Notes on Pharmacovigilance

Definition & Aim

Pharmacovigilance is defined as the science and activities relating to the detection, assessment, and prevention of adverse drug reactions in humans. It is regarded as a type of continuous monitoring of unwanted effects and other safety-related aspects of drugs, which are already placed in markets.
Pharmacovigilance also plays an important role in rational use of drugs, by providing information about the adverse effects possessed by the drugs in general population.

Scope of Pharmacovigilance:

1. Exhibiting the efficacy of drugs by monitoring their adverse effect profile for many years from the lab to the pharmacy.
2. Tracking any drastic effects of drugs improving public health and safety in relation to the use of medicines.
3. Encouraging the safe, rational and cost-effective use of drugs.
4. Promoting understanding, education and clinical training in pharmacovigilance and effective communication to the generic public.
5. Providing information to consumers, practitioners and regulators on the effective use of drugs.
6. Designing programs and procedures for collecting and analyzing reports from patients and clinicians conclude to the objectives of pharmacovigilance studies.

The activities involved in pharmacovigilance are:

a. Post marketing surveillance and other methods of ADR monitoring such as voluntary reporting by doctors (e.g. yellow card system of UK), prescription event monitoring, computerized medical record linkage and other cohort/case control studies

b. Dissemination of ADR data through 'drug alerts'. 'medical letters' , advisories sent to doctors by pharmaceuticals and regulatory agencies (such as FDA in USA. committee on safety of medicines in UK).
c. Changes in the labelling of medicines indicating restrictions in use or statuary warning ,precautions, or even withdrawal or the drug, by the regulatory decision making authority.

Phamacovigilance centers have been set up in most countries. **The Uppsala Monitoring Centre (Sweden)** is the international collaborating centre.

In India. the Central Drug standard Control Organization (CDSCO) is coordinating the pharmacovigilance programme, under which peripheral, regional and zonal monitoring centres have been set up along with a National Pharmacovigilance Advisory Committee.
The pharmacovigilance centers collect, communicate and disseminate ADR data by linking with hospitals as well as practitioners and are also expected to provide experts for assessing causality and severity of ADRs by using standard algorithms and rating scales like **the Naranjo algorithm (causality assessment)** and **Modified Hartwig scale (severity grading**).

Pharmacovigilance Programme of India (PvPI)

• The Central Drugs Standard Control Organization (CDSCO), Directorate General of Health Services under the Ministry of Health & Family Welfare, Government of India in association with Indian Pharmacopeia commission, Ghaziabad is initiating a nation-wide Pharmacovigilance Programme for protecting the health of the patients by promising drug safety.
• The Programme shall be coordinated by the Indian Pharmacopeia commission, Ghaziabad as a National Coordinating Centre (NCC). The center will operate under the supervision of a Steering Committee.
• The Pharmacovigilance Programme of India (PvPI) was started by the Government of India on **14th July 2010** with the All India Institute of Medical Sciences (AIIMS), New Delhi as the National Coordination Centre for monitoring Adverse Drug Reactions (ADRs) in the country for safe-guarding Public Health.
• In the year 2010, 22 ADR monitoring centres including AIIMS, New Delhi was set up under this Programme.
• To safeguard implementation of this programme in a more effective way, the National Coordination Centre was shifted from the All India Institute of Medical Sciences (AIIMS), New Delhi to the Indian Pharmacopoeia Commission, Ghaziabad, Uttar Pradesh on 15th April 2011

Mission: Safeguard the health of the Indian population by ensuring that the benefits of use of medicine outweigh the risks associated with its use.
Vision: To improve patient safety and welfare in Indian population by monitoring the drug safety and thereby reducing the risk associated with use of medicines.

Short term goals

• To develop and implement pharmacovigilance system in India
• To enroll, initially, all MCI approved medical colleges in the program covering north, south, east and west of India
• To encourage healthcare professionals in reporting of adverse reaction to drugs, vaccines, medical devices and biological products
• Collection of case reports and data

Long term goals

To expand the pharmacovigilance programme to all hospitals (govt. & private) and centers of public health programs located across India
To develop and implement electronic reporting system (e-reporting)
To develop reporting culture amongst healthcare professionals
To create a nation-wide system for patient safety reporting
To identify and analyze the new signal (ADR) from the reported cases
To make ADR reporting mandatory for healthcare professionals

Key Definitions & Adverse Drug Reactions Classification:

Adverse drug reaction (ADR)—The World Health Organization defines an ADR as "any response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." In other words, an ADR is harm directly caused by the medicine at normal doses, during normal use. An unexpected ADR refers to a reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or is unexpected from characteristics of the medicine.

The term adverse drug effect is interchangeable with adverse drug reaction. Side Effect—Any unintended effect of a pharmaceutical product occurring at doses normally used in humans which is related to the pharmacological properties of the medicine. Such effect may be either positive or negative. Such effects may be well-known and even expected and may require little or no change in patient management.

Serious Adverse Effect— Any untoward medical occurrence that at any dose and results in death, requires hospital admission or prolongation of existing hospital stay, results in persistent or significant disability or incapacity, or is life threatening.
Adverse Drug Event-Any untoward medical occurrence that may be present during treatment with a medicine but does not necessarily have a causal relationship with this treatment, that is, an adverse outcome that occurs while the patient is taking the medicine but is not, or not necessarily, attributable to it.
Causality—The probability that a particular medicine or substance is responsible for an isolated effect or ADR.
Signal—Reported information on a possible causal relationship between and adverse event and a medicine, the relationship being previously unknown or incompletely documented. Usually more than one signal report is required to generate a signal, depending on the seriousness of the event and the quality of the information.
Prescribing error—Incorrect medicine ordering by a prescriber.
Medication error—Administration of a medicine or dose that differs from the written order.
Negligence—Medical decision making or care below accepted standards of practice.

Adverse Drug Reactions and its Classification:

ADRs are unexpected, unintended, undesirable, or excessive responses to a medicine, and they may be harmful to the patient. By contrast, side effects are known reactions to a medicine and are typically listed in the medicine's labeling. The American Society of Health-System Pharmacists2 provides another definition of ADR. It describes an ADR as any unexpected, unintended, undesirable, or excessive response to a medicine that—

- Requires discontinuing the medicine (therapeutic or diagnostic)
- Requires changing the pharmaceutical therapy
- Requires modifying the dose (except for minor dosage adjustments)
- Necessitates admission to a hospital
- Prolongs the patient's stay in a health care facility

• Necessitates supportive treatment
• Significantly complicates diagnosis
• Negatively affects prognosis
• Results in temporary or permanent harm or disability, or in death

ADRs can be classified into six types—

• **Type A reactions (dose-related)**—These reactions are an exaggerated, but otherwise normal pharmacological responses to the effects of the medicines given in therapeutic dose, cause significant morbidity but are rarely severe. The reaction is treated by reducing the dose or withholding the medicine and considering alternative therapy. **Examples** of such reactions include– *Pharmacodynamic (e.g., bronchospasm from beta-blocker administration) or Toxic (e.g., deafness from overdosing of aminoglycosides)*

• **Type B reactions (non-dose related)**—These reactions are bizarre(unusual) and unpredictable with no relation to dose or pharmacological action of the medicine and are often allergic in nature. They are uncommon but are often severe and cause high mortality. The reaction is treated by stopping the medicine and avoiding it in the future. **Examples** of such reactions include– *Medicine- induced diseases (e.g., antibiotic-associated colitis), Allergic reactions (e.g., anaphylactic reaction to penicillin administration) , Idiosyncratic reactions (e.g., irreversible aplastic anemia caused by chloramphenicol)*

• **Type C reactions (dose-related and time-related)—**These reactions are chronic (long term)and related to cumulative dose. The reaction is treated by reducing the dose or withholding the medicine, which may have to be withheld for a long time. **Examples** of such a reaction include— *Osteoporosis with oral steroids, Hypothalamic-pituitary-adrenal axis suppression by corticosteroids*

• **Type D reactions (time related)—**These reactions are delayed (i.e., have a lag time) after the use of a drug. They are uncommon but their treatment is often intractable. **Examples** of such reactions include— *Teratogenic effects with anticonvulsants or lisinopril , Carcinogenesis, Tardive dyskinesia*

• **Type E reactions (withdrawal)**—These reactions occur soon after the end of use (i.e.,withdrawal) and are uncommon. The reaction is treated by reintroducing the medicine and then withdrawing it slowly. **Examples** of this reaction include— *Withdrawal syndrome with benzodiazepines,Opiate withdrawal syndrome, Myocardial ischemia after beta-blocker withdrawal*

• **Type F reactions (unexpected failure of efficacy)**—These reactions occur when there is a failure of efficacy. Such reactions are common, may be dose-related and are often caused by drug interactions. The reaction is treated by increasing the dose and considering the effects of concomitant therapy. **Examples** include— *Resistance to antimicrobials, Inadequate dosage or oral contraceptives, particularly when used with specific enzyme inducers.*