- **Principles of pharmacology:**
  - **psychopharmacology** The study of the effects of drugs on the nervous system and on behavior.
  - **drug effect** The changes a drug produces in an animal’s physiological processes and behavior.
  - **site of action** A location at which molecules of drugs interact with molecules located on or in cells of the body, thus affecting some biochemical processes of these cells
  - **pharmacokinetics** The process by which drugs are absorbed, distributed within the body, metabolized, and excreted.

- **Routes of administration:**
  - **intravenous (iV) injection** Injection of a substance directly into a vein.
    - Fast, precise, direct access to brain
    - Drug of abuse, adrenaline
  - **intraperitoneal (iP) injection** Injection of a substance into the peritoneal cavity—the space that surrounds the stomach, intestines, liver, and other abdominal organs.
    - Fast indirect access to brain
    - Chemotherapy
  - **intramuscular (im) injection** Injection of a substance into a muscle.
    - Slower (capillaries), direct access
    - Vaccine, antibiotics
  - **subcutaneous (SC) injection** Injection of a substance into the space beneath the skin.
    - Slow absorption (fat tissue), indirect
    - Insulin
  - **oral administration** Administration of a substance into the mouth, so that it is swallowed.
    - Easy, delayed (has to go through stomach/intestines and liver)
    - Aspirin
  - **sublingual administration** Administration of a substance by placing it beneath the tongue.
    - Easy (for humans). Bypass digestive system. Capillaries of tongue
    - Steroids, cardiovascular (hypertension, vasodilator)
  - **intrarectal administration** Administration of a substance into the rectum.
    - Slow, bypass stomach
    - Suppositories
  - **inhalation** Administration of a vaporous substance into the lungs.
    - Fast, easy, requires volatile sub
    - Nasal decongestant, drugs of abuse, asthma
  - **topical administration** Administration of a substance directly onto the skin or mucous membrane.
    - Fast, local, (skin)
    - Nasal, eye (herpes, glaucoma) ear drops
  - **intracerebral administration** Administration of a substance directly into the brain.
    - Bypass the BBB. Local (specific brain area) - mostly research
  - **intracerebroventricular (iCV) administration** Administration of a substance into one of the cerebral
    - Bypass the BBB (brain, blood barrier), global effect, emergency ventricles.

- **Kinetics of absorption:**
  - Study effects of some specific brain areas. Mov through BBB
• **Lipid-soluble** (heroin) sub pass through BBB. **Water soluble** sub (morphine) do not

**Drug effectiveness**:

• **dose-response curve** A graph of the magnitude of an effect of a drug as a function of the amount of drug administered.
  • If the effect was proportional to amount of drugs = linear curve
  • Most drugs are non-linear

• **therapeutic index** The ratio between the dose that produces the desired effect in 50 percent of the animals and the dose that produces toxic effects in 50 percent of the animals

• **affinity** The readiness with which two molecules join together.
  • Drugs may have same end result, but may vary in effectiveness
  • Different sites of action:
    ▪ Morphine: Analgesic: inhibits pain perception neurons
    ▪ Aspirin: Analgesic. Surpress 'chemical sig' from damaged cells to the NS
  • Diff affinity:
    ▪ Drugs bind to receptors

• **Margin of safety**: diff betwn mid points of 2 graphs - good effect / bad effect graphs
  • Morphine: helps relieve pain (good) / slows heart rate and breathing (bad)
  • TI - therapeutic index (margin of safety) = LD50 (lethal dose for 50% of the animals) / ED50 (effective dose for 50% of animals)
  • Ex: valium (tranquilizer, anxiety reducer) - TI = 100 (good TI)
  • Ex: barbiturate - TI = 3 (bad TI) requires measurements in the blood and monitoring

\[
TI = \frac{LD_{50}}{ED_{50}}
\]

• **Effects of repeated administration**:
  • **Effects decrease w/ repeated use**:
    • **tolerance** A decrease in the effectiveness of a drug that is administered repeatedly.
      ▪ Need more drugs
      ▪ Decrease in affinity, decrease in receptor numbers
    • **withdrawal symptom** The appearance of symptoms opposite to those produced by a drug when the drug is administered repeatedly and then suddenly no longer taken.
      ▪ Compensatory mechanism alone
      ▪ Opposite behavir/emotional effect
      ▪ Euphoria <- Depress

  • **Effects increase w/ repeated use**:
    • **sensitization** An increase in the effectiveness of a drug that is administered repeatedly.
      ▪ Antidepressants: need time to be effective

  • **Effect can be psychological**:
    • **Placebo effect** An inert substance that is given to an organism in lieu of a physiologically active drug; used experimentally to control for the effects of mere administration of a drug.
      • Mainly used in research
• Control for anxiety (human)
• Control for the effect of drug administration (animals)
  ○ Drug reinforcing effect depends on environment - nicotine and cues

• Sites of drug action:
  ○ **antagonist** A drug that opposes or inhibits the effects of a particular neurotransmitter on the postsynaptic cell.
    ● Closes receptor - blocks neurotransmitter
    ● Decrease neurotransmitter effect
  ○ **agonist** A drug that facilitates the effects of a particular neurotransmitter on the postsynaptic cell
    ● Same postsynaptic effect as a particular neurotransmitter - open receptor
    ● Increase neurotransmitter effect

• Effects on receptors:
  ○ **direct agonist** (competitive binding) A drug that binds with and activates a receptor.
  ○ **receptor blocker** A drug that binds with a receptor but does not activate it; prevents the natural ligand from binding with the receptor.
  ○ **direct antagonist** A synonym for receptor blocker.
  ○ **noncompetitive binding** binding of a drug to a site on a receptor; does not interfere with the binding site for the principal ligand.
  ○ **indirect antagonist** A drug that attaches to a binding site on a receptor and interferes with the action of the receptor; does not interfere with the binding site for the principal ligand.
  ○ **indirect agonist** A drug that attaches to a binding site on a receptor and facilitates the action of the receptor; does not interfere with the binding site for the principal ligand.

• Amino acids: glutamate
  ○ **Synthesis:** from proteins in food
  ○ **Found:** everywhere in CNS
  ○ **Receptors:**
    ● Always excitatory
    ● Ionotropic for Na+ (AMPA, Ketinate)
    ● Ionotropic for Na+ and Ca2+ (NMDA)
    ● Metabotropic glutamate receptor
  ○ **Psychopharmacology:**
    ● NMDA involved in learning and mem
    ● AP5 blocks glutamate binding site on NMDA receptors
      ▪ Alcohol blocks NMDA receptors (indirect competitor to glutamate)
    ● PCP blocks NMDA and Calcium entry in the cell (indirect competitor to glutamate) - hallucination and aggression - animal model for schizophrenia
    ● Too much glutamate binding results in excitotoxicity (cell death from too much activity)

• Amino acids: GABA
  ○ **Synthesis:** From glutamate
  ○ **Found:** everywhere in CNS
  ○ **Receptors:**
    ● Always inhibitory
    ● Ionotropic for Cl- (GABAa)
    ● Metabotropic for K+ (GABAb) exists presynaptically (autoreceptor)
  ○ **Psychopharmacology:**
- Controls spread of excitation
- Muscimol opens and bicuculline blocks GABAa
- Benzodiazepines - open GABAa
- GABAa is clocked by picrotoxin (convulsions)
- Barbituates

- **Amino acids**: Glycine
  - **Synthesis**: in sugar cane
    - Endogeneous production unknown - non essential - produced by body for external source
  - **Found**: spinal cord
  - **Receptors**: always inhibitory
    - Ionotropic for Cl-
  - **Psychopharmacology**:
    - Prevents excessive muscle contraction
    - Tetanus: bacteria produces a chem that blocks glycine release
    - Strychnine blocks glycine receptor - convulsion and death