Adverse Drug Reaction

- An adverse drug Reaction is an unwanted or harmful reaction experienced following the administration of a drug or combination of drugs under normal conditions of use.
- WHO: "Any response to a drug which is noxious, unintended and occurs at doses used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiological functions."

Common ADRs

- Constipation with opioids
- Sedation with antihistamines
- GI upset with NSAIDs
- Dryness of mouth with atropine
- Hypoglycaemia with sulfanamides

Adverse Drug Reaction

- Any unintended, undesirable or unexpected effect of a prescribed medication that:
  - Requires discontinuing a medication or modifying the dose
  - Requires treatment with a prescription medication
  - Requires initial or prolongation of hospitalization
  - Results in a disability or is life threatening
  - Results in death

Classification of ADR

Onset of event:

1. **Acute**
   - within 60 minutes
2. **Sub-acute**
   - 1 to 24 hours
3. **Latent**
   - > 2 days

Severity of reaction:

1. **Mild**: bothersome but requires no change in therapy
2. **Moderate**: requires change in therapy, specific treatment, hospitalization
3. **Severe**: life-threatening causes permanent damage or requires intensive medical treatment
4. **Lethal**: Directly or Indirectly contributes to death of the patient

Classification of ADR cont..

1. **Type A reactions (Augmented)**
2. **Type B reactions (Bizarre)**
3. **Type C reactions (Continuous)**
4. **Type D reactions (Delayed)**
5. **Type E reactions (End of use)**

Classification of ADR cont..

1. **<u>Type A reactions</u> (Augmented)**
- 80% of ADRs
- Based on the normal pharmacological properties of the drug.
- *Predictable, dose dependent,* and *most often preventable*
- Relatively common but do not cause serious illness
- Usually resolves when the dose is reduced
- e.g., hypoglycaemia with sulphonylureas
  dry mouth with anticholinergics

2. <u>Type B reaction</u> (Bizarre)
- *unrelated to the normal pharmacological effect* of the drug
- *Unpredictable and unpreventable*
- *Independent of drug dose, concentration or clearance*, and are *rarely avoidable.*
- comparatively rare but often serious need to withdrawal of the drug.
- Include **hypersensitivity or idiosyncratic** mechanism
- e.g. haemolysis with methyldopa
  Penicillin induced hypersensitivity
  Thrombocytopenia with ACE inhibitors

3. **Type C reactions** (Continuous)
- associated with long-term use
- involves dose accumulation
- e.g., phenacetin and interstitial nephritis , antimalarials and ocular toxicity, NSAIDs induced peptic ulcer

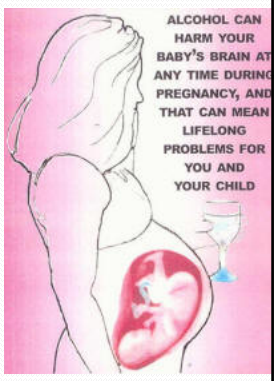
4. **Type D reactions** (Delayed effe
- delayed effects (dose independe
- Carcinogenicity (e.g., immunosu
- Teratogenicity (eg thalidomide-phocomelia)

5. **Type E reactions (End of use)**
- Withdrawal syndromes

E.g.
- Corticosteroid- Acute adrenal insufficiency
- Opoids- narcotic withdrawal
- Benzodiazepines- rebound insomnia
- Worsening of angina pectoris or myocardial infarction may result from stoppage of β blockers.
- Frequency of seizure may increase on sudden withdrawal of antiepileptic drugs

Teratogenecity

- Capacity of a drug to cause foetal abnormalities when administered to the pregnant mother.
- **Thalidomide** (phocomelia)



Drug can affect the foetus at 3 stages

- **Fertilization and implantation-** conception to 17 days- failure of pregnancy.
- **Organogenesis**- 18-55 days of gestation- most vulnerable period, deformities are produced.
- **Growth and development**- 56 days onwards-development and functional abnormalities can occur. ACE inhibitors can cause hypoplasia of organs

FDA category of Drugs during Pregnancy

Category	Description	Examples
A	**No risk in controlled human studies**	Inj. Mag sulfate thyroxine
B	**no controlled studies conducted in human, No risk in other studies,**	amoxicillin Penicillin V
C	**Animal studies- risk,but Risk not ruled out in human** (No adequate and well controlled studies)	Morphine, Codiene gabapentin
D	**Positive evidence of risk on human studies**	Aspirin, Phenytoin, lorazepam
X	**Contraindicated in Pregnancy (fetal abnormalities shown in animal as well as in human studies)**	Estrogen, warfarin Methotrexate

Prevention of adverse effects to drugs

- Avoid all inappropriate use of drugs
- Use appropriate dose, route and frequency of drug administration on patients specific variables
- Elicit and take into consideration previous **history of drug reactions**
- elicit **history of allergic diseases**
- Rule out possibility of **drug interactions** when more than one drug is prescribed.
- Adopt correct drug administration technique
- Carry out appropriate laboratory monitoring (warfarin/heparin)