Pharmacodynamics

- Pharmaco: drug and dynamic: change
- Refer to how drug changes the body.
- Concerned with the mechanism of drug action and the relationship between drug concentration and responses in the body.
- Has important nursing applications.
- Knowledge of Therapeutic index, dose-response relationships and drug receptor interactions----- provides safe and effective treatment.

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Pharmacodynamics

Therapeutic Index / Therapeutic Ratio:

$$\text{Therapeutic ratio} = \frac{\text{LD}_{50}}{\text{ED}_{50}} \qquad \text{Therapeutic ratio} = \frac{\text{TD}_{50}}{\text{ED}_{50}}$$

LD_{50} (median lethal dose): Dose of drug that will be lethal in 50% of the group.
ED_{50} (median effective dose): dose of drug that will be effective in 50% of the group.
TD_{50} (median Toxic dose): dose of drug that causes adverse effect in 50% of subjects.

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Potency Vs Efficacy

Potency (strength) refers to the amount of drug needed to produce an effect, such as relief of pain or reduction of blood pressure. For instance, if 5 milligrams of drug A relieves pain as effectively as 10 milligrams of drug B, drug A is twice as potent as drug B.

Efficacy is a drug's capacity to produce an maximum effect (such as lowering blood pressure).

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Principles of Drug action

1. **Stimulation** : enhancement of the level of activity of specialized cells. E.g. adrenaline stimulates heart.
2. **Depression**: diminution of activity of specialized cells. Eg. Barbiturates depress CNS
3. **Irritation**: nonselective, noxious effect and is particularly applied to less specialized cells (epithelium, connective tissue).
4. **Replacement**: use of hormones, natural metabolites in deficiency states. Eg. Iron in anaemia, insulin in diabetes.
5. **Cytotoxic action**: selective cytotoxic action for invading parasites or cancer cells, attenuating them without significantly affecting the host cells. E.g. Penicillin, chloroquine, cyclophosphamide

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Mechanism of Drug action

1 Physical action

Charcoal: adsorptive property

2 Chemical action

Antacid ($AlOH_3$) neutralize gastric HCl

Acidiying (NH_4Cl) and alkalinizing ($NaHCO_3$) agents react with buffers in plasma and alter pH of urine.

3 Through enzymes

Stimulation: adrenaline stimulates adenylcyclase

Inhibition: aspirin inhibit cyclooxygenase

4 Through receptors

Receptor and Drug action

Drug act by modulating or changing existing physiological and biochemical processes.

To exert such changes requires that drugs interact with specific molecules and chemicals normally found in the body.

A cellular macromolecule to which a drug binds in order to initiate its effect is called a receptor.

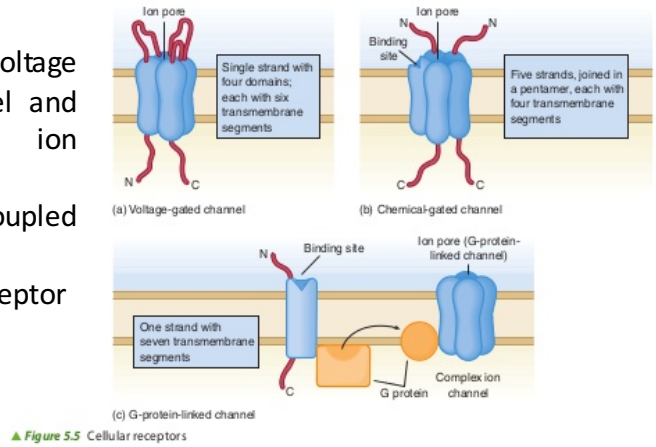
These receptors do not exist in the body to bind drugs.

Their normal function is to bind **endogenous molecules** such as *hormones, neurotransmitters and growth factors*.

Found in plasma membrane (mostly), cytoplasm and nucleus.

Types of Receptor

- Ion channel (Voltage gated ion channel and Ligand gated ion channel
- G protein coupled receptor
- Enzyme linked receptor



▲ *Figure 5.5* Cellular receptors

Types of Drug-Receptor Interactions

Agonist

- is a chemical that binds to a receptor and activates the receptor to produce a biological response.

Partial Agonist

drug produces weak or less efficacious response than agonist.

Antagonist

- binds to receptors but do not activate them. This results in a receptor blockade.

(Self- Competitive Vs non competitive antagonist)

Inverse Agonist

- binds to a receptor and produces a pharmacological response that is opposite to that of the corresponding agonist.

Examples???

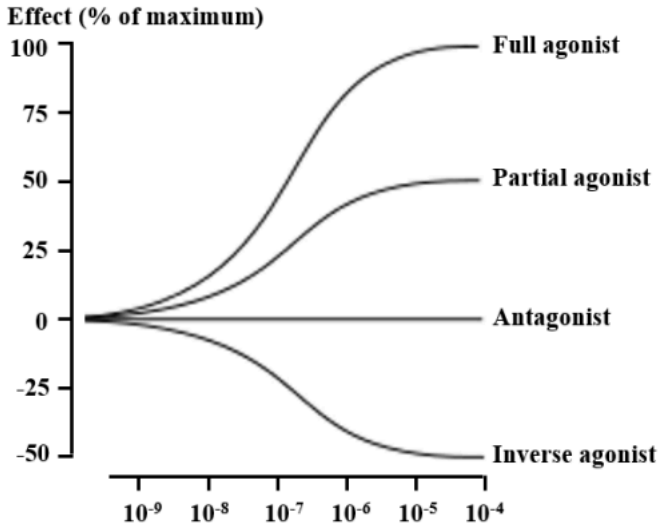


Fig. dose-response curves for different types of actions of drugs at receptors

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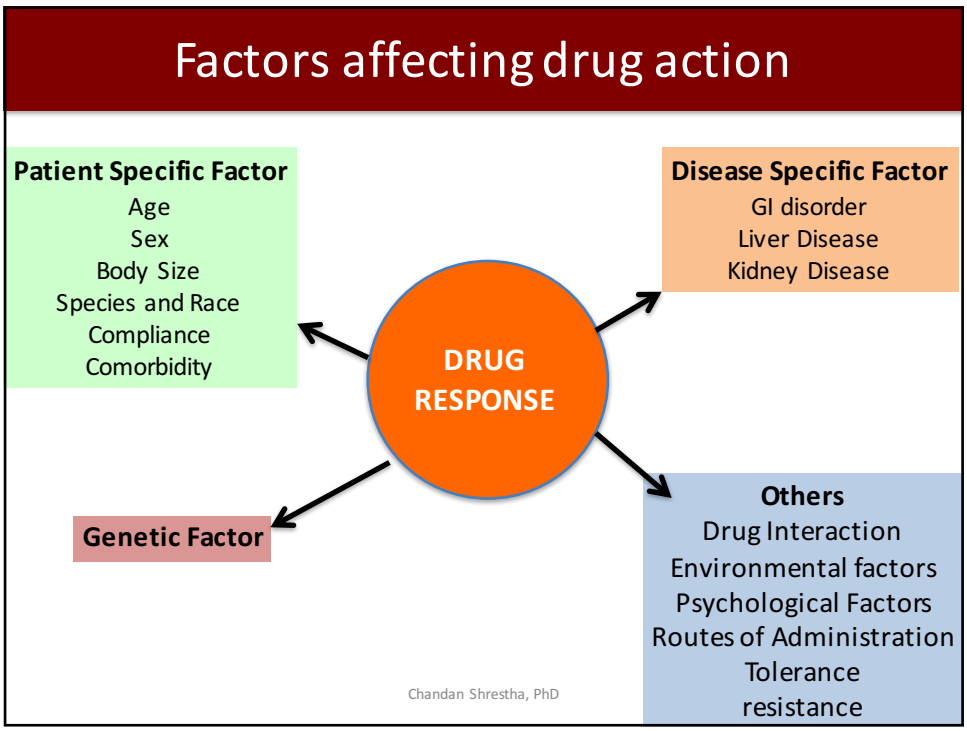

Factors affecting Drug response

- ✓ Body size
- ✓ Body weight
- ✓ Sex
- ✓ Species and race
- ✓ Genetics
- ✓ Route of Administration
- ✓ Environmental factors and time of administration
- ✓ Psychological factor
- ✓ Placebo
- ✓ Pathological states
- ✓ Drug-Drug Interaction
- ✓ Tolerance

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Patient Related Factors

Body Size: A large person generally needs more of a drug than a smaller person need for the same effect.

$$\text{Individual dose} = \frac{\text{BW (Kg)}}{70} \times \text{average adult dose}$$

$$\text{Individual dose} = \frac{\text{BSA } (m^2)}{1.7} \times \text{average adult dose}$$

$$\text{BSA } (m^2) = \text{BW (Kg)}^{0.425} \times \text{Height (cm)}^{0.725} \times 0.007184$$

BSA- Body surface area

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Patient Related Factors

Age:

Infants and older people particularly have problems with drug response. Their liver and kidneys function less effectively, so drugs that are broken down by the liver or excreted by the kidneys tend to accumulate, thus potentially causing problems.

Child dose calculation

Young's formula

$$\text{Child dose} = \frac{\text{Age}}{\text{Age} + 12} \times \text{average adult dose}$$

Dilling's formula

$$\text{Child dose} = \frac{\text{Age}}{20} \times \text{adult dose}$$

Fried's formula

$$\text{Child dose} = \frac{\text{Weight of child in lbs}}{150} \times \text{adult dose}$$

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Patient Related Factors

Sex:

Females have smaller body size and require doses that are on the lower side of the ranges.

Comorbidity:

Older people typically have more disorders and thus usually take more drugs. The more drugs people take, the more likely they are to have problems caused by one drug interfering with another drug or disease. (Drug Drug interaction or Drug-disease interaction)

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Patient Related Factors

Compliance (*Adherence) is the degree to which a person takes prescribed drugs as directed.*

Reason for non compiance

- Forget to take the drug at specific times
- Unable to avoid certain foods restrictions.
- Encountering obstacles (for example, having difficulty swallowing tablets or capsules, having problems opening bottles, or being unable to obtain the drug)
- Believing that the drug cannot help or is not needed
- Finding the drug to taste or smell bad
- Experiencing side effects (the treatment may be perceived as worse than the disorder)

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Disease Related Factors

GI diseases:

- Alter the absorption of orally administered drugs.
- Changes are complex and drug absorption can be increased or decreased.
- Coeliac disease absorption of amoxycillin is decreased but that of cephalexin and cotrimoxazole is increased.

Liver diseases:

- Bioavailability of drugs having high first pass effect is increased.
- Serum albumin is reduced---- protein binding is reduced and more drug is present in free form
- Metabolism and elimination of some drugs (morphine, lidocaine) is decreased and their dose should be reduced.
- Prodrug needing hepatic metabolism for activation e.g. prednisone, sulindac are less effective and should be avoided.

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Disease Related Factors

Kidney diseases:

- Affects pharmacokinetics of many drugs as well as alters the effect of some drugs.
- Plasma proteins, specially albumin are often low with renal disease----binding of acidic drugs is reduced----acidic drug are available in free form.
- But basic drugs is not much affected.

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Others

Routes of Administration

Route of administration governs the speed and intensity of drug.

Oral- delay action, under goes hepatic bypass

Parenteral- rapid action

Environmental factors

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Others

Psychological factor

- Efficacy of a drug can be affected by patient's belief, attitudes and expectation.
- *Placebo*

Tolerance

- Requirement of higher dose of a drug to produce a given response.

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Drug Interaction

Drug Drug Interaction

- occurred when two or more drug is given together.
- Results into increase or reduce effect.
- Ibuprofen (NSAIDs) and Hydrochlorothiazide (Diuretics) results into reduced effectiveness of the diuretics (opposite action)
- Aspirin + codiene = pain relief (additive effect)
- Alprazolam + cetrizine- enhanced sedative effect (synergistic)

Drug Food Interaction

Tetracycline + milk

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