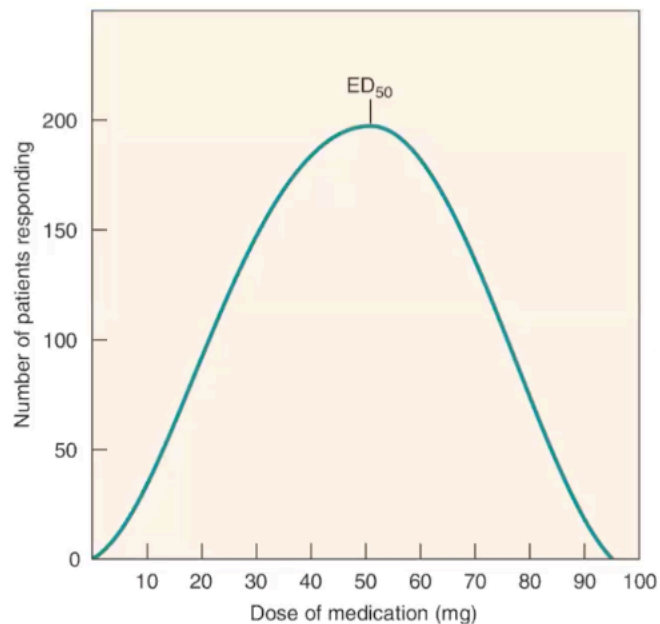


Pharmacodynamics and Pharmacogenetics

- **Pharmacodynamics**
 - *Pharmaco* = medicines
 - *Dynamics* = change
 - How a drug changes the body
 - Involves drug mechanism of action
 - Involves effect of drug concentration on body responses
- **Interpatient Variability**
 - Patients have widely different responses to drugs, which can be depicted on a frequency distribution curve.
 - Individuals have different responses to drugs
 - Responses are related to:
 - Dose–response relationships
 - Therapeutic index
 - Drug receptor interactions
- Frequency distribution curve

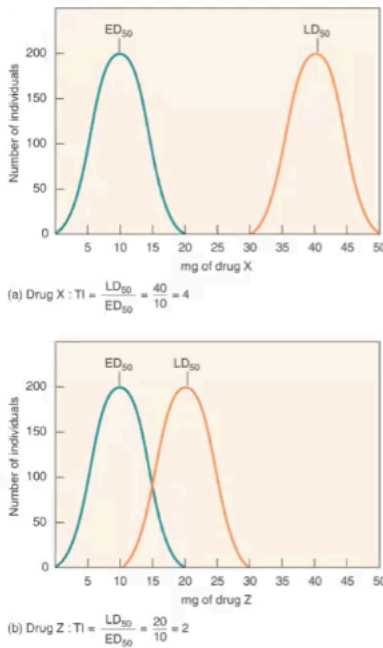
Figure 4.1



- Number of patients responding to a drug action at different doses
 - Horizontal axis shows range of responses.
 - Peak curve shows largest response.
- Median effective dose (ED₅₀)
 - Desired drug response in 50% of subjects (Top of the curve) – best response
- Clinical implications
 - Average dose predicts therapeutic response in 50%
 - Low and slow when prescribing
 - Client may need less or more of a drug.

- Need to monitor drug effect on client
- Dosage adjustment may be indicated.
- **Therapeutic Index**
 - The therapeutic index describes a drug's margin of safety.
- Identifies safety index of drugs
- Median lethal dose (LD₅₀) – use animals in testing
 - Lethal to 50% of test subjects
- Therapeutic index (TI)
 - Ratio of a drug's median lethal dose (LD₅₀) to its median effective dose (ED₅₀)

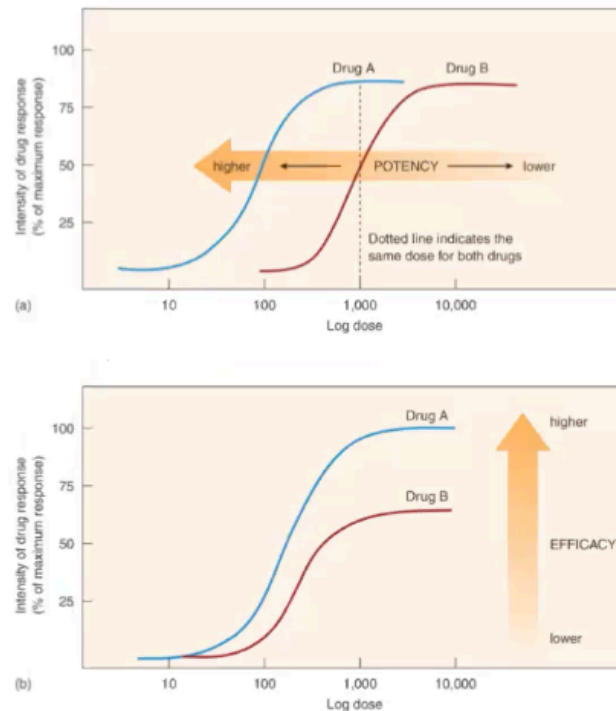
Figure 4.2



Therapeutic index: (a) Drug X has a therapeutic index of 4. (b) Drug Z has a therapeutic index of 2.

- Median toxicity dose
 - Produces toxicity in 50% of subjects
 - Extrapolated from animal data or adverse effects in clinical trials
- Margin of safety (MOS)
 - Amount of drug lethal to 1% of animals divided by amount of drug that produces therapeutic effect in 99% of animals
- **Potency and Efficacy**
 - Potency and efficacy are fundamental concepts of pharmacodynamics that describe a drug's activity.

Figure 4.4



- Potency and efficacy: (a) Drug A has a higher potency than drug B. (b) Drug A has a higher efficacy than drug B.
 - Not all drugs have equal efficacy.
 - Drugs in same class can differ in potency and efficacy.
 - Potency
 - Amount of drug needed to produce a specified effect
 - Compares doses of two different drugs in the same class
 - Efficacy
 - Maximum response produced by drug
 - Compares desired therapeutic effect of two drugs
 - When two different drugs are compared, one cannot assume that the drug with lower dose gives fewer adverse effects.
 - **Agonists and Antagonists**
 - Agonists, partial agonists, and antagonists compete for cellular receptors and can modify drug action.
 - Agonists
 - Mimic the action of endogenous substances
 - Response may be greater than endogenous activity.
 - Partial agonists
 - Produce weaker action than endogenous substances
- Ex. Serotonin theory: can increase by exercise, eating and feeling good etc, but you can also take a serotonin reuptake inhibitor which increases the serotonin by decreasing the level of uptake
- Antagonists

- Prevent action of endogenous substances
 - May compete with agonists
 - Useful in blocking excess endogenous activity
 - May reverse adverse effects of overdoses
- Antagonists
 - Antagonists do NOT have intrinsic activity.
 - Functional antagonism inhibits the effects of an agonist
 - Ex. Narcan
- **Pharmacogenetics**
- In the future, pharmacogenetics may allow customization of drug therapy.
- Branch of pharmacology that studies role of genetic variation in drug responses.
 - Human Genome Project
 - Genetic differences in drug-metabolizing enzymes
 - FDA identified pharmacogenetic biomarkers for over 150 medications
 - Ex. People who are sensitive to medication, or people who need higher doses of medication
 - Use often in psychiatry and oncology
 - After pt have failed two antidepressants in major depressive disorder use genetic testing.