Cardiovascular Pharmacology

- Heart disease: leading cause of death in the U.S.
- ~80,000,000 people in the U.S. have some form of cardiovascular disease
  - HTN
  - Coronary disease
    - AMI
    - Angina
  - CVA
  - Heart failure
- CV disease is responsible for ~35.4% of all deaths (1:2.8 deaths)
Hyperlipidemia

**Cholesterol (CHO):**
- Risk of developing CHD is directly related to increased levels of blood cholesterol (LDL)
- Many *physiologic roles*:
  - Component of all cell membranes
  - Required for the synthesis of certain hormones
    - Estrogen
    - Progesterone
    - Testosterone
    - Corticosteroids
  - Required for the synthesis of bile salts (digestion and fat absorption)
  - Deposited in the stratum corneum of the skin (reduces evaporation of water and blocks transdermal absorption of water-soluble compounds)
- Total CHO = dietary (exogenous) + liver (endogenous: #1)

Lipoproteins

- Cholesterol and triglycerides
  - Carried in bloodstream by serum proteins (lipoproteins)
- 3 classes of lipoproteins are most relevant to CAD:
  - VLDL-C (*contain mostly triglycerides*)
  - LDL-C
    - Transport cholesterol from the liver to tissues/organs
    - Forms a platform for clot formation
    - 30% decrease in LDL-C will yield an ~ 30% decrease in CAD and stroke
  - HDL-C
    - Removes cholesterol from tissues to the liver
Pathogenesis of Plaque Rupture

**Functions of the Endothelium:**

- Not simply a barrier between the blood and smooth muscle as once thought
  1. Non-adhesive surface endures unimpeded blood flow
  2. In healthy people, exhibits antithrombotic and fibrinolytic properties
  3. Releases several vasoactive substances that regulate smooth muscle tone:
     - Bradykinin prompts the endothelium to synthesize and release nitric oxide → vasodilation

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**Functions of the Endothelium – continued:**

- Controls cell proliferation
- Endothelial dysfunction → vasoconstriction, coagulation and cellular growth inhibition
- Foam cells form when LDL-C penetrates the damaged epithelial layer and becomes oxidized

- Need to focus on lipid core and stability of the fibrous cap
  - Statin drugs stabilize the cap
  - HDL-C: “The Paxil or Zoloft of foam cells!!”
Management of Hyperlipidemia

◆ Therapeutic Lifestyle Changes – FIRST!
  ◆ TLC diet
    ◆ 5-6% calories: Saturated fat
    ◆ < 200 mg/day of cholesterol
    ◆ Increase soluble fiber + plant stanols/sterols to enhance LDL reduction
  ◆ Smoking cessation
  ◆ Increase physical activity
  ◆ Control HTN, diabetes and metabolic syndrome
  ◆ Stress management
  ◆ 2013 Lifestyle Management Work Group Guideline

Lipid Levels

◆ When should cholesterol screening begin?
◆ Total Cholesterol
  ◆ Desirable: < 200 mg/dL
◆ Triglycerides (VLDLs)
  ◆ < 150 mg/dL
◆ HDL
  ◆ > 40 mg/dL
◆ LDLs
  ◆ < 100mg/dL: Optimal
  ◆ [Consider values: < 130? < 100? < 70?]