**Module-3**

**ADVERSE DRUG REACTIONS:**

**Medicinal product:**

“(a) Any substance or combination of substances presented as having properties for treating or

preventing disease in human beings; or (b) Any substance or combination of substances which may

be used in or administered to human beings either with a view to restoring, correcting or modifying

physiological functions by exerting a pharmacological, immunological or metabolic action, or to

making a medical diagnosis.”

(medicinal product” defined in an EU Directive (2001/83/EC)).

**Side effect:**

Unintended effect occurring at normal dose related to the pharmacological properties. (WHO definition)

**Adverse event:**

A noxious and unintended response to a medicinal product for which there is no reasonable possibility that the product caused the response.

**Adverse Drug reaction:**

A noxious and unintended response to a medicinal product for which there is a reasonable possibility that the product caused the response.

The response to the medicinal product explains that there is a causal relationship between a medicinal product and the adverse event.

Reasonable possibility states that there are facts and/or evidence to support a causal association with the medicinal product.

**SUSAR- Serious unexpected suspected Adverse reaction:**

The serious adverse drug reaction which is not consistent with the product information**.** The term is used in clinical trials.

Types of Adverse drug reactions (ADRs):

Based on the time taken to onset:

* Acute: If the event occurs less than 60 minutes
* Sub- acute: Event occurs 1-24 hours
* Latent: Event occurred greater than or more than 2 days.

**Type of Adverse drug reactions: (Rawlins and Thompson classification later modified as Wills & Brown classification)**

**Type A:**

* Type A are considered as Augmented reactions
* Reactions can be explained from the pharmacology of the drug
* Dose dependent reactions.
* Cane be reduced by dose reduction

Examples:

1. Beta blockers—Bradycardia
2. Anti-coagulants--- Bleeding
3. Nitrates--Headache

**Type B:**

* Type B are Bizarre reactions.
* Cannot be explained from the pharmacology of the drug
* Not dose dependent
* Host depended factors can be an alternate explanation.

Examples:

1. Penicillin- Anaphylaxis.

**Type C:**

* Chronic effects
* Adverse reactions associated with prolonged use of drugs.

Examples:

1. Phenothiazines- prolonged use causes orofacial dyskinesia
2. Chronic use of prednisolone- Cushing’s syndrome
3. Aspirin- Analgesic nephropathy

**Type D: (**Delayed reactions)

* Adverse events occurring in patients’ years after treatment or effects occurring in their children who did not receive that treatment.
* Teratogenic effects also come under Type D adverse reactions.

Examples:

1. Clear cell carcinoma of vaginal in the daughters of women who took diethylstilbestrol during pregnancy.
2. Chemotherapy-secondary tumors.

**Type E:**  End of treatment effects.

These ADRS occurs when a drug is suddenly discontinued.

Examples:

1. Adrenocortical insufficiency after sudden stopping of glucocorticoid.
2. Rebound hypertension after sudden withdrawal of Beta blocker.
3. Phenytoin withdrawal- Seizures

**Type F**: Familial.

Reactions occurring in the genetically predisposed patients.

Examples:

1. G6PD deficiency individuals—Hemolytic anemia with primaquine.

**Type G**: Genotoxicity.

Reactions with irreversible genetic damage

Examples:

Thalidomide—Teratogenetic causing genetic damage in fetus.

**Type H**: Hypersensitivity.

* Reactions occurred due to immune system.
* Reduces once the medicine is withdrawn.

Examples:

Allergic reaction with antibiotics.

**Type U**: Unclassified

Mechanism is not clear to explain the adverse reaction.

Example:

Simvastatin: Taste disturbances

**Based on the severity the Adverse drug reactions are:**

Minor/less Severe: No need of management required or prolongation of hospitalization necessary.

Examples: Opioids—constipation; Cetirizine- Drowsiness

Moderately severe: A change in treatment is required (dose modification, addition of a drug), but not necessarily discontinuation of the drug is required. Hospitalization may be prolonged or specific treatment may be required.

Example: Hormonal Contraceptive: Venous thrombosis

Severe ADRs: Adverse reaction is potentially life threatening & requires discontinuation of the drug and specific treatment of the ADR.

Example:

Angiotensin converting enzyme Inhibitor (ACEI): Angioedema.

Lethal ADRS: ADRS directly or indirectly contributes to death.

Example: Anticoagulants: Hemorrhage.