Drug Combination

Two or more drugs are taken at the same time (Drug-drug interaction).

TYPES of Drug-drug interaction
1. Harmful
2. Useful (multidrugs treatment of T.B.)
Clinically important D-D interactions:

1. Patients with impaired liver or kidney functions.
2. Elderly patients.
3. Drugs known as enzyme inducers and inhibitors.
4. Drugs with small therapeutic index (digoxin-Lithium).
5. Drugs used for prolonged time and precise plasma levels (lithium-antiepileptics).
Drug Combination

Where
1. Outside the body.
2. Inside the body.
Drug interaction outside the body.

- Soluble insulin and protamine zinc → delayed absorption

- **incompatibility**

  Diazepam or phenytoin + Infusion fluid (saline) → Precipitation.

Carbenicillin + Gentamycin → Inactive gentamycin

Thiopental + Suxamethonium → Precipitation
Drug INTERACTION INSIDE THE BODY

Mechanisms

Pharmacokinetic interactions
- Absorption
- Distribution
- Metabolism
- Elimination

Pharmacodynamics Interactions
- Synergism
  - Potentiation
  - Addition
- Antagonism
I. Interactions During Absorption

A. Direct chemical interaction

- Iron and tetracyclines form complex.
- Antacids: Aluminium or magnesium chelate with tetracyclines ↓ bioavailability of tetracycline (2 hr apart).

- Cholestyramine interfere with absorption of:
  - Digoxin
  - Warfarin.
  - Thyroxine
(B) Alteration of GIT Motility

- Purgatives ↓ absorption
- Antidepressants & anticholinergic drugs e.g. Atropine ↓ gastric emptying & delay absorption.
- Prokinetics e.g. Metoclopramide ↑ gastric emptying and absorption.
(C) Alteration in GIT Flora

- Broad spectrum antibiotics
- Potentiates anticoagulants → ↓
- Bacterial synthesis of Vit K.

(D) Absorption from other sites

- Local anesthetic (lidocaine) + Adrenaline
- Delay in absorption → ↑ duration of action
II. Distribution

A) Displacement from plasma protein binding sites.

Sulphonamide + Bilirubin $\rightarrow$ Kernicterus

B) Displacement from other tissue binding sites.

Quinidine + digoxin $\rightarrow$ more digoxin $\rightarrow$ toxicity
III. **Biotransformation**

A) **Enzyme Induction.**

Rifampin + Contraceptives → Failure of conception

Barbiturates + Warfarin → ↓ Anticoagulant effect

B) **Enzyme Inhibition.**

Cimetidine → potentiates effects of Warfarin, theophylline.
IV. Interaction During Excretion

a) Interference with active transport.

<table>
<thead>
<tr>
<th>Primary Drug</th>
<th>Competing Drug</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>Probenicid</td>
<td>↑ Penicillin Level</td>
</tr>
<tr>
<td>Salicylates</td>
<td>Probenicid</td>
<td>Salicylate toxicity</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Probenicid</td>
<td>Indomethocin toxicity</td>
</tr>
</tbody>
</table>
Pharmacodynamic Interactions

- DRUG SYNERGISM.
- DRUG ANTAGONISM.
Synergism

When the therapeutic effect of one drug is enhanced by another drug.

Types:

- Addition.
- Potentiation.
Addition

- When the effect of two drugs having similar action are additives
- the net effect of two drugs used together is equal to the sum of the individual drug effect.

\[ 1 + 1 = 2 \]

Thiazide diuretics + Beta blocker have an additive antihypertensive action.
Potentiation

- When the net effect of two drugs used together is greater than the sum of the individual drug effects.
  \[1 + 1 > 2 \text{ or } 1 + 0 > 2\]

- When one drug increases the action of other drug e.g. sulphaematuxazole + trimethoprim → cotrimoxazole (bactericidal) \[1 + 1 > 2\]

- Or when drug has no effect as own but increases the effect other drugs \(1 + 0 > 2\)
  
  L-dopa and carbidopa.
Antagonism

The effect of one drug is decreased or abolished by the administration of another one.

- Physiological antagonism.
- Chemical antagonism.
- Pharmacological antagonism.