Adverse drug reactions

An adverse drug reaction is a response to a drug which is undesirable and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or for alteration of physiological function.

All drugs are capable of causing adverse reactions and whenever a drug is given a risk is taken. The magnitude of risk has to be considered along with the magnitude of the expected therapeutic benefit in deciding whether to use or not to use a particular drug in a given patient.

ADR may develop promptly or only after prolonged medication or even after stoppage of the drug.

ADR may be classified:

Predictable (type A or augmented) reactions – These are based on the pharmacological properties of the drug, they are normal response to the drug; they include; side effects, toxic effects and consequences of drug withdrawal.

Unpredictable (Type B or Bizarre) reactions – these are based on patient peculiarities and not drug's known actions; includes; allergy and idiosyncrasy. They are less common, often non dose related, generally more serious and require drug withdrawal.

Severity of drug reactions has been graded

? **Minor** – No therapy, antidote or hospitalization required.
? **Moderate** – Requires change in drug therapy, specific treatment, prolongs hospital stay.
? **Severe** – potentially life threatening causes permanent damage and requires intensive medical treatment.
? **Lethal** – Directly or indirectly contributes to death of the patient.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse drug reactionsor any other drug related problems. It has an important role in the rational use of medicines, as it provides the basis for assessing safety of medicines.

Prevention of adverse drug reactions

Adverse drug reactions can be minimized but not altogether eliminated:

i. Avoid all inappropriate use of drugs in the context of patient's clinical condition.
ii. Use of appropriate dose, route and frequency of drug administration.
iii. Consideration of patient's previous drug history including allergies.
iv. Rule out possibilities of drug interactions when more than one drug is prescribed.

v. Adopt correct drug administration technique e.g. anticancer drugs.
vi. Carry out appropriate laboratory monitoring e.g. prothrombin time with warfarin.

Adverse drug effects can categorized

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 drug. They can be predicted from the pharmacological profile of a drug and are known to occur in a given percentage of patients.

Reduction of dose may reduce the symptoms. For example atropine used in preanaesthetic medication for its antisecretory action; it also causes dryness of mouth.

Secondary effects – These are indirect consequences of primary action of the drug e.g. suppression of bacterial flora by tetracyclines paves way for superinfection.

Toxic effects – the result of excessive pharmacological action of the drug due to overdosage or prolonged use. Overdosage may be absolute (accidental, homicidal, suicidal) or relative. The effects are predictable and dose related.

Drug allergy – It is an immunologically mediated reaction producing symptoms which are unrelated to the pharmacodynamic profile of the drug; occurs generally even with smaller doses and have different time course of onset and duration. Allergic reactions occur only in a small proportion of the population exposed to the drug and cannot be produced in other individuals at any dose. Examples include; penicillin, sulfonamides, salicylates, tetracyclines etc.

Photosensitivity – a cutaneous reaction resulting from drug induced sensitization of the skin to UV radiation e.g. sulfonamides, fluoroquinolones, chloroquine, chlorpromazine.

Drug dependence – Drugs capable of altering mood and feelings are liable to repetitive use to derive euphoria, withdrawal from reality, social adjustment e.t.c.

Drug withdrawal reactions – Sudden interruption of therapy with certain drugs can result in adverse consequences e.g. clonidine sudden withdrawal results in severe hypertension, restlessness; sudden withdrawal of antiepileptic drugs may increase frequency of seizures.

Teratogenicity – Capacity of a drug to cause foetal abnormalities when administered to the pregnant mother; e.g. thalidomide, anticancer, tetracyclines. The placenta does not constitute a barrier and any drug to a greater or lesser extent can cross it.

Mutagenicity / carcinogenicity – The capacity of a drug to cause genetic defects and cancer respectively, e.g. anticancer, radioisotopes tobacco, estrogens.

Drug induced diseases (iatrogenic) – Are functional disturbances caused by drugs which persist even after the offending drug has been withdrawn and largely eliminated; e.g. peptic ulcer by salicylates and corticosteroids; hepatitis by isoniazid.

Drug use in Pregnant Women

When women first learn they are pregnant most will embark on a program of good nutrition, exercise and general wellness to avoid causing harm to themselves and their growing baby.

Although some women may forgo treatments without any health consequences, mothers who require medication for a chronic health condition will be faced with a dilemma: continue therapy and possibly risk harm to their baby or risk under-treating a serious illness, which can be harmful to both.

The Food and Drug Administration (FDA), the government agency that oversees the safety of drugs, evaluates all the available research studies that test the safety and efficacy of new drugs.

Experimental drugs are first tested on animals to determine an initial level of safety. If they are deemed sufficiently safe, the drugs are then tested on humans.

These studies are often "well controlled", meaning that the study includes a group of patients receiving the experimental drug and another group receiving either an approved drug, or an inactive substance (placebo).

Most drugs however, are not tested in pregnant women to avoid the potential harm to the mother and fetus. Additionally, if a drug is considered safe to take early in the first trimester, it may turn out to be harmful during the last few months of pregnancy as the body's physiology changes throughout pregnancy. Still, there are some drugs that initially had an unclear safety rating but later received a safe rating after many women taking the drug during pregnancy had no ill effects.

So the FDA has created a system that assigns a safety category -- A, B, C, D and X -- which must be applied to the labels of all drugs. These letters represent very important information about drug safety during pregnancy. Since 1996, every drug label includes a statement about the drug's known effects on pregnancy.

This system, which has been criticized for its vague definitions and use of medical jargon, can be difficult to interpret. But an understanding of how these categories are assigned can help pregnant women make very important decisions.

FDA Pregnancy Category Chart

The safest drugs falling under the category A, the least-safe drugs in category X.

Category A - Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities. Drugs that fall under category A have had several well-controlled studies that found no harmful effects or increase in birth defects. These drugs have all had studies conducted in pregnant woman with positive results. Very few drugs fall into this category. Prenatal vitamins receive a category A rating.

Category B - Animal studies have revealed no evidence of harm to the fetus, however there are no adequate and well-controlled studies in pregnant women or animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus. Drugs assigned a category B rating are not likely to pose a threat to the fetus from the evidence in animal studies, but no well-controlled studies have been performed in pregnant women. However, a drug may also receive a category B rating if animal

studies have shown evidence of fetus damage but the same drug tested on pregnant women posed no threat.

Category C- Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women. or No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women.

Category D- Studies, adequate well-controlled or observational, in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.

Category X - Studies, adequate well-controlled or observational, in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.