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

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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.

MECHANIISM;
Type B reactions may result from the following causes:
>Pharmaceutical:
Use of wrong excipients in a drug formulation
>Pharmacokinetics:
Formulation of toxic metabolites or electrophillic 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;immunosupressants)
>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 re_appearing the ADRs

Multiple drug therapy(polypharmacy)

Incidence of ADRs from drug interactions increase sharply with the number of drugs taken.

CURRENT DISEAS:

>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 KNOWLWDGE

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 leads 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

Safe monitoring of herbal medicines:

- Ingestion of traditional medicines generally produces minimal toxicity, life threatening events from severe intoxication may also occur.
- Herbal preparations are often complex mixtures of chemicals. Their composition may vary with regard to the constituents and their concentrations. When an adverse reaction occurs the identification of the causative factor may be difficult or impossible.
- Traditional medicines are also covered by the ADR reporting system.

Eg: market withdrawal of preparations containing kava kava because of liver toxicity.

Counterfeit medicines / fake medicines:

- Containing nothing or very little of the active ingredients. They may also contain toxic ingredients.
- Outcome of the sales of the fake medicine is a lack of intended effect.
- Far reaching consequences when contraceptive agents, vaccines, or antibiotics are counterfeited.
- If the fake medicine contains a toxic product, such as ethylene glycol instead of propylene glycol, serious toxicity may occur.
- Pharmacovigilance centres should also encourage the reporting of unexpected lack of therapeutic effect.

ROLE OF PEARMACISTS IN THE MANAGEMENT OF ADR:

- Monitoring the patients who are at greater risk of developing ADRs.
- Monitoring the patients who ate prescribed with drugs highly susceptible cause ADRs.
- As session and documenting the patients previous allergic status.
- Assessing the patients drug therapy for its appropriateness.
- Assessing health care professionals in detection and assessment of ADRs.
- Documentation of suspected reported reactions for future reference educating patients
- Follow up of patients to assess the outcome of all reaction and management.
- Educating health care professionals about the importance of reporting of ADR.
- Creating awareness about ADRs among healthcare professionals, patients and public.
- Presentation of reports in meeting and conferences.
- Conducting workshops or conference or seminars on ADRs for healthcare professionals.

- Dissemination of signals generated through publications of reports in bulletin or journals.
- Encouraging or stimulating health care professionals in reporting ADR.

DRUG INFORMATION

The provision of drug information is among the most fundamental responsibility of clinical pharmacist. Drug information [DI] 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 as an integral part of pharmaceutical care or relative to a group of patient, such as in the. context of a disease management program

The drug information may be also be needed for academic or, research purpose. Most pharmacist will needed to provide drug information at some stage of their career irrespective of their place of employment Hence it is important for pharmacist to learn the technique of drug information search and response. The term Drug Information Service; refers to activities that are part of all the overall pharmacy service or pharmaceutical care process. The term Medicine Information; is sometime used to highlight that the service's functions relate to medicinal drugs rather than drug of abuse. This term has now been officially adopted in the United kingdom. Drug Information Centre [DIC] refer to the specialized facility that provide drug information to those who needed it.

The term Drug Information developed in the early 1960s. The first drug information center was established at university of Kentucky in 1962 .This center was established to act at source of selected, comprehensive drug information for staff physicians and dentists to evaluate and compare drugs this center was shortly followed by several other drug information centers in the US as well as in the UK , Australia and Canada. A new breed of pharmacists known as ' drug information specialists' developed at this time. A survey was conduct in the US in 1963 by the National Library of medicine to identify the availability of drug literature and the complexities involved in accessing drug information. The results of the survey published in 1965 clearly justified the incorporation of drug information center in healthcare delivery Salient conclusions of the survey included.

- Drug literature is vast and complex
- Drug literature, as well as literature on the clinical experience of drug is growing rapidly in size making it difficult for clinicians to interpret.
- Competent evaluation of masses of drug information is particularly necessary.

In the US more than 80% of DICs are located in hospitals and are apart of pharmacy services' are available in private organizations and other are within educational institutions. Some information service are available in the pharmaceutical industry though these are not considered as DICs. According to the2000 Red book, there are 109 DICs in the US alone However, it is difficult to determine the actual number of centers due to the lack of listing. by any single agency, and the number of DICs is probably higher.

Drug Information in India

Given the ever increasing patient load on the clinicians, the demand for better health care delivery and decreasing budgeters support, drug information services are very relevant in India. However, drug information services and centers are still in their infancy, we have only a few services that qualify as drug information centers. Most of these are located in hospitals and are enlisted.

Lack of well-defined criteria for using the titles of DIC or services adds to the difficulty. Some so- called DICs here are in the pharmaceutical industry. These medical information departments may provide some useful information about, the company's product but they do not provide independent, unbiased drug information.

There is considerably scope for significant growth in the area of drug services. Even though India has been slow to catch up with the Western world in this regard, the process has been definitely started. Salient features that will in fluence the evolution of drug information in India are:

- Growth of clinical pharmacy education and practice - Drug information pharmacists need to have a good knowledge of pharmacotherapeutics, broad clinical experiences, and good written and verbal communication skills. Until recently the development of drug information have been restricted by a lack pharmacists with this training and experiences. This shortage is being addressed as pharmacist shortage.
- Grow the of information technology- Developments in information technology have improved our ability to store and access the vast amount of drug information. Computer based databases are now available for a variety of requirements. However, many of these databases are expensive and can't be affordable. The interest too has been with access to online information for millions of users including scientific literature, government publications and many more.
- Focus on evidence - based medicine- Evidence based medicine isa n approach to practice and teaching that integrates current clinical research evidence with pathophysiologic rationale, professional expertise and patient preferences. Drug information skills helps pharmacist to access EBM resources which can: be used in drug information, the development and implementation of therapeutic guidelines and clinical pathways, drug use evaluations and advice on disease state management.
- Complexity of drug use- Drug therapy is a complex issue in our country. The high cost of some diagnostic and treatment procedures, together with patient demand for fast-acting, symptomatic treatment often results in empirical drug therapy.
- Consumer awareness - Consumers in India have been slow to developed awareness on medication use. However, their awareness has improved in recent years, largely due to increasing healthcare costs and improved access to health information's. Even though patients in India do not participate in healthcare decisions fully as like other western peoples.

STEP: 6 Formulate and Provide Response

This involves a series of steps that must be performed completely, objectively and in a logic sequence. Patient factors, disease factors, medication history and other relevant background information and special circumstances should be considered: The way in which answers are communicated plays a major role in determining how drug information is accepted by physicians

Clinical pharmacists who have broad clinical experience will find out this step easier, as they understand the type of clinical information which may be relevant to a particular question, and are therefore able to specifically ask about this. When a question involves a patient, the patient's age, weight and sex are usually needed. In addition thepatient's diagnosis, other medications, and pertinent medical information such as co-morbidities, and hepatic and renal function are often important to assess.

The response to the question must include restating the request and clearly identifying the problems, issue and circumstances that are relevant to the question. Conflicting viewpoints or considerations should be clearly stated. In the hospital setting the majority of questions will be I answered verbally and responses should be brief, concise and accurate and provided ni a timely manner.

STEP: - 7 Conduct Follow-up and Documentation

Follow-up is the process of verifying the appropriateness, correctness, and completeness of a response after it has been given. When recommendations are made follow-up should always be done in timely manner. This allows pharmacist to know if the recommendations were accepted and implemented. Patient-specific request generally provide opportunities for follow-up. In hospital setting this may involve visiting the ward and offering additional advice and information. This type of follow-up provides opportunities for pharmacist to become involved in direct patient care, independently of ward round participation or routine patient counselling.

Drug Information Centre

The term 'drug information service can be applied to any activity where information about drug use is transferred, and includes patient-related aspects of pharmaceutical care. A drug information Centre is an area where pharmacist (or other health professional) specializes in providing information to health professional or the public. The unique aspects of the drug information Centre are that it draws together a range of information resources and makes these accessible to people who know how to make the best use of them.

Drug information centers vary in size according to the volume of requests. A Centre can be large (national or regional) and focus solely on providing information, or be incorporated into clinical service units with patient care functions. Most are operated by pharmacists but some also use the services of librarians and medical specialists (usually clinical pharmacologist). What makes it a "center" is the concentration of resources and trained

professionals which together have a greater potential value than if the same resources were disseminated and used by individuals in multiple locations.

The term "medicines information" can be used to avoid confusion with services which are limited to problems relating to drugs of abuse. Medicines information has been adopted as the preferred description in the United Kingdom but is used less frequently in other countries where English is à major language. In some languages, 'drugs' and 'medicines" are not distinguished with specific words, so the potential difference in meaning can be lost in translation.

Drug information centers were first established in the USA in the early 1960s and developed in parallel with clinical pharmacy services. Centers are usually located in hospitals or support clinical training programmers, and exist in most countries which have well developed clinical pharmacy services. There has been limited momentum in establishing drug information centers in developing countries in conjunction with patient care services.

Drug information centers can limit their services to health professionals but some also offer a service to the public. There are also centers which are specializing in information for the public. The training and skills required for public focused services differ from those for health professionals, and can be more challenging. A drug information centers can also contribute to pharmacovigilance (adverse drug reaction reporting), drug use reviews, health education programmes and clinical research. Poison information services can be co-located with drug information services, but specific training and resources are required to provide poison information to health professionals and the public.

DRUG INFORMATION RESOURCE

Drug information is stored in a variety of media including textbooks, journals, newsletter, microfiche, optical disks and computer system. Skills to identify, the most appropriate resources to consult in a given clinical situation and to apply these resources determine the quality of drug information provided. This requires the knowledge of the content of t h e resources as well as proficiency. in searching.

The usual approach too many DI queries are to first consult tertiary and secondary resources, followed by primary resources if necessary. The type of requester may dictate which resources are used in answering queries.

Information to patients may be provided from tertiary resources whereas information to physicians may often require reference to the primary and secondary literature.

1) **Primary Resources:**

Primary literature consists of research studies or clinical experience which has not been previously published. This includes clinical trials, short report, case reports and letters: to the editor which describes clinical events• such as adverse drug reactions or unexpected clinical outcomes. The term primary literature refers to the type of article rather than the source of publication. For example, the results of a clinical trial of a new antihypertensive drug published in a medical journal is an example of

primary literature, whereas a general review of antihypertensive drug therapy published in the same journal could not be considered as primary literature.

The primary literature is growing at an exponential rate. Over 20,000. biomedical journals are published annually. Examples of journals which publish primary literature include Annals of Internal medicine. These are usually the most up to day resources for information. For drug information purposes annals should be consulted so. that the strength of the research methods and the generalization of the results can be evaluated. Literature evaluation skills are essential for pharmacist providing drug information. Pharmacist must learn to systemically review and critique biomedical literature so as to efficiently and effectively determine the validity of the results of studies, and the applicability in clinical practice.

2) **Secondary Resource**

Secondary resources provide an overview of previously published work, and include indexing and abstracting service of the primary literature. Examples of secondary resource include the abstracting scenes DRUGDEX and International Pharmaceutical abstracts and the inducing services BIOSIS Preview, ClinAlen Drug Information System. An indexing system provides only bibliographic information that is indeed the topic and provides the original abstract. Although most of the resources provide access to primary literature, each covers different biomedical journals, meeting abstract and newsletters. Accessing more than one secondary resource may therefore allow more thorough information retrieval.

While secondary resources are available both online and in CD-ROM format, they may. be preferred when numerous individuals use the same system. Online searching is especially useful for searching, to access information from remote locations without networking capabilities and for use by single users. Examples of online resources include PubMed from the National library of Medicine. This is available free of charge and may be of help to pharmacist or organizations who cannot afford to pay for a CD version but who can have access to the internet. These consist of general literature including textbooks and full-text computer databases. Examples of tertiary resources include united Sources: Pharmacopeia Drug Information, Meyer's Side Effects of Drugs, Remington's Pharmaceutical Sciences, Merck index, Red Book; Martindale. The Complete Drug reference, The Merck Manual, and Applied Therapeutics. In addition, review articles in biomedical journals are sometimes classified as tertiary 'literature, as is much of the information found on them. General review articles contain background information on the subject discussed along with a comprehensive review of the literature by acknowledged experts of the literature by an acknowledged expert in the field.

3) **Tertiary resources:**

The most commonly used sources of information because they are easy to use, convenient, concise, and compact. However there are some disadvantages associated with use of tertiary literature. First the information may not be complete. Topics may be presented in insufficient detail due to space limitations of the textbook or the topic by the author. Secondly, even 'new' textbooks may be several years out of date owing to the time lag that occurs from the time a book is written

POISON INFORMATION

Definition

Poison information is a specialized drug information which includes information about the toxic effects of chemicals and pesticides, hazardous material spills, household products, overdose of therapeutic medicines ,plants including mushrooms ,animal toxins from the bites of snakes, spiders and other venomous creatures, and stings.

Goal

The goal of poison information services is to reduce the morbidity and mortality caused by poisoning and improve patient's health related quality of life.

Poison Information Centre

Poison information services are provided by a specialized center known as a poison information center (PIC) or poison control center (PCC):

Organization

The organization pattern of a PIC should be based on the anticipated "ideal human exposure call volume." The PIC is usually staffed by a physician (medical director), a pharmacist (technical director), an administrator, at least one clinical toxicologist and a poison information specialist with the required secretarial assistance.

Functions

- Patient management
- Toxicological analytical services
- Toxicovigilance
- Education and training of healthcare professionals and public
- Prevention of poisoning
- Research in poisoning
- Development of therapeutic guidelines / protocols for poison management.

Facilities

- **Location:** A feasible location for the PIC is within a hospital providing emergency and intensive care services. Ideally, the PIC should be co-located with a hospital clinical toxicology service which is concerned with the identification, treatment and prevention of the harmful effects of chemicals, including natural substances on humans. This type of setup will provide ready access to a network of medical disciplines that will support and enhance the

work of the center. Other locations include a medical or pharmacy college. Regardless of the location, it is wise to have a liaison with a hospital/ university medical library.

- **Space:** The PIC should be placed in a spacious. facility to accommodate the service staff and needs. A work area of 200 square feet per workstation is recommended, with a separate office for the medical director and manager supervisor. The working area should have adequate lighting and ventilation.
- **Equipment:** The PIC should be well equipped with the necessary basic facilities, including furniture ,communication equipment's like telephone, fax, email, etc photocopying machine, book shelves, filing cabinets, lockable cabinets etc.
- **Information Resources:** There are 3types of information resources:

1. **Primary resources**
2. **Secondary resources**
3. **Tertiary resources**

Primary Resources:

Human and experimental toxicology, neuro-toxicology. clinical toxicology, Pharmacology and toxicology, Indian journal of toxicology, Journal of medical toxicology, Indian journal of Environment and Toxicology.

Secondary Resources:

Example-POISINDEX, MEDLINE, Toxbase, Toxline , Toxicology abstracts, Index medicus.

Tertiary Resources:

Indian pharmacopeia, United states pharmacopeia, British National Formulary, Oxford Medical dictionary, Medical and general toxicology, Occupational and industrial toxicology.

"Systemic Approach In Handling Poison Information Queries"

Handling a poison information query is the ultimate responsibility of the poison information specialist. To handle the query the specialist should have good skills in communicating clearly and concisely to elicit or present explanatory or interpretive information It is necessary to establish and maintain effective working relationships with other employees of relevant organizations. The following steps should be adopted to systematically approach a poison information query.

STEP 1: OBTAIN THE REQUESTERS DEMOGRAPHICS

Receive and accept the query related to the service either over the phone or in person. Establish the identity of the enquirer by gathering contact details. Also obtain all required information from the requester that will allow you to reply to the query. If the enquirer is a healthcare professional the position and anticipated knowledge of the enquirer should be determined. If the it takes time to obtain information, ask the enquirer to call back or note their contact number