



# ***ADVERSE DRUG REACTIONS***

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## ***Adverse Reaction***

- Harmful or seriously unpleasant effects occurring at doses for therapeutic, prophylactic or diagnostic effect and which call for reduction of dose or withdrawal of the drug and forecast hazard from future use.

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# ***Toxicity***

Implies a direct action of drug at high dose, damaging cells.

- Liver damage – Paracetamol overdose.
- Eighth cranial nerve damage – Gentamicin.
- All drugs toxic in overdose.
- Oculotoxicity by Ethambutol, Chloroquine.
- Mutagenecity, Carcinogenecity, Teratogenecity.

# ***Secondary Effects***

- Indirect consequences of a primary drug action.
- Vitamin deficiency or oppurtunistic infections occur in patients whose normal bowel flora has been altered by antibiotics like tetracyclines.
- Diuretic induced hypokalaemia causes digoxin intolerance.

## ***Idiosyncrasy***

Implies an inherent qualitative abnormal reaction to a drug, usually due to genetic abnormality, e.g. Porphyria.

“ Cur'd yesterday of my disease,  
I died last night of my physician”

## ***Idiosyncrasy...***

- Haemolytic anaemia caused by Priamquine in Glucose-6-Phosphate Dehydrogenase deficiency in RBCs.
- Prolonged apnoea caused by pseudo-cholinesterase deficiency.
- Salicylism, Iodism & Cinchonism.
- Aspirin produces Bronchial Asthma.

## ***Intolerance***

- Appearance of ADR at therapeutic dose.
- Chloroquine causes vomiting and abdominal pain.
- Phenobarbitone may cause excitement and mental confusion.

## ***Drug Withdrawal Reactions***

- Clinical condition may worsen after sudden withdrawal.
- Acute adrenal insufficiency on sudden withdrawal of corticosteroids.
- Severe hypertension on clonidine withdrawal.
- Worsening of angina pectoris or myocardial infarction on withdrawal of  $\beta$ -blockers.
- Anti-epileptic drug withdrawal may increase seizures.

# ***Side Effects***

- Extension of pharmacological effects in therapeutic doses.
- Predictable, dose-related and minor in nature.
- Dryness of mouth & skin by Atropine.
- Postural hypotension by Prazosin.
- Hypokalemia by Furosemide.
- Constipation by Morphine.
- Headache by Nitrates.

# ***Adverse Event ( AE )***

An AE can be any unfavourable and unintended sign, symptom or disease temporarily associated with the use of a medicinal product.

- Exacerbation of a pre-existing episodic event or condition.
- Condition detected or diagnosed after “study drug” administration.
- Continuous persistent disease or symptoms present at baseline that worsen following start of study drug.

# ***Serious Adverse Event (SAE)***

An SAE is any adverse event occurring at any dose that results in any of the following outcomes:

- a. Death
- b. A life-threatening adverse event.
- c. Inpatient hospitalisation or prolongation of existing hospitalisation.
- d. A disability / Incapacity.
- e. A congenital anomaly in the offspring of a subject who received drug.

# ***Allergic (Hypersensitivity) Reactions***

- Immunologically mediated.
- Unrelated to dose & effects.
- Prior cell sensitisation needed.
- Latent period of one to two weeks after first exposure.
- Re-exposure produces antigen-antibody reaction, may be mild or serious.
- Targets: Skin, Respiratory tract, Blood & Vessels.

# **Types of ADRs**

## **PREDICTABLE OR TYPE 1 REACTIONS**

- Side Effects.
- Secondary Effects.
- Drug Withdrawal Reactions.
- Toxic Effects.
- ✓ More common, dose dependent, based on pharmacological properties of drug.

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# **Types of ADRs...**

## **UNPREDICTABLE OR TYPE 2 REACTIONS**

- Intolerance.
- Idiosyncrasy.
- Allergy or Hypersensitivity.
- ✓ Based on patient & not on drug action.
- ✓ Less common, dose independent.
- ✓ More serious & require drug discontinuation.

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# Unavoidable ADRs

- Pharmacological effects in therapeutic doses:  
Dryness of mouth & skin by Anticholinergics.  
Palpitation & tachycardia by Catecholamines.
  - Sequelae of pharmacological effects in therapeutic doses:
  - Postural hypotension with Prazosin & Hydralazine.
  - Throbbing headache & syncope by Nitrates
- Low safety margin of drugs:

## Digoxin, Lithium, Anticancer drugs

## Causation

- **Definite** – event corresponds to what is known; ceases on stopping drug, event returns on restarting.
- **Probable** – event ceases on stopping drug, not explained by patient's disease.
- **Possible** – event does not correspond to the drug, could not be explained by patients disease.

# **Recognition of ADR**

When an unexpected event, for which there is no obvious cause, occurs in a patient already taking a drug, it may be induced.

Distinction between natural disease progression & drug-induced deterioration is challenging,

Sodium in antacids may aggravate cardiac failure.

Antidepressants may provoke epileptic seizures.

Aspirin may cause bronchospasm in asthmatics.

**THANK YOU**