitoring is often ^{مذكور} cited as the major reason for therapy failure. It may lead to:

- Failure to detect and resolve inappropriate therapeutic decisions and/or
- Failure to monitor the effects of treatment.

- Therefore it is very important to review each part at the beginning of therapy and during treatment

to ensure that the desired outcomes has been achieved.

these will 4Ss that is, signs, symptoms side effects and sequelae. This applies for all disease. The expectations of active treatment is that it should produce a positive effect or the disease resulting in an improvement or amelioration of signs and symptoms. At the same time treatment should prevent progression of disease that is sequelae.

-The clinical pharmacist has a big role to play, in all these event. Some of the job, that pharmacist will have to do ensure good monitoring out comes are as follows:

1. The pharmacist regularly reviews subjective and objective monitoring parameters to ensure, if satisfactory progress is being made towards outcomes, according to therapeutic plan.

2. The ph and the pt determine, if original plan should continue, or it needs, modification.

-If modifications are needed, ph works with the patient and his other health care providers to modify the plan and implement the revised plan.

3. The ph reviews ongoing progress in achieving desired outcomes with the patient and provides the report to the pat's other health care providers.

4. Ph provides a mechanism or for the follow up with the pat. He then notifies the pat's other health care providers about the level of adherence to the plan by the patient.

Identify the PRIME pharmacotherapy problems:

1. P = Pharmaceutical based problems

Patient not receiving a prescribed drug, device or intervention.

2. R = Risk to patient

Adverse drug reaction / drug allergy

Potential for overlap of adverse effect.

3. I=Interactions

Drug-drug, drug-food interactions

4. M=Mismatch between medication and condition/p_t need

5. E= Efficacy issues

□ Documentation of pharmaceutical care:

Format of a FARM note.

a. F=Findings: The patient specific information that gives a basis for, or leads to the recognition of a pharmacotherapy problem. Finding includes subjective as well as objective information.

b. A=Assessment

1. Any additional information that is needed to best assess the problem in order to make recommendation.
2. The severity, priority or urgency of the problem.
3. The short-term and long-term goals of the intervention proposed or provided.

^{dis, ds}
C. R = Resolution (including prevention)

1. Observing, reassessing
2. Counseling or educating the patient/care giver
3. Making recommendations to the patient/care giver
4. Informing the prescriber
5. Making recommendations to the prescriber
6. Withholding medication or advising against use

D. M = Monitoring and follow up:

1. The parameter to be followed e.g. pain, depressed mood
2. The intent of the monitoring e.g. efficacy, toxicity, ADR event.
3. How the parameter will be monitored e.g. patient interview, serum drug level, physical examination.
4. Frequency of monitoring e.g. weekly, monthly
5. Duration of monitoring e.g. until resolved, while on antibiotic etc.
6. Anticipated or desired finding e.g. no pain.
7. Decision point to alter therapy when or if outcome is not achieved e.g. pain still present after 3 days, mild hypoglycemia more than 2 times a week.

SOAP format:

- Subjective:

Information that explains or delineates the reason for the encounter. Information that the Pt reports concerning symptoms, treatments tried, medications used adverse effects encountered.

Objective:

Information from physical examination, laboratory results, diagnostic tests, pill counts and pharmacy Pt profile information.

→ It is the interpretation of the subjective and objective findings and the methods by the pharmacist derives the recommendation or plan.

Assessment:

A brief, but complete, description of the problem, including a conclusion or diagnosis that is supported logically by the above subjective and objective data.

→ or: It is the action, intervention and recommendation made by pharmacist.

Plan:

A detailed description of recommended or intended further work up (lab, radiology, consultation),

treatment (e.g. continued observation, physiotherapy, diet, medications, pt education, etc.

Focused areas of practice:

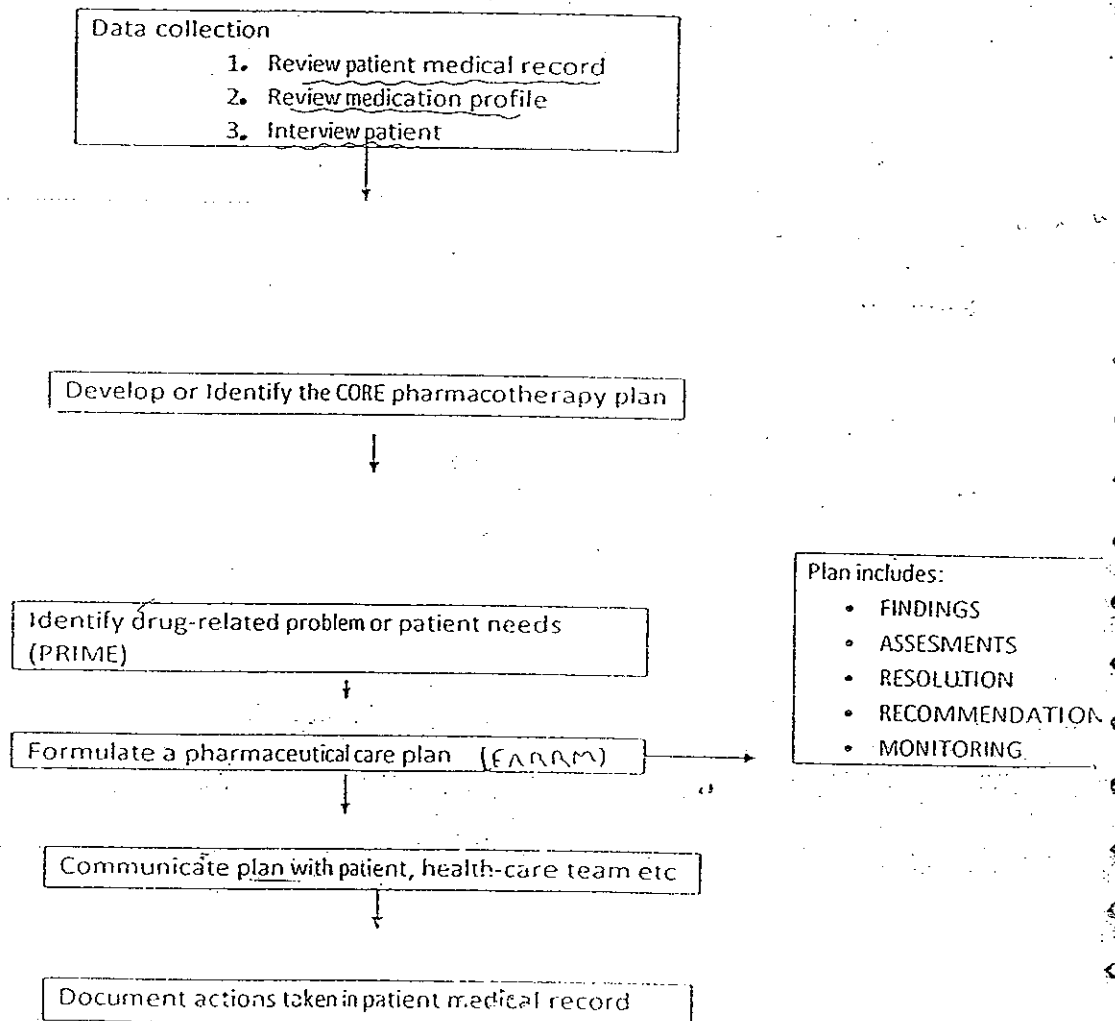
- A. Drug monitoring
- B. Disease monitoring
- C. Drug/disease management protocol
 - 1. Disease & drug monitoring with patient counseling
 - 2. Disease & quality of life outcomes identified & agreed upon by patient, medical provider & pharmacist
 - 3. Application of a drug-disease management protocol includes:
 - i) Process by which the physician refers the patient to the pharmacist
 - ii) Drugs, devices, medical treatment, tests & procedures that may be prescribed, administered or ordered as appropriate for the treatment of health problem addressed by protocol
 - iii) Limited physical assessment
 - iv) Integration of the pharmaceutical care plan into the total medical care plan for the patient
 - v) Predetermined plan for emergency services
 - vi) Written communication/documentation to/from medical provider
e.g. chart access & note entry

CLINICAL SKILLS AND PHARMACIST'S ROLE IN PHARMACEUTICAL CARE:

- A. Patient assessment
 - 1. Physical assessment
 - 2. Barriers to adherence
 - 3. Psychosocial issues
- B. Patient education & counseling
 - 1. Interview skills
 - 2. Communication skills e.g. empathy, listening, speaking or writing
 - 3. Ability to motivate, inspire
 - 4. Develop & implement a patient education plan based on an education
 - 5. Identification & resolution of compliance barrier
- C. Patient specific pharmacist care plans
 - 1. Recognition, prevention & management of drug interactions
 - 2. Pharmacology & therapeutics
 - 3. Interpretation of laboratory tests
 - 4. Knowledge of community resources

- 5. Community & rapport with community medical providers
- D. Drug treatment protocols
 - 1. Develop & maintain (update) protocols
 - 2. Follow up protocols as a pharmacist clinician
 - 3. Monitor aggregate adherence to treatment protocol e.g. drug-utilization evaluation
- E. Dosage adjustment
- F. Selection of therapeutic alternative
- G. Prevention services
 - 1. Immunizations
 - 2. Screenings
 - 3. Health & wellness education

Pharmaceutical care as the model for pharmacy practice:



Documentation of information:

One of the jobs of a ph is to regularly update records of the pat with documentation (info). This is a critical component of PC. Documenting is to improve the quality of patient care.

Documentation provides a record of care provided & history of the decisions made for a specific patient. Besides this it also helps to provide for:

- A. Reimbursement requirements.
- B. Managing some risk of legal litigations.
- C. Indicate pharmacist decisions taken for pat's welfare.
- D. Proof of his reasonable judgment.
- E. Provides valuable tool to identify the new activities & roles that ph can play.
- F. Provides a method to evaluate cost-benefit or cost effectiveness of the services.
- G. Provides necessary papers, to get reimbursement of the PC services, to the pharmacist.
- H. It provides recognition to the pharmacist, for his valuable PC services, by other health care service providers.

Activities that should be documented are:

A. Pharmaceutical care related activities:

- 1. Drug related problems: as detected & where a change in drug therapy is made.
- 2. Identification of drug, allergies, diseases.
- 3. Type of problem or need.
- 4. Identification of activities, care & services provided
- 5. Identification of recommendations & potential outcomes.

B. Other non-dispensing, non-technical but patient related activities:

- 1. Consultations with other HC providers.
- 2. Consultations especially tailored to pats needs.
- 3. Assessments of pat's understanding.
- 4. Self care consultation or advice.
- 5. Pat's referrals to other HC providers/professionals.
- 6. Those specific pat related activities, which consume a lot of time.
- 7. Any pat related encounter or activity, which may have bearing on future decisions (sequels).

The documentation, should be pat & related problem oriented, & should have 4 components, such as

- Identification of the patient & the event (encounter)

This information should include information as to date of the event, the person who is making the event & the person who is facing it & trying to resolve it. Time spent to resolve & level of significance of the event i.e., life saving, major, moderate or minor incident.

- Identification of problem &/or need

In identifying the problem or need, the medications, diseases or allergies/hypertensives involved should be included. This will be critical part of the documentation if the pharmacist should need to refer to it for later use.

- Identification of the activities, services or care provided

This info should include the actions taken by the ph or any initiative taken by him. It should also include calls made to the physician, other HC providers & third party payer, to solve the potential problem. If a non-prescription product is recommended, after review of the patient medical record: should be documented.

- Identification of the recommendations & potential outcomes

This info should contain, complete listing of all medications, that the pat is utilizing, & for what purpose (i.e. expected outcome) they are prescribed. This part of the documentation helps the ph for getting payment for his services, demonstrates value of his service & knowledge to HC professionals.

Pharmaceutical care plan:

Establish pharmacist-patient relationship



Collect data



Interpret data



Identify drug related problems



Determine priority of Drug related problems



Determine desired outcomes



Develop therapeutic plan



Develop monitoring plan



Implement & follow up pharmaceutical care plan

PHARMACEUTICAL CARE: AN ONGOING PROCESS.

The patient profile (data base) is revised and reassessed each time a new drug is added to or deleted from the medication regimen, a new disease or condition is diagnosed: when the patient returns to the pharmacy or is readmitted to the health system facility, the pharmacist uses the patient profile, PWDI, and FARM (or SOAP) notes as the basis for ongoing pharmacist-patient interactions.

IMPORTANCE OF PHARMACEUTICAL CARE IN TODAY'S PHARMACY PRACTICE:

A. The potential for medication error is growing.

1. The use of prescription & non-prescription medications is growing and now constitutes the primary therapeutic modality available to health care practitioners and patient.
2. The number, complexity, and potency of prescription & non-prescription drug products is increasing.

B. The need of pharmaceutical care secures an enduring role for the pharmacist in U.S. health care system. Every encounter with patients, regardless of practice setting, provides pharmaceutical care. Pharmaceutical care activities integrate pharmacists into the health care system of the future.

The clinical pharmacist has a big role to play, in all these event. Some of the jos, that pharmacist will have to do ensure good monitoring out comes are as follows:

5. The pharmacist regularly reviews subjective & objective monitoring parameters to ensure, if satisfactory progress is being made towards outcomes, according to therapeutic plan.
6. The ph & the pat determine, if original plan should continue, or it needs, modification. If modifications are needed, ph works with the patient & his other health care providers to modify the plan & implement the revised plan.
7. The ph reviews ongoing progress in achieving desired outcomes with the patient & provides the report to the pat's other health care providers.
8. Ph provides a mechanism or for the follow up with the pat. He then notifies the pat's other health care providers about the level of adherence to the plan by the patient.

The ph, regularly updates pat's medical &/or pharmacy records with information concerning patient progress

Reference:

Clinical pharmacy by Tipinis Baja

Text book of clinical pharmacy by Parthasarathi.G

Comprehensive pharmacy by Leon shargel

Critical Literature Evaluation:

- For health and science professional, the term 'literature' refers to the body of articles published in biomedical and scientific journals.
- It is this literature we turn to when we need to answer questions such as 'which is the best drug for this disease' or 'is this new drug for this disease'.
- Many of the articles in biomedical journals describe research studies investigating various aspects of disease causation, diagnosis, screening, prognosis and management.

Types of drug therapy research papers:

- The studies of greatest interest to clinical pharmacists include those that focus on clinical efficacy, short and/or long term drug toxicity, drug pharmacokinetics, drug response relationships and drug therapy monitoring.
- What is critical appraisal? It is the ability to

read original research papers in a way that allows us to judge its scientific value and to consider how the results can be applied to practice.

The major aim of critical appraisal can be summarized as: Should this paper in conjunction with others relevant literature and clinical experience change the clinical practice.

□ Choosing paper for critical appraisal:

How do the clinical pharmacist decide which research papers are important to read? The filter the articles to select those that are most likely to be of greatest clinical relevance and significance.

Importance of a paper consideration needs to be given to factors such as:

1. Is this paper addressing an important controversial therapeutic issue which is of relevance to

my patients?

2. Is this study the first evidence for efficacy of a new drug class or treatment?

3. Does this study involve more patients, or continued for longer than previous studies?

4. Does methodology address methodological problems identified in previous studies of this drug.

- If the answer of these questions are "yes" then it is likely that the paper may be worthy of critical appraisal.

□ Critical appraisal of primary research papers:

They conform to a standard format known as

IMRAD:

• Introduction

• Methods

• Results

• Analysis

• Discussion

Terms used to design of drug trials:

Terms	Meaning
Double blind	Neither <u>subjects</u> nor <u>investigators</u> know treatment allocation
Single blind	<u>Subjects</u> do not know which <u>treatment</u> they are receiving <u>but</u> <u>investigators</u> are <u>aware</u> of Rx allocation
Placebo controlled	<u>Control subjects</u> receive <u>inactive treatment</u> , which should be identical in appearance and <u>method</u> of administration to <u>active</u> medications.
Open label study	<u>Subjects</u> and <u>investigators</u> are <u>aware</u> of treatment allocations.
Prospective study	A study using data to be <u>gathered</u> in the <u>future</u>
Retrospective study	A <u>study</u> using data which are <u>available</u> in <u>past</u> .
Case control study	A study that <u>identifies</u> a <u>group</u> of <u>patients</u> <u>having</u> the <u>outcome</u> of interest and <u>compares</u> them to <u>matched</u> group of patients who <u>do</u> not have the outcome of interest.
Cross over	<u>Each</u> <u>subject</u> receive both the <u>intervention</u> and <u>control</u> <u>treatments</u> , usually <u>separated</u> by <u>washout</u> period during which subjects receive no treatments.

Cohort study

A non-experimental study design
which follows a group of people
prospectively and then examines
how events differ among people
within the group.

-The best choice of study design depends on the research question, but in general when testing the efficacy of drug Rx the randomized controlled trials (RCT) is considered the preferred study design. In an RCT subjects are randomly allocated to either an intervention group or control group. Both groups are then followed up for a specified time period and analyzed in terms of specific outcomes which are defined at the outset of the study.

Typical selection criteria may relate to age, sex, severity of disease and co-morbid conditions, exclusion criteria are often used to ensure patient safety.

-RCT investigators will study a variety of outcomes or endpoints to evaluate the effects of the study treatments. The outcome considered by the investigators to be of greatest importance is the primary outcome. Other outcomes of interest are called secondary outcomes.

□ Statistics:

-The types of statistical tests used in the study are also described in the methods sections. Research papers use statistics for both descriptive and inferential purposes.

-In general parametric tests are more powerful than non-parametric and so should be used possible.

□ Evaluating the results sections:

-When examining the results section the first thing you should look for is that the randomization process did indeed produce similar groups.

-Another factor to consider when interpreting the results is the subjects who withdraw from a study. These may include those who do not respond adequately to treatment who experiences adverse effects.

□ Confidence intervals (CI): are another measure often reported in study results. A confidence interval is the range within which the true size of effect lies with a given degree of assurance.

The statistical methods used to define the relationship b/w 2 variables. The statistical methods used to define the relationship b/w 2 variables are termed correlation and regression.

Correlation analysis: provides a measure of the strength of relationship.

Regression analysis: is a way of mathematically describing the relationship b/w variables. It aims to allow one dependant variable to be predicted from one or more independent predictor variables.

Absolute risk is the probability that an individual will experience a specified outcome during

a specified time period. The change in absolute risk or absolute risk reduction (ARR) is the difference between how often an outcome occurs in the Rx group compared to control gp.

Evaluating the introduction and other parts of the paper:

-The introduction provides background information about the topic and should explain why the current research is needed. Other parts worth examining include the title author affiliation, and knowledge and reference.

Reaching a conclusion:

-At the end of the critical appraisal process you ask yourself: should this paper in conjunction with other relevant literature and clinical experience change clinical practice.

□ Critical appraisal of a systemic review or

meta-analysis:

- For any research question, result of individual RCT may vary, with some studies studying the same intervention, producing large effects other smaller effects, and others perhaps even negative effects. A systematic review applies a rigorous and usually replicable method to summarize research findings from different primary studies relating to the same research question. Sometimes the results of a systematic review are combined numerically this is called a meta-analysis.

Medication Errors

- Any preventable event that may cause or leads to inappropriate medication use or patient harm while the medication is ⁱⁿ the control of the Health care Professionals, Patients or consumers.

Types of errors: CAMP PP

1. Prescription errors:

These errors involved prescribing missing or inaccurate allergy information, improper or omitted dose, route of administration, improper or omitted frequency, medication ^{omission} omission, medication incorrect or unspecified medication, unauthorized drugs, duplication, missing or inaccurate patient weight. These errors are made by the busy treating clinicians.

These errors, which lead to the administration of wrong dose, may sometimes be life-threatening misplacement of the decimal point while calculating the dose is a potentially fatal error.

- Inappropriate or inadequate instructions for

use of a medication ordered by a physician or other authorized prescriber.

- Prescribing injections in milliliters instead of milligrams without mentioning the strength of injections is an error often made by the doctors.

- Prescribing syrups in teaspoons is another inaccurate way of prescribing because variable size of spoons may be used resulting in inadequate or excessive dose.

Dispense ^{دواء}
وصف

2. Dispensing errors:

- Dispensing is an integral part of the quality use of the medicines and together with the patient counseling form the core professional activities of a pharmacist. These activities allow the safe and efficient provision to the general public of what would normally be dangerous or restricted drugs.

- Dispensing errors generally refers to errors in the dispensing process e.g. Wrong drug or dose strength, incorrectly labeled directions or drug

dispensed to wrong patient that are not detected and corrected prior to the patient leaving the pharmacy and which may be to sub optimal outcome of treatment for the patients.

- Main risk factors associated with the Dispensing errors were found to be prescription ^{load} overload, lighting levels, noise, ^{less} interruptions and ^{for or because} distractions. Also the major parts of the dispensing errors were related to wrong drug or wrong strength.

- Dispensing error originating from the point that medication was dispensed from the pharmacy.

- Dispensing errors includes incorrect admixtures of medications within the pharmacy and dispensed to the floor for administration of the dose.

3. Administration Errors:

- An error originating during the process directly associated with medication administration at the nursing unit.

4. Monitoring Errors:

Failure to review a prescribed regimen for appropriateness or failure to use appropriate clinical or laboratory data for adequate assessment of resident response to prescribed therapy.

5. Potential errors:

- A mistake in prescribing, dispensing or planned medication administration that is detected and corrected through intervention before actual medication administration.

6. ^{Control} Compliance errors:

Inappropriate resident behavior regarding adherence to a prescribed medication administration.

7. Clerical errors:

- These errors often arise on one hand due to the errors in copying out doctor's instruction and on the other hand due to the mistaken

identity of patient leading to the administration of authorized drug.

II Causes of medication errors:

- i- insufficient or inadequate information about the patient
- ii- lack of knowledge about drug therapy
- iii- Poor communication of drug information
- iv- Poor hand writing
- v- Confusing or misleading drug labeling, packing and nomenclature.
- vi- Poor drug storage and stocking
- vii- Problems with standardization and distribution
- viii- Poor safety assessment of drug delivery devices before purchase and during their use.
- x. Misinterpreted verbal orders
- xi. lack of time

III Medication errors includes:

1. Over dose/under dose
2. Missing information

3. Wrong dosage form/wrong drug/wrong route out ordered

4. Allergy to ordered drug

5. Duplicate therapies and wrong Patient.

How to prevent Medication errors: ^{5M}

- Because of the medication errors, the hospitalization of the patients are becoming higher and also because of the same, many more patients are seen in ambulatory settings such as Physicians offices, clinics, urgent care centers, nursing homes and home health services.

The emergence of new technology offers greater potential to improve both the efficiency and accuracy of care, resulting in improved patient safety.

- The following applications of technologies can prevent medication errors:

1- Computer Physician Orders Entry System (CPOE):

Computer Physician Orders Entry is a computer

برای کاربر (کارت)

application that accepts the prescribers order for diagnostic and treatment services electronically rather than recording them in writing on an order sheet or prescription pad which includes orders against standards for dosing, check for allergies or interactions with other medications and warn the prescribers about potential problems. Hence ... can reduce serious medication errors.

2. Bar Code Bed Side Care System:

Bar Coding System is another recommended top-priority action for preventing adverse drug events in hospitals through a machine-readable coding e.g Bar coding. It has been suggested that the checking and documentation function that occur when medications are administered. It could be done more effectively and accurately if aided by bar code scanning. A bar code drug administration system could linked to clinical information and the medication profile, so that when the dose is administered, an automatic check be made to assure the fact that the drug has prescribed for the patient.

-NDC is a unique 10-digit, 3-segment number. It is a universal product identifier for human drugs in the United States.

NDC 0777-3105-02

the dose, time and route of administration was correct and then the patient does not having an allergy to the medication have been given etc.

3. Scanners:

For those pharmacies with scanners all medication bottle taken from shelf should be scan against the barcode on the patient price sheet/information sheet to make sure that it is the correct medication, before counting.

4. National Drug Code Numbers (NDC):

- Those who work in pharmacies that do not have bar code scanners, the National drug code numbers along with the drug must first verify before counting begins. There are three segments for National drug code numbers,

- The first segment is labeler code, a label any ^{شركة - بئانه} firm that manufactures, repacks or distributes a drug product.

- The second segment the product code, which identifies a specific strength, dosage form and

formulation for a particular firm.

- The third segment, package code that identifies the package sizes.

- By verifying all these conditions pharmacists can tell that where error occur and they can correct it suddenly.

5. Automated Dispensing:

- Hospital pharmacies increasingly using drug dispensing machines or robots.

- Some of these machines work like banking ATMs, Pre packed medications are dispensed instead of cash or postage stamps. Healthcare workers enter a user identification and password and swipe their ID cards through the machines electronic reader.

- Also a new robotic drug dispensing are implemented and called as Rapid script.

These systems decrease errors made by pharmacists. It does not eliminate errors that come either from physicians or errors that may occur while the pharmacist attempts to read and interpret the physician's order etc.

6. Other methods to reduce medication errors:

- Providers also can use simple non-technological procedures to easily cut the error rates.

- Pharmacists and physicians should counsel the patient to know what medications they are taking, what all the possible side effects, etc.

Also patient should be encouraged to inform their doctor or pharmacist, about their treatment discrepancies and side effects very early.

Early, and frank conversation by patients with their healthcare can help to minimize the effects, if not help to prevent errors.

□ The following outlines are some of the recommendations developed by various individuals and groups to assist in reducing medication errors.

→ Hospital-wide Actions and Policies to decrease Medication Errors:

1. Establish and maintain functional formulary system with policies for drug evaluation, selection and therapeutic use.

2. Provide an adequate number of well-trained persons to prepare, dispense, and administer medications.
3. Provide a suitable work environment for safe, effective drug preparation.
4. Establish a clearly defined system for drug ordering, dispensing, and administration that includes review of the original drug order before dispensing and administration.
5. Provide ongoing formal quality improvement of the therapeutic use of medications including a drug-use evaluation (DUE) program.
6. Maintain medication profiles for both inpatients and ambulatory patients receiving care at the hospital.
7. Computerize systems, where possible, to check dose and dosage schedules, drug interactions, allergies, and duplicated therapies.

Medication ordering to reduce errors:

- Physician prescriptions and drug orders are a means of communicating, so they must be legible, clear and unambiguous.

The following steps may help to ensure that medication orders communicate safely and effectively.

- Confirm that the patient's weight is correct for weight based dosages.
- Identify drug allergies in patients
- Write out instructions rather than using abbreviations
- Avoid ^{clear} vague instructions
- Specify exact dosage strength
- Avoid use of a terminal zero to the right of the ^{correct} decimal point. (e.g. use 5 rather than 5.0) to minimize 10-fold dosing errors.
- Use a zero to the left of a dose less than 1 (e.g. use 0.1 rather than .1) to avoid 10-fold dosing errors.
- Avoid abbreviations of drug names (e.g. MS may mean morphine sulfate or magnesium sulfate).

- Spell out dosage units rather than using abbreviations (e.g. milligram or microgram rather than mg or µg; units rather than U).

→ Prescribers Actions to decrease Medication Errors:

- Stay current concerning appropriate treatment of medical conditions they manage.
- Review the patient's existing drug therapy before prescribing new medications.
- Remain familiar with individual hospital medication ordering systems.
- Ensure that drug orders are complete, clear, unambiguous, and legible.
- Reserve verbal orders for instances when it is impossible or impractical to write an order or enter it in the computer.
- When possible, speak with the patient or caregiver about the medication that is prescribed and any special precautions or observations that should be noted, such as allergic or hypersensitivity reactions.

Pharmacy Actions to Decrease Medication Errors:

- Remain available to prescribers and nurses to participate in drug therapy development and monitoring
- Never guess or assume the intent of confusing medication orders.
- Review an original copy of the written medication order before dispensing a medication, except in emergency situations.
- Prepare drugs in a clean and orderly work area with a minimum of interruptions.
- Dispense medication in a timely fashion using a unit-dose, ready to administer form whenever possible.
- Provide counsel to patients or caregivers about their medications.

Nurses Actions to Decrease medication Errors:

- Be familiar with medication ordering and use system.
- Verify drug orders before medication administration

- Confirm patient identity before administration of each dose.
- Check medication calculations with a second individual.
- Usually large volumes or dosage units for a single patient dose should be verified.

□ Patients and Families:

- Inform physicians and hospital staff of any old or new allergy.
- Be responsible for knowing the medication names, strength and dosing. Ensure that dosing interval followed as prescribed. Ask questions to ensure understanding of medication administration. When possible, bring all current medications to the hospital for confirmation and review.
- Ask questions about the purpose of each medication to be used.
- Inform physicians and hospital staff about a child's use of complementary or alternative methods of health maintenance or therapeutic treatment, including herbal or dietary supplements.

□ Avoiding Medication Errors at home:

- Make a list of medications you are now taking. Include the dose, how often you take them, the imprint on each tablet or capsule, and the name of pharmacy.
- Any time your medications change, be sure to change your list, too.
- Keep medications in their original containers.
- Read the label every time you take a dose to make sure you have the right drug and you are following the instructions.
- Don't store medications in the bathroom medicine cabinet or in direct sunlight. Humidity, heat and light can affect medications potency and safety.
- Flush old medications down the toilet. Some drugs become toxic after the expiration date.

Systematic Approach In Answering DI

Queries:

Aim: is to promote the safe, effective and economic use of medicine.

Steps:

Step 1:

Secure demographic of requestor

- obtain initial question
- Secure requestor demographics.
- Determine a method for delivery of the response.

Step 2:

Obtain Background Information

→ Sufficient background information must be obtained in a limited period of time by the clinical pharmacist.

→ When a question involves a patient, the patient's age, weight, sex are usually needed. and patient's diagnosis, other medications, hepatic and renal are assessed.

Step 3:

Determine and categorize the ultimate question:

- The ultimate question may be differ significantly from the original question.
- Adequate background information is need to determine UQ.
- Then categorize Q to help in developing the research strategy.

Step 4:

Develop Strategy and conduct Search:

- Select the resources based on probability of containing the desired information.
- Conduct a systemic search (Ex) →

Step 5:

Perform evaluation, Analysis and synthesis:

- review of information and confirm it (evaluation).
- Analyze and synthesize the information
- consideration of background information.

Step 6:

Formulate and provide response

→ The response must include restating the request and clearly identifying the problems, issues and circumstance

Step 7:

Conduct Follow-up and Documentation:

- Document the question and response, and conduct follow-up
- Methods of documentation
- Reasons for "
- Follow-up is the final portion of the process
- Methods of follow-up
- Reasons of follow up

- Methods of Documentation (ex):

Paper form

Logbook

Computer database

- Reasons of documentation:

- Further reference for repetitive drug information requests
- Protective measure against legal liability

Methods of Follow-up:

Phone call, Mail survey, Written communication

Reasons:

- Provide the requestor with additional information that supports or changes a prior recommendation

- Obtain feedback concerning the quality of the service.

Conduct a systematic search:

Ex:

If the question is classified as a Drug Interaction, then a logical and efficient search would begin with a text specific for drug interactions (e.g. Drug Interaction Facts and Comparisons). If a text specific for drug interaction is not available, other references likely to contain the desired information (e.g. Drug Facts and Comparisons etc.) should be selected as opposed to references with a decreased probability of containing the information (e.g. American Drug Index).

ANNEXURE I

	Department Of Pharmacy Practice Drug Information Centre – V.I.P.S. KIMS Hospital and Research Centre 4th Floor, New Building, K.R. Road, Bangalore 560 004	
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Drug Information Request Form

Date: - _____ Time: - _____ Received by: - _____

Name of the Enquirer: - _____ Contact no _____ Unit: - _____

Enquirer's Professional Status:

Physician ☐ Surgeon ☐ Resident ☐ PG ☐
Intern ☐ Nurse ☐ Pharmacist ☐ Others ☐

Details of Enquiry:

Query: _____

Purpose of Enquiry: Update knowledge ☐ Better patient care ☐ Others ☐

Answer Needed: Immediately ☐ within 30 min ☐ within 2h ☐ more than 24h ☐

Patient Details:

Age: _____ years Weight: _____ kg Sex: M ☐ F ☐

Liver/renal function	Allergies	Current medical problem	Relevant drug therapy

Other details

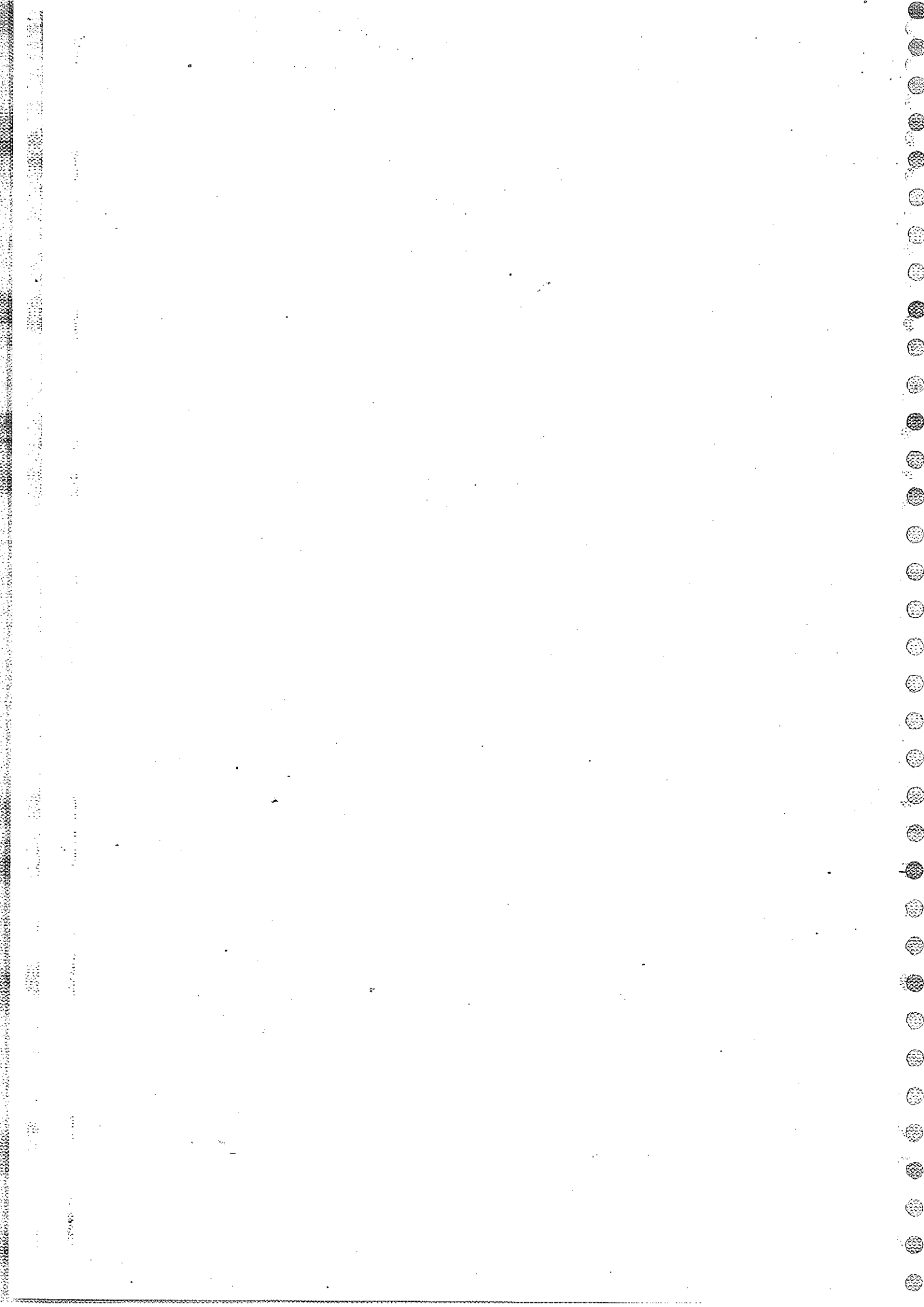
If pregnant: - first trimester ☐ second trimester ☐ third trimester ☐

If breast feeding age of infant: - _____

Pharmacist's notes:-

Signature of Attending Pharmacist

Signature of Enquirer



ANNEXURE 2

 DRUG INFORMATION SERVICES	Department of Pharmacy Practice Drug Information Centre – V.I.P.S. KIMS Hospital and Research Centre 4th Floor, New Building, K.R. Road, Bangalore 560 004	
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Drug Information Documentation Form

Date:- _____ Time:- _____ Received by:- _____

Name of the enquirer:- _____ Department:- _____

Unit:- _____ Contact no.: _____

The Enquirer's Professional Status:-

- ☐ Physician ☐ Surgeon ☐ Resident ☐ PG
☐ Intern ☐ Nurse ☐ Pharmacist ☐ Any Other (Specify)

Details of enquiry:-

Query:- _____

Patient details:-

Age _____ weight _____ kg Sex:- ☐ M ☐ F

Liver/renal function	Allergies	Current medical problem	Relevant drug therapy

Others details:

If pregnant:- ☐ first trimester ☐ second trimester ☐ third trimester

If breast feeding, age of infant:- _____

Mode of Request : ☐ Direct access ☐ During ward rounds ☐ Telephone
☐ E-Mail ☐ Others

Purpose of Enquiry: ☐ Update Knowledge ☐ Better Patient Care ☐ Other

Category : ☐ Indication ☐ Availability / Identification
☐ Administration / Dosage ☐ Drug Profile
☐ Dosage Recommendation ☐ Drug of Choice / Therapeutics

- ☐ Pharmacokinetics ☐ Adverse Drug Reactions (ADR)
☐ Pharmacoeconomics ☐ Drug Interactions
 (Drug-Drug, Drug-Lab, Drug- Disease, Drug - Food)
☐ Pregnancy / Teratogenicity ☐ Poisoning / Toxicology
☐ Lactation / Infant risk ☐ Compatibility / Stability
 (Chemical, Pharmaceutical, Sorption, Solubility, etc.)
☐ Efficacy ☐ Other

Date of reply : _____ Time of Reply: _____

Answer needed Immediately ☐ with in 30 mins ☐ within 2 hours ☐
 more than 24 hours ☐

Delay in Answer : ☐ Yes ☐ No

If Yes, Reason for Delayed Answer _____

Follow-up if any;- _____

Form of Reply : ☐ Written ☐ Verbal ☐ Both ☐ Printed Material
 ☐ Telephone ☐ E. Mail

Information provided _____

Reference consulted _____

Name of the clinical pharmacist

Signature of H.O.D

Normal Reference Range Table

Hematology Tests

Blood Gas

Thyroid

Chemistry

Urinalysis

Endocrine

Cardiac Tests

CSF

Miscellaneous

Hematology Tests

Hematocrit (Hct)

40-52% (Male)

37-46% (Female)

31-43% (Child)

Hemoglobin (Hgb)

13.2-16.2 gm/dL
(Male)

12.0-15.2 gm/dL
(Female)

Red Blood Cell Count (RBC)

4.3-6.2x10⁶/μL (Male)

3.8-5.5x10⁶/μL
(Female)

3.8-5.5x10⁶/μL
(Infant/Child)

White Blood Cell Count (WBC)

4.1-10.9x10³/μL

Diff

Polymorphonuclear Cells (polys) 35-80%

Immature Polys (bands) 0-10%

lymphocytes (lymp) 20-50%

monocytes (mono) 2-12%

eosinophils (eos) 0-7%

	basophils (bas)	0-2%
Platelet Count (Plt)		140-450x10 ³ /μL
Red Cell Distribution Width (RDW)	Coefficient of variation	11.5-14.5%
	standard deviation	35-47 fL
RBC Mean Cell Volume (MCV)		82-102 fL (Male)
		78-101 fL (Female)
Mean Cell Hemoglobin Concentration (MCHC)		31-35 gm/dL
CD4+		31-63%
		416-1751/μL (Absolute #)
Reticulocyte		0.5-1.5% (Adult)
		1.1-4.5% (Newborn)
		0.5-3.1% (Infant)
Prothrombin Time (PT)		12-14 seconds
Partial Thromboplastin Time (PTT)		18-28 seconds
Fibrinogen		170-420 mg/dL

Iron Studies

Total Serum Iron (TSI)	76-198 μg/dL (Male)
	26-170 μg/dL (Female)
Total Iron-Binding Capacity (TIBC)	262-474 μg/dL
Transferrin	204-360 mg/dL

Ferritin	18-250 ng/mL (Male)
	12-160 ng/mL (Female)

Chemistry Tests

Aspartate aminotransferase (AST)	5-35 U/L
Alanine aminotransferase (ALT)	7-56 U/L
Albumin	3.5-4.8 U/L
Alkaline phosphatase (ALP)	38-126 U/L
Amylase	30-110 U/L
Anti-streptolysin O Titer (ASO)	<250 (school age)
	<125 (adult)
Bicarbonate	22-26 mEq/L
Bilirubin, direct	<0.3 mg/dL
Bilirubin, total	0.2-1.3 mg/dL
Calcium	8.9-10.4 mg/dL
Cholesterol	120-200 mg/dL
Creatinine	0.5-1.4 mg/dL
Gamma GT	8-78 U/L
Glucose	65-110 mg/dL
Lipase	7-60 U/L
Potassium	3.6-5.0 mEq/L
Sodium	137-145 mEq/L
Total Protein	6.3-8.2 gm/dL

Triglyceride	50-250 mg/dL
Uric Acid	3.5-8.5 mg/dL
Urea Nitrogen (BUN)	7-21 mg/dL

Cardiac Tests

Total CK	38-120 ng/mL
CK-MB	0-3 ng/mL
CK-index	0-3
Troponin	<0.4 ng/mL

Blood Gas

pH	7.34-7.44
pCO ₂	35-45 mmHg
pO ₂	75-100 mmHg
HCO ₃	22-26 mEq/L

Urinalysis

Specific gravity	1.002-1.030
pH	5-7
Protein	negative-trace
Glucose	negative
Ketone	negative

Bilirubin	negative
Blood	negative
Nitrite	negative
Leukocyte	negative
Urobilinogen	0.2-1.0 Ehr U/dL

Micro

RBCs	0-2/HPF
WBCs	0-2/HPF
RBC casts	0/HPF

CSF

Glucose	50-80 ng/dL
Protein	15-45 mg/dL
RBCs	0/ μ L
WBCs	0-3/ μ L

Thyroid

T ₃ -total	60-181 ng/mL
T ₄ -free	0.8-1.5 ng/dL
T ₄ -total	5.5-12.3 ng/mL
TBG	12-30 mg/L
Thyroid Stimulating Hormone (TSH)	0.4-4.5 μ IU/mL

Endocrine

17-OHCS	<4 mg/day
Adrenocorticotrophic Hormone (ACTH)	20-100 pg/mL
Alpha-Fetoprotein (AFP), serum	0-44 ng/mL
Beta-HCG	<5 mU/mL (Male, non-pregnant Female)
CA 19-9	<40 U/mL
Prolactin	0-14 ng/mL

Miscellaneous

Rheumatoid Factor	<30 IU/mL
Prostatic Specific Antigen (PSA)	0-4 ng/mL

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DOCTOR OF LITERACY
1947

Reza Rahimi
DOCTOR OF PHARMACY

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