FACTORS AFFECTING DOSE AND ACTION OF A DRUG

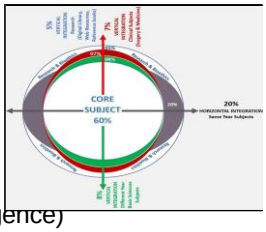
SOURCES:

- BERTRAM G. KATZUNG BASIC & CLINICAL PHARMACOLOGY 15TH EDITION
- GOODMAN AND GILMAN'S THE PHARMACOLOGICAL BASIS OF THERAPEUTICS 13TH EDITION.

Sequence Of Lecture

- Spiral Integration
- Horizontal Integration
- Vertical integration
- Core Subject
- EOLA(End of lecture assessment)
- Digital Library References

(Research, Bioethics, Artificial Intelligence)



LEARNING OBJECTIVES

- At the end of session, the students of 3rd year should be able to:
- Discuss different factors affecting drug dose and action regarding Physiological, Pathological,Psychological,Genetic, Drug related (drug interactions) and Environmental factors
- Explain Synergism, Summation and Potentiation , Accumulation

Which of the following factors primarily affects the absorption of a drug?

A) Blood pressure
B) Route of administration
C) Liver function
D) Plasma protein binding
E) Renal function

Which of the following factors increases the rate of drug metabolism?

A) Age
B) Drug interactions
C) Liver disease
D) Genetic polymorphisms
E) All of the above

Which of the following can happen when two drugs compete for protein-binding sites?

A) Increased drug clearance
B) Decreased drug absorption
C) Increased free drug concentration of one drug
D) Decreased drug metabolism
E) Increased drug excretion

How does a high-fat meal affect drug absorption?

A) Increases absorption of lipophilic drugs
B) Decreases absorption of hydrophilic drugs
C) Has no effect on drug absorption
D) Increases the clearance of drugs
E) Increases the rate of renal elimination

Which of the following describes functional/ physiological antagonism?

A) Two drugs bind to the same receptor but do not compete for the same binding site

B) A drug binds to a receptor and prevents another drug from binding

C) Two drugs produce opposite effects through different mechanisms in the body

D) One drug chemically neutralizes the other

E) One drug changes the pH to reduce the activity of another drug

In which type of drug antagonism does one drug reduce the effects of another by binding to a different site on the receptor?

A) Competitive antagonism
B) Non-competitive antagonism
C) Functional antagonism
D) Chemical antagonism
E) Physiological antagonism

What effect does drug tolerance have on drug action?

A) Increases drug effectiveness
B) Decreases drug effectiveness
C) Has no effect on drug effectiveness
D) Makes the drug less toxic
E) None of the above

What type of drug interaction occurs when two drugs with similar effects are taken together, and the combined effect is equal to the sum of the individual effects?

A) Synergism
B) Antagonism
C) Additive effect
D) Potentiation
E) Sensitization

In which type of drug interaction do two drugs produce a combined effect greater than the sum of their individual effects?

A) Antagonism
B) Synergism
C) Additive effect
D) Potentiation
E) Chemical antagonism

What is the primary characteristic of drug summation?

A) The effects of drugs are opposite and cancel each other out.
B) The effects of drugs combine to produce a response greater than the sum of their effects.
C) The drugs do not interact and their effects are simply added together.
D) One drug enhances the effects of the other drug.
E) The drugs block each other from producing their effects.

Factors Modifying Doses and Action of Drugs

1. **Physiological Factors**
2. **Pathological Factors**
3. **Environmental factors**
4. **Psychological factors**
5. **Genetic Factors**
6. **Interaction with other drugs** (drug-drug interactions)

Physiological Factors

1. **Age**
2. **Gender**
3. **Pregnancy & Lactation**
4. **Body size**
5. **Racial Difference**
6. **Food**

1. **AGE**

- Formula for calculating dose in infants & children
- YOUNG'S FORMULA:

Child Dose = (Age/ Age + 12) adult dose

- DILLING'S FORMULA:

Child Dose= Age (Adult Dose/ 20)

2. BODY WEIGHT & BODY SURFACE (BSA)

- Individual Dose= (BW (kg)/ 70) x Average Adult Dose
- Individual dose=BSA(m2)/1.7 x Average Adult Dose

3. GENDER

- Females generally have smaller body size & require lower doses.
- Differences In metabolism (alcohol)
- Many anti-hypertensive drugs (beta blockers) interfere with sexual dysfunction in males but not in females.
- Androgens & estrogens have different effects in males & females.

4. PREGNANCY

- GIT motility is reduced causing slowed absorption.
- Plasma & ECF volume increases,Vd increases.
- Plasma albumin decreases, alpha 1 acidic glycoprotein increases; acidic drugs less bound, basic drugs more bound.
- Hepatic microsomal enzymes undergo induction-many drugs are metabolized faster.

Category	Description
A	Studies in women fail to demonstrate a risk to fetus in first trimester (& there is no evidence of a risk in late trimesters)
B	Adequate human studies are lacking, but animal studies have failed to demonstrate a risk to fetus OR in humans adequate studies in pregnant women have failed to demonstrate a risk to fetus, but animal studies have shown an adverse effect on fetus
C	Animals studies revealed adverse effects on fetus (teratogenic) & there are no controlled studies in women OR studies in women & animals are not available. *Drugs should be given only if potential benefit justifies potential risk to fetus*
D	There is positive evidence of human fetal risk, *but benefits from use in pregnant women may be acceptable despite risk* (eg, if a drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective)
X	Studies in animals or human beings have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both & risk of use of drug in pregnant women clearly outweighs any possible benefit. *The drug is contraindicated in women who are or may become pregnant*

5. DIET

- Milk decreases absorption of Tetracyclines.
- Presence of food decreases the absorption of most of the drugs.

6. RACE

- Beta blockers are less effective anti-hypertensive drugs in blacks as compare to whites.

7. ENVIRONMENT

- High altitude with concomitant low barometric pressure diminishes the capacity of body to oxidize drugs & this may precipitate drug toxicity.
- Dose of hypnotics required to cause sleep at daytime is much higher than required at night.

HORIZONTAL INTEGERATION WITH PATHOLOGY

8. PATHOLOGICAL STATES

- GIT Disease – Absorption
- Liver Disease – Metabolism, Plasma proteins
- Kidney Disease – Excretion, half life

VERTICAL INTEGERATION WITH PSYCHIATRY

9. EMOTIONAL/ PSYCHOLOGICAL FACTORS

- A patient's beliefs, attitudes & expectations can affect efficacy of a drug.
- The personality of physician may influence drug effect considerably.
- PLACEBO

- **PSYCHOLOGICAL DEPEDENCE:**

"A condition in which drug produces a feeling of satisfaction and a psychic drive that requires periodic or continuous administration of drug to produce pleasure or to avoid discomfort."

Characterized by craving for drug & an overwhelming concern for obtaining & using it.

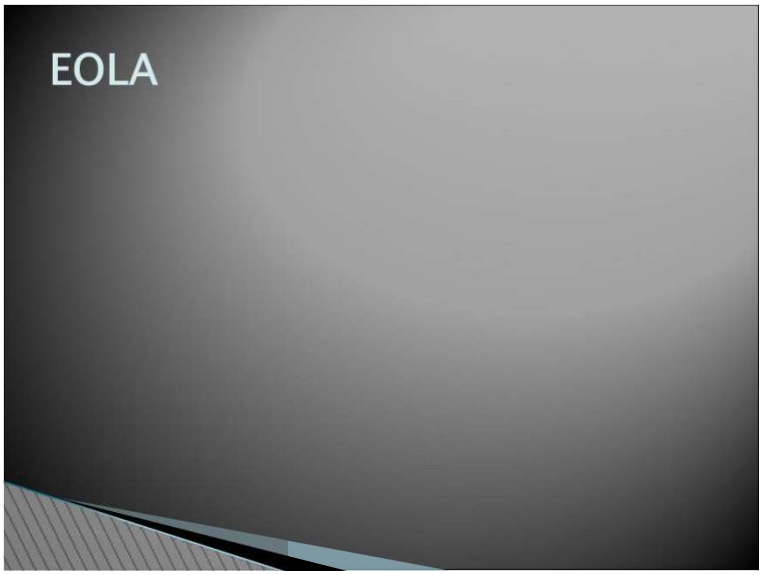
- **PHYSICAL DEPENDANCE:**

"Body achieves an adaptive state that manifests itself by intense physical disturbances when the drug is withdrawn (withdrawal syndrome)."

- **16. MISCELLANEOUS FACTORS**
- Wrong diagnosis or incomplete diagnosis.
- Poor patient compliance or over compliance.

EXAMPLE

- To improve patients compliance, we use (DOTs)



- Trimethoprim and sulfamethaxazole are bacteriostatic drugs when given alone. However the combination is bactericidal. Which of the following term best defines this drug interaction:
- 1. Additive effect
- 2. Summation
- 3. Potentiation
- 4. Sensitization
- 5. Tolerance

- Chen C, Liu F, Ren Y, Suttner L, Sun Z, Shentu Y, Schmidt EV. Independent drug action and its statistical implications for development of combination therapies. Contemporary Clinical Trials. 2020 Nov 1;98:106126.
- D'Alessandro C, Benedetti A, Di Paolo A, Giannese D, Cupisti A. Interactions between food and drugs, and nutritional status in renal patients: a narrative review. Nutrients. 2022 Jan 4;14(1):212.