General Pharmacology

Combined Effort of:

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What Is a Drug

- Chemical agents used in the diagnosis, treatment, or prevention of disease
- Any substance that when taken into the body changes one or more of the body's function
- The science of drugs including the study of the origin, ingredients, uses and actions on the body is pharmacology

Our Approach

- Lecture on General Pharmacology
- 3 lectures on Specific Emergency Drugs
  - Mechanism of Action
  - Indications
  - Interactions
  - **Contraindications**
  - Precautions
  - Dose
  - How supplied
  - Adverse Reactions
- ***Calculations***

Information about Drugs

- Physicians Desk Reference (PDR)
- Merck Manual
- The Pill Book
- ePocrates
  - Available for Palm and Windows OS.
- Many others
- **→ Very useful for patient assessment**

Pharmacology

- Branches include:
  - Phamacokinetics – movement of drug in the body with emphasis on its distribution, duration of action, and method of excretion
  - Pharmacodynamics – study of drugs and their actions on body tissues
  - Pharmacotherapy – use of drugs in treatment of diseases
  - Toxicology – study of poisons and adverse drug effects
  - Pharmacogenetics – study of influence of heredity factors on the response to drugs

History of Pharmacology

- Earliest written records from Egypt
- Greece-Hippocrates
- Renaissance
- Welsh “foxglove”
- Sulfa 1935
- PCN 1940

History of Pharmacology Important Discoveries

- 17th century
  - Opium, coca, and ipecac
- 1785 – digitalis discovered
- 19th century
  - Beginning of large scale manufacturing plants
- 1815 – morphine used to treat pain
- Early 1800's – ether and chloroform allowing surgical treatment

History of Pharmacology Important Discoveries

- 1922- insulin
- Mid-1940's – antibiotics like PCN
- 1955 – polio vaccine
- Mid- 1970's - antivirals

Sources of Medications

- Plant
  - Alkaloids – group of organic substances that react with acids to form salts (morphine, atropine)
  - Glycosides – on hydrolysis, produce a sugar in addition to one or more active substances (digoxin)
  - Gums – plant exudates. When water added, forms gelatinous mass (natural laxatives, tropical preparations to sooth skin)
  - Oils – volatile or fixed
    - Volatile – puts off a pleasant odor or taste and used as a flavoring agent (peppermint)
    - Fixed – greasy (castor oil)

Sources of Medications

- Animal and human
  - Drugs used to replace insufficient glandular secretions (ACTH, Insulin)
- Mineral
  - Iron, iodine, and mineral salts (“bicarb”)
- Synthetic
  - Laboratory-produced chemicals (lidocaine)

Drug Legislation

- 1906-pure food and drug act
  - Established the FDA
  - United States Pharmacopoeia (USP)
- 1914-Harrison narcotic act
- 1938-food,drug and cosmetic act
- Durham/Humphrey Amendment
  - **Required verbal/written prescriptions**
- 1970- controlled substance act
  - Established the DEA

Drug Names

- Chemical
  - Ethyl 1-methyl-4-phenylisonipecotate hydrochloride
- Generic
  - Meperidine hydrochloride
- Trade
  - Demerol
- Official
  - Meperidine hydrochloride, USP

Drug Classifications

- Alpha Adrenergic Blockers
  - Proscar, Hytrin
- Aminoglycosides
  - "Mycin" antibiotics – Streptomycin, Tobramycin
- Amphetamines
  - Diet "drugs"
- ACE Inhibitors
  - Vasotec, Zestril, Lisinopril, Accupril, Altace, Diovan
- Antianginals – Nitroglycerine, Isosorbine (Isordil), CC Blockers
- Antianxiety
  - Valium, Xanax, **Prozac**, Thorazine

Drug Classifications

- Antiarrhythmic – correct dysrhythmias
  - Group I – decrease rate of sodium during depolarization and decrease rate of phase O of cardiac action potential (lidocaine, phenytoin)
  - Group II – block beta receptors and depress phase 4 depolarization (atenolol)
  - Group III – prolong duration of action potential (relative refractory period) without changing phase of depolarization (amiodarone)
  - Group IV – calcium channel blockers and glycosides (digitalis, verapmil)

Drug Classifications

- Anticoagulants – affect blood clotting
  - Anticoagulant – prevents or slows coagulation
    - Coumadin, Heparin, Lovanox
  - Thrombolytics - increase rate at which clot dissolves
    - TPA, ASA, Streptokinase
  - Hemostatics – prevent or stops internal bleeding
    - Vitamin K
- Anticonvulsants – depress neuronal discharge in the CNS that may cause seizures
  - Dilantin, Depakote, Valium, Lorazepam
- Antidepressants – cause adaptive changes in the serotonin and NE receptor systems
  - Elavil, Tofranil ("Tricyclic Antidepressants")
- Antihistamines – blocks effect of histamine (H_1)
  - Benadryl (Diphenhydramine)
- Antihypertensive – lower B/P
  - Beta Blockers, CC Blockers, Diuretics, ACE Inhibitors, Alpha Blockers
- Antipsychotic blocks dopamine receptors in brain
  - Ziprasidone

Drug Classifications

- Beta-adrenergic blockers – block response of sympathetic nerve impulses
  - Inderal (Propranalol), Lopressor, Tenormin (Atenalol)
- Bronchodilators – reverse bronchospasm
  - Albuterol, Xopenex, Alupent, Terbutaline, Atrovent
- Calcium channel blockers – inhibit influx of ca through cell membrane results in depression of automaticity and conduction velocity
  - Verapamil, Cardizem, Procardia
- Cardiac glycosides – increase force and velocity of myocardial contraction
  - Digitalis (Digoxin, Lanoxin)
- Cholinergic agonist – strengthens, prolongs or prevents breakdown of acetylcholine
  - Physotigamine (Antilirium)
- Cholinergic blocker – prevents Ach from combining with receptors on the postganglionic nerve terminal
  - **ATROPINE**

Drug Classifications

- Corticosteroids – two functions
  - regulation of metabolic pathways involving carbohydrates, protein and fat
  - electrolyte and water balance
    - Solu-Medrol, Decadron
- Diuretics – inhibit reabsorption of sodium and chloride in proximal and distal tubules and loop of Henle
  - Lasix, HCTZ, Bumex
- Histamine (H_2) blockers – block production of gastric acid secretion
  - Nexium, Prilosec, Protonix, Aciphex
- Inotropics – increase cardiac contractile force
  - Dopamine**, Dobutamine, Epi
- Medicinal gases – maintain partial pressure of oxygen in arterial blood
  - Oxygen, General Anesthesia gasses

Drug Classifications

- Narcotic analgesics – attach to specific receptors in CNS
  - Morphine, Demerol (Meperidine), Fentanyl, Nubain
- Narcotic antagonists – block action of narcotic analgesics
  - Narcan
- Sympathomimetics – mimic action of norepinephrine or epinephrine
  - Dopamine, Dobutamine
- Vasodilator- relaxes blood vessels
  - Nitroglycerine, Isosorbide, Ismo, CC Blockers
- Vasopressor – causes contraction of muscles of capillaries and arteries increasing Peripheral Vascular Resistance
  - Epi, Vasopressin

Drug Preparations

- Local effects
  - Topical use
    - Aerosol
    - Colloid
    - Liniment
    - Lotion
    - Ointment
    - Paste
    - Plaster
    - cream
- Oral use
  - Liquids
    - Solution
    - Suspension
    - Spirits
    - Elixirs
    - Tinctures
    - Extract
  - Solids
    - Capsule
    - Pill
    - Powder
    - Tablet
    - Lozenge

Drug Preparations

- Parenteral use
  - Ampule
  - IV infusion
  - Prefilled syringe
  - Vial
- Oral preparations for systemic effects
  - Inhalants
  - Suppositories

Drug Development

- Screening process required by FDA that needs the following sequence
  - Animal studies to determine
    - Toxicity
      - Acute toxicity – medial lethal dose (LD_{50}) dose lethal to 50% of animals tested
      - Subacute and chronic toxicity- speed at which toxicity develops
    - Therapeutic index – ratio of LD_{50} to median effective dose
    - Modes of absorption, distribution, biotransformation, and excretion

Drug Development

- Human studies
  - Phase I - initial pharmacologic evaluation. Goal to prove drug's safety and to identify tolerable dosages
  - Phase II – limited controlled evaluation. Designed to test drug's effect on the specific illness it was designed for. After completion of this phase, a new drug application can be submitted to the FDA. If approved, we move to phase III
  - Phase III – extended clinical evaluation. Full-scale evaluation on large number of subjects to determine therapeutic effects, side effects and its tolerability and to establish tolerable dose ranges

Pharmacological Terminology

- Antagonism
  - The opposition between two or more medications
- Bolus
  - A single, often large dose of a medication
- Contraindications
  - Medical or physiological conditions in a patient that would make it harmful to administer a medication

Terminology (Cont.)

- Cumulative action
  - Occurs when a drug is administered in several doses, causing an increased effect
- Habituation
  - Act of becoming accustomed
- Hypersensitivity
  - reaction to a substance that is normally more profound than in the normal population
- Idiosyncrasy
  - reaction to a drug that is unusually different

Terminology (Cont.)

- Indication
  - the medical condition in which the drug has proven of therapeutic value
- Physiologic action
  - Effect on body function
- Potentiation
  - The enhancement of one drug's effects by another
    - E.g. Alcolhol and Barbiturates
- Refractory
  - When there is no response to a drug

Terminology (Cont.)

- Side effects
  - Known, unavoidable, undesired effects seen in a drug
- Synergism
  - The combined action of two drugs – generally for the same purpose
    - E.g. HCTZ and Accupril
- Therapeutic action
  - The desired, intended action of a drug given in the appropriate medical condition

Terminology (Cont.)

- Tolerance
  - Progressive decrease in effectiveness or response to drug
- Untoward reaction
  - Harmful side effect

Mechanism of Action

- The biochemical events that take place resulting in the desired physiological actions
- The study of these actions are termed pharmacodynamics

Drug Absorption

- The process of movement of a drug from the site of application to the extracellular compartment of the body

Factors Affecting Drug Absorption

- Solubility of the drug
- Concentration of the drug
- Body pH
  - Most drugs are weak acids or bases
  - Acidic vs. Alkaline Drugs
- Site of absorption
  - E.g. skin vs. IV vs. IM…
- Absorbing surface area
  - E.g. lungs
- Blood supply to the site of absorption
- Bioavailability

Drug Distribution

- The process whereby a drug is transported from the site of absorption to the site of action
  - A certain amount of drug may become bound to blood proteins rendering it unavailable for further distribution until released
  - Amount that binds to protein is called bound protein
  - Amount not bound is called free drug

Factors Affecting Drug Distribution

- Cardiovascular function
  - E.g. in cardiogenic shock, kidneys are not well perfused – drugs for kidneys (e.g. ????) are less effective
- Regional blood flow
- Drug storage reservoirs
  - Plasma/tissue reservoirs – Delay onset, BUT, prolong the action of drugs
- Physiological barriers
  - E.g. Blood/Brain Barrier
    - Excludes ionize (water-based drugs) such as Dopamine
    - Allows nonionized drugs such as barbiturates to enter the brain

Biotransformation

- Active drugs are converted to inactive form
- Usually occurs in the liver
- Converted to water soluble metabolites
  - if slow, can cause cumulative drug effects
  - Consider the "aging" liver and biotransformation
    - Lidocaine dosage variations

Elimination

- Drugs are eliminated in original form or as a metabolite
- Kidneys (urine)
- Liver(bile)
- Intestines (feces)
- Lungs(air)

Pharmacodynamics

- Time from administration to production of therapeutic response called onset of drug action
- Drugs must bind to receptors
  - Affinity – attraction to receptor
  - Efficacy – capacity to produce pharmacological response
  - Affinity & Efficacy need not be directly "proportional"
- Proteins present on the cell membrane
- **Lock & Key theory**
  - **Agonist vs. Anagonists**
  - **Partial Agonists (Nubain)**
  - **Classic Example: Epinephrine and Inderal**

Special Considerations

- Pediatrics
- Geriatrics
- Pregnancy & Lactation

Pregnancy & Lactation

- FDA assigned categories
  - I A controlled studies show no risk
  - I B no evidence of risk in humans
  - I C risk cannot be ruled out
  - I D positive evidence of risk
  - I X contraindicated in pregnancy

Drug Administration

- Medication
- Dose
- Route
- Rate

Six Rights of Med. Administration

- Right Patient
- Right Medication
- Right Dose
- Right Route
- Right Time (rate)
- Right Documentation

Administration Routes

- Enteral (Alimentary) vs. Parenteral

Enteral Routes

- Oral
- Sublingual
- Rectal

Parenteral Routes

- Topical
- Intradermal
- Subcutaneous
- Intramuscular
- Intravenous
- Endotracheal
- Intaosseous
- **Intranasal**
- Inhalation
- Vaginal

Cardiac Output

- Stroke Volume x Heart Rate
- **CO = SV x HR**
- Typical adult SV = 70ml/beat
- Typical adult HR: 60-100 beats/minute
- Therefore, typical adult CO = ?

Tropic Agents

- Chronotropic = Rate
- Inotropic = Contractile force
- Dromotropic = Rate of nerve impulse conduction (electrical conduction)
- **Positive Tropic Agents**
  - Epi/Norepi
- **Negative Tropic Agents**
  - Beta Blockers (e.g. Inderal)

Blood Pressure

- Blood Pressure = Cardiac Output x Peripheral Vascular Resistance
- BP = CO x PVR
- What might increase PVR?

Shock (Hypoperfusion)

- BP= SV x HR x PVR

- What is my first and most reliable vital sign?
- What is my least reliable sign?

Tonight's Scenario

You come to the scene and find a semiconscious 51 YO male lying prone on the floor. There is a small cut on the forehead that looks a few days old.