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ADVERSE DRUG REACTIONS

'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 modifications of physiological function'.

Adverse events are unintended pharmacologic effects that occur when a medication is administered correctly while a side effect is a secondary unwanted effect that occurs due to drug therapy.

Adverse drug reactions (ADRs) are the undesirable effects of drugs even when administered in daily normal doses. It has been seen that ADRs may arise even after single administration of drug(s),

Types:

1. Type A reactions – sometimes referred to as augmented reactions – which are ‘dose-dependent’ and predictable on the basis of the pharmacology of the drug
2. Type B reactions – bizarre reactions – which are idiosyncratic and not predictable on the basis of the pharmacology.

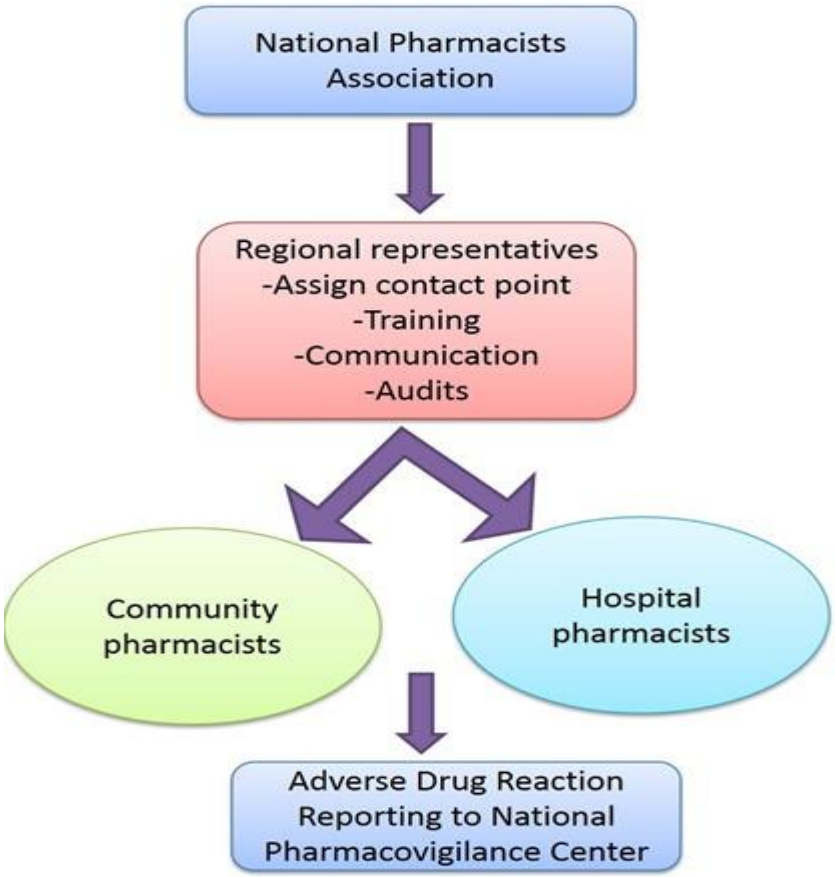
Reduction of ADR:

1. Identify the subgroup of patients who are likely to be susceptible to the adverse effect and modify the treatment choice accordingly.
2. Ensure the treatment plan mitigates any possible adverse effects.

Reasons for ADR:

- Drug-related factors
  - Nature of the drug
  - Degree of exposure (dose, duration, frequency)
  - Route of administration
  - Cross-sensitization
- Host-related factors
  - Age : (elderly & neonates)
  - Sex : (pregnancy)
  - Genetic factors (HLA type, Acetylator status)
  - Concurrent medical illness (e.g. viral infection, bronchial asthma)
  - Previous drug reaction
  - Multiple allergy syndrome

Role of Pharmacist in ADR:



DRUG INDUCED DISEASES

Drug induced disease is defined as the unintended effect of a drug that results in mortality or morbidity with symptoms sufficient to prompt a patient to seek medical attention and/or to require hospitalization and may persist even after the offending drug has been withdrawn.

Drug-induced liver diseases are diseases of the liver that are caused by physician-prescribed medications, over-the-counter medications, vitamins, hormones, herbs, illicit ("recreational") drugs, and environmental toxins.

Types of Drug Induced Diseases:

- Predictable
- Unpredictable

Drug induced liver diseases:

Drug-induced liver diseases are diseases of the liver that are caused by physician-prescribed medications, over-the-counter medications, vitamins, hormones, herbs, illicit ("recreational") drugs, and environmental toxins.

Drugs and chemicals can cause a **wide spectrum of liver injury**. These include:

- Mild elevations in blood levels of liver enzymes without symptoms or signs of liver disease
- Hepatitis (inflammation of liver cells)
- Necrosis (death of liver cells) that often is caused by more severe hepatitis
- Cholestasis (decreased secretion and/or flow of bile)
- Steatosis (accumulation of fat in the liver)
- Cirrhosis (advanced scarring of the liver) as a result of chronic hepatitis, cholestasis, or fatty liver
- Mixed disease, for example both hepatitis and necrosis of liver cells, hepatitis and fat accumulation, or cholestasis and hepatitis.
- Fulminant hepatitis with severe, life threatening liver failure
- Blood clots in the veins of the liver

Examples of drugs that can cause **acute hepatitis** include acetaminophen (Tylenol), phenytoin (Dilantin),aspirin, isoniazid (Nydrazid,Laniazid), diclofenac (Voltaren), and amoxicillin/clavulanic acid (Augmentin).

Examples of drugs that can cause **chronic hepatitis** include minocycline (Minocin), nitrofurantoin (Furadantin, Macrodantin),phenytoin (Dilantin), propylthiouracil, fenofibrate (Tricor), and methamphetamine.

Drug induced kidney diseases:

What drugs are toxic to kidneys?

- **Antibiotics**.
- Diuretics.
- **Non-Steroidal Anti-Inflammatory Drugs** (**NSAIDs**)
- Proton Pump Inhibitors (PPIs)
- Supplements.
- Laxatives.

Drug-induced nephrotoxicity is increasingly recognized as a significant contributor to **kidney** disease including acute **kidney** injury (AKI) and chronic **kidney** disease (CKD). **Nephrotoxicity** has a wide spectrum, reflecting damage to different nephron segments based upon individual **drug** mechanisms.

Drug induced Hematologic diseases:

- The most common drug-induced hematologic disorders include aplastic anemia, agranulocytosis, megaloblastic anemia, hemolytic anemia, and thrombocytopenia.
- Drug-induced hematologic disorders are generally rare adverse effects associated with drug therapy.
- The incidence of rare adverse drug reactions (ADRs) is usually established by postmarketing surveillance and reporting.
- Rechallenging a patient with an agent suspected of inducing a blood disorder is not generally recommended.
- Drug-induced hematologic disorders can occur by two mechanisms: direct drug or metabolite toxicity or an immune reaction.
- The primary treatment of drug-induced hematologic disorders is removal of the drug in question and symptomatic support of the patient.

Drug induced GI disorders:

Medications produce symptoms,

- by altering GI physiology (eg, constipation induced by anticholinergic medication),
- by causing tissue toxicity and damage (eg, ulcers from non-steroidal anti-inflammatory drugs (NSAIDs)),
- by changing the intestinal microbiota (eg, antibiotics causing *Clostridium difficile* infection), or
- by unknown mechanisms, such as with metformin.

The pharmacologically active compound, as well as the excipient (or packaging) of the tablet or capsule can cause problems.

Nausea and vomiting may be caused by mechanisms remote from the GI tract.

Drug induced dermatologic reactions:

Drug-induced skin disorders are often classified as either **acute or chronic.**

Acute diseases include erythematous eruptions; urticaria, angioedema, and anaphylaxis; fixed-drug eruptions; hypersensitivity syndrome; Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN); warfarin-induced skin necrosis; vasculitis; serum sickness–like reaction; acute generalized exanthematous pustulosis (AGEP); and photosensitivity.

Chronic disorders include drug-induced lupus, drug-induced acne, and pigmentary changes.

TERATOGENECITY

The capability of producing fetal malformation is teratogenicity.

Teratogens are substances that may cause birth defects via a toxic effect on an embryo or fetus. **Teratogens** are classified into **four** types:

- Physical agents,
- Metabolic conditions,
- Infection,
- Drugs and chemicals.

Known Teratogens are,

- angiotensin converting enzyme (ACE) inhibitors, such as Zestril and Prinivil.
- alcohol.
- aminopterin.

- androgens, such as methyltestosterone (Android)
- busulfan (Myleran)
- carbamazepine (Tegretol)
- chlorobiphenyls.
- cocaine.

For example, in the early 1960's, a drug known as thalidomide was used to treat morning sickness. Exposure of the fetus during this early stage of development resulted in cases of phocomelia, a congenital malformation in which the hands and feet are attached to abbreviated arms and legs.