

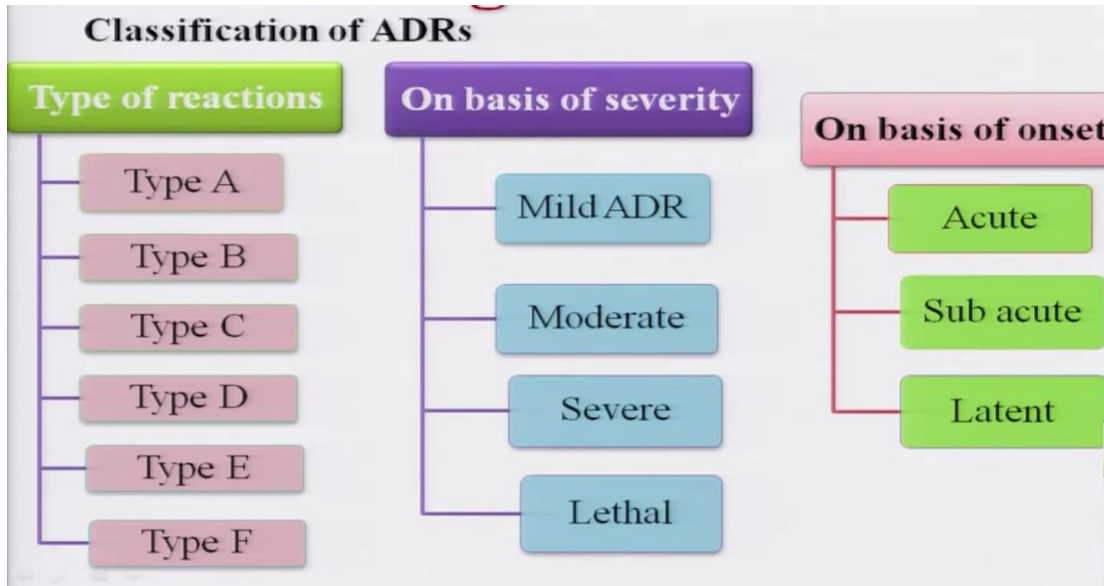
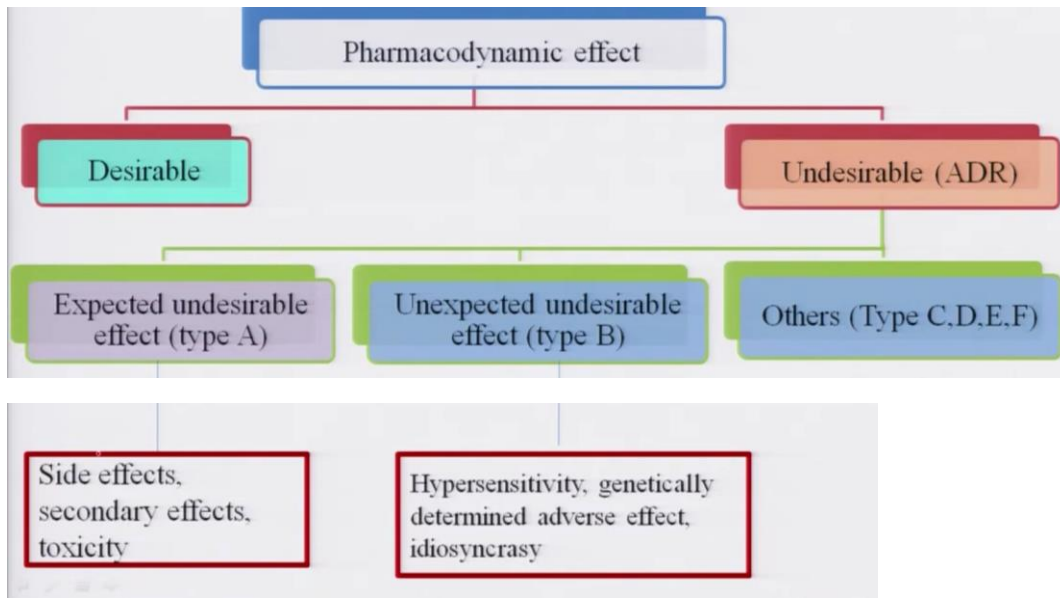
Adverse Drug Reactions (ADRs)

ADR:

✓ WHO defined ADR as a response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of physiologic function”

Adverse Drug Reactions

Causes of ADR	Factors effecting ADR
✓ Fail to take at correct times	✓ Sex, age, diet, smoking.
✓ Overdose	✓ Genetic influences
✓ Taking other drugs or preparations that interact with the medicine	✓ Previous ADR
✓ Taking a medicine that was prescribed for someone else	✓ Total number of medications
✓ Combining the medicine with alcohol	✓ Concurrent diseases (renal ,liver , cardiac)



Adverse Drug Reactions

Type A Reactions or Augmented:

Extension effects

- Predictable
- Dose - Related responses
- Prevention - Adjustment of dosage regimen

Examples

- Benzodiazepines - **Sedation**
- Furosemide - **Water and electrolyte imbalance**
- Heparin, warfarin - **Spontaneous bleeding**
- Insulin - **Hypoglycemia**

Adverse Drug Reactions

Type B Reactions or Bizarre:

- ✓ Abnormal effects, High mortality Unrelated from the drug's known pharmacological actions.
- ✓ Uncommon, Unpredictable.
- ✓ Not related to the pharmacologic action of the drug.



Example

- ✓ Immunologic reactions: anaphylaxis to penicillin.
- ✓ Idiosyncratic reactions: malignant hyperthermia with general anesthetics.

Management: Withhold and avoid in future.

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Adverse Drug Reactions

Type C Reactions or Continuous / Chronic

- ✓ Long term effects are usually related to the dose and duration of treatment
- ✓ Uncommon, related to the cumulative dose
- **Examples**
 - Ethambutol - Retinopathy
 - NSAIDs – Nephrotoxicity
 - Colonic dysfunction due to laxatives



Osteonecrosis of Jaw with Bisphosphonates

Management

- ✓ Reduce dose or use an alternate day therapy
- ✓ Withdrawal may have to be prolonged

Adverse Drug Reactions

Type D Reactions or Delayed:

- ✓ Uncommon
- ✓ Usually dose related
- ✓ Occurs or becomes apparent sometime after use of the drug



Example

- ✓ Carcinogenesis
- ✓ Teratogenesis
- ✓ Thalidomide

Management

- ✓ Often intractable

Type E Reactions or Ending of Use:

Features

- Uncommon
- Occurs soon after withdrawal of the drug

Example:

- ✓ Benzodiazepines – Rebound insomnia, agitation, anxiety
- ✓ Clonidine, β blockers – Rebound hypertension
- ✓ Corticosteroids – Acute adrenal insufficiency

Management

- ✓ Reintroduce drug and withdraw slowly

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Type F Reactions or Failure of Efficacy:

Features

- ✓ Common, dose related
- ✓ Under dosing of medications
- ✓ Often caused by drug interactions

Example

- ✓ Oral contraceptive when used with an enzyme inducer.
- ✓ Resistance to antimicrobial agents

Management

- ✓ Increase dosage

Adverse Drug Reactions

On bases of onset:

1. Acute (observed with in 60min)

e.g. Anaphylactic shock, N&V, Bronchoconstriction

2. Sub acute (observed in 1 to 24 hours)

e.g. Serum sickness, antibiotic associated diarrhoea

3. Latent (observed > 2 days): e.g. Organ toxicity

On bases of severity:

1. Mild ADR: No Hospitalization

2. Moderate: Hospitalization

3. Severe: life threatening cause permanent damage.

4. Lethal: directly or indirectly leads to death

Adverse Drug Reactions

Adverse Drug Effects may be Categorized into

1. Side effects:

Undesirable effects at therapeutic doses

✓ Atropine, dicyclomine - undesirable effect dry mouth

✓ Codeine - undesirable effect Constipation

2. Secondary effects:

e.g. Suppression of bacterial flora by tetracycline's

Corticosteroids - Latent T.B. activated

3. Toxic effect:

Due to over dose it may accidental, suicidal

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3. Toxic effect (Contd..)

- ✓ High dose heparin - Bleeding
- ✓ Prolonged use of streptomycin - Ototoxicity, nephrotoxicity
- ✓ Paracetamol - Liver damage
- ✓ Barbiturates - Coma
- ✓ Digoxin - A.V blockade
- ✓ Morphine - Respiratory failure

4. Intolerance:

- ✓ Characteristic toxic effects at therapeutic dose
- e.g. Single dose triflupromazine - muscular dystonia
- Single dose of chloroquine may cause abdominal pain

- ✓ More common e.g. Tetracycline

Photoallergy: less common, long wave length, Sulfonamide

7. Allergy/Hypersensitivity

- Humoral -Type I,II,III
- Cell mediated-Type IV

Type I- Anaphylactic reactions due to IgE antibodies, minimum 2-3 hrs. e.g. urticaria, angioedema, anaphylactic shock

Type II - Cytolytic reactions due to antigen antibody complex within 72 hours e.g. hemolytic anemia

Type III - Retarded /Arthus reaction due to immune complex mediated reactions subsides 1-2 weeks. E.g. serum sickness

Adverse Drug
7. Allergy/Hypersensit

Type IV- Delayed hypersensitivity reaction.
E.g. Contact dermatitis