Cardiovascular 3

Lipids and Hemostasis

New Guidelines meant be out in 2012...

The National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP) is composed of experts who study the research and make clinical practice recommendations.

Current guidelines updated in 2006

The NCEP-ATP guidelines

Patients at a **HIGH risk** for Coronary Heart Disease (CHD) have any 1 of 5 “CHD Risk Equivalents”

1. Diabetes mellitus or metabolic syndrome
2. Peripheral vascular disease
3. Carotid artery disease
4. Abdominal aortic aneurysm
5. **Calculated** 10 year risk of a coronary event the is greater than 20%

Patients at an **intermediate risk** have 2 or more of these:

1. BP greater than 140/90 or are on anti-HTN medication
2. Smoker
3. HDL less than 40 mg/dL
4. Age over 45 years for men and 55 years for women
5. 1st degree relative with CHD onset age younger than 55 years if a male and younger than 65 years if female

**Low risk** patients have less than 2 of the intermediate risk factors.

Metabolic Syndrome

Includes any 3 of these:

- Abdominal obesity
  - In men waist > 40 inches
  - Women > 35 inches
- High triglycerides
  - ≥ 150 mg/dL
- Low HDL
  - Men <40 mg/dL
  - Women < 50 mg/dL
- High BP
  - ≥ 130/85 mmHg
- High fasting glucose
  - ≥ 110 mg/dL indicates insulin resistance

For every 5 cm the waist circumference increases, the mortality risk increases by 17% for men and 13% for women.
Clotting Agents

Hemophilia is a genetic condition. There are many types of hemophilia. It is caused by mutations that prevent the synthesis of various clotting factors. Treatment generally entails infusions of clotting factors that have been harvested from pooled human plasma. Pooled human plasma may carry blood-borne diseases.

Factor IX Complex (BeneFIX) is used to treat hemophilia B or deficiencies of clotting factors VII and VIII.

Conditions requiring drugs to control bleeding

- Hemophilia
- Liver disease
- Child birth
- Bone marrow disorders
- Repeat coronary artery bypass graft surgery
- Surface injuries with extensive (abrasion or other) damage

Fibrinolytic bleeding

Fibrinolytic bleeding occurs when the fibrin holding the clot together is dissolved too soon. The following conditions are associated with fibrinolytic bleeding:

- Surgery on heart, prostate or kidney
- Amegakaryocytic thrombocytopenia with aplastic anemia
- Abruptio placenta
- Hepatic cirrhosis
- Cancer of the prostate, lung, stomach or cervix
- Increased production of urokinase, an enzyme produced by the kidney to lyse blood clots in the urinary system

Aminocaproic acid (Amicar) is used to treat fibrinolytic bleeding.
Treatment of hyperlipidemias

There are a number of lipid fractions that are examined. Total cholesterol combines LDL + HDL + other cholesterol components. It should be below 200 mg/dL. LDL should be less than 100 mg/dL, HDL should be more than 40 mg/dL in men and more than 50 mg/dL in women. Triglycerides should be less than 150 mg/dL.

**Atorvastatin** (Lipitor) is a statin drug used to lower LDL cholesterol and raise HDL cholesterol. It also leads to reductions in inflammatory proteins. It acts by blocking a key enzyme in cholesterol metabolism in the liver.

The statins are pregnancy category X. They alter liver enzymes and are associated with elevating blood glucose. Rarely, they cause Rhabdomyolysis (break down of skeletal muscle) that can lead to kidney damage. There are reports of memory loss in patients taking statins.

**Cholestyramine** (Questran) is a bile acid sequestrant. This is a drug that does not get absorbed; it absorbs lipids and lipid-soluble materials, including drugs and vitamins, from the GIT. Because cholesterol is the sole precursor of bile acids, and most bile acids are normally recycled, when cholestyramine binds the bile acids, they are excreted in the feces. This lowers cholesterol.

**Nicotinic acid** is niacin, the vitamin B₃ (Niacor). Niacor is not simply concentrated OTC vitamin B₃ and patients need to be instructed to not take mega doses of OTC B vitamins.

Fibric acids, or fibrates, include the drug Gemfibrozil (Lopid). Fibrates lower triglycerides dramatically while substantially elevating HDL levels. They don’t affect LDL. A number of HIV antiviral drugs cause hypertriglyceremia that is treated using a fibrate such as gemfibrozil.

**Ezetimbe** (Zetia) is a unique, fairly new drug. It acts on the cells of the GIT epithelium to block the uptake of dietary and biliary cholesterol.
Anticoagulants affecting clotting factors....

Warfarin (Coumadin) is primarily used chronically as an oral anticoagulant. It is pregnancy category X. Patients should be genotyped for CYP2C9 and VKORC1 prior to therapy.

Warfarin interferes with Vitamin K dependent activation of clotting factors. Its effects can be reversed by consuming or administering Vitamin K.

Warfarin has a long delay between the onset of therapy and the onset of action. While waiting for the warfarin effect to kick in, patients will typically be treated with Heparin. Warfarin requires substantial monitoring and patient compliance with taking the drug as prescribed as well as controlling their diet.

Heparin is the most common anticoagulant used in the hospital setting, but it can cause heparin-induced thrombocytopenia (HIT). This is happens when heparin binds to platelets, causing WBCs to clear the affected platelets from circulation.

Dabigatran (Pradaxa) is an oral alternative to heparin. It is a direct thrombin inhibitor.

Enoxaparin (Lovenox) is a parenteral alternative to heparin that doesn't require nearly so much monitoring and doesn't have the high risk of side effects associated with chronic heparin use such as osteoporosis.

Bivalirudin (Angiomax) is also a parenteral alternative to heparin, but due to expense is mainly used during cardiac procedures.

Patients taking anticoagulants should report any:

- Unusual bruising
- Pink or brown urine
- Red or black, tarry stools
- Coughing up any blood
- Vomiting blood
- Coffee-grounds looking vomit
- Pain or swelling in a joint
- Reoccurring nose bleeds
- Cuts that bleed too long
- Heavier than normal menstrual bleeding
Aspirin, and other NSAIDs, inhibit COX. This interferes with the synthesis of thromboxane and limits platelet activation and aggregation. Thromboxane, along with the prostaglandins, is synthesized from Arachidonic acid by cyclooxygenase.

**Clopidogrel (Plavix)** is a Prodrug. Patients should be screened for CYP2C19 activity prior to starting therapy with Plavix (boxed warning) because poor metabolizers will see little if any benefit from taking Plavix. Clopidogrel blocks ADP receptors on platelets that are a trigger for platelet activation and aggregation.

**Cilostazol (Pletal)** is a 3-PDE with specific effects. It is only used to treat intermittent claudication and should not be used in heart failure patients.

**Eptifibatide (Integrilin)** is the only parenteral antiplatelet anticoagulant we cover. It is derived from a protein in the venom of pygmy rattlesnakes, and it is a biologic.

**Alteplase (Activase)** is a recombinant form of tissue plasminogen activator (t-PA). It is not an antiplatelet anticoagulant; it is a fibrinolytic. These drugs are known as “clot busters.” They must be given ASAP to have much benefit.
Platelets have many surface receptors for different ligands that trigger activation and aggregation

- Thrombin
- Thromboxane (TXA$_2$)
- Adenosine diphosphate (ADP)
- Epinephrine
- Collagen
- Arachidonic acid
- Shear stress forces
- Fibrinogen
- Serotonin
- Von Willebrand factor
- Platelet activating factor
- ADH/Vasopressin

Homework and Exercises

1. Read the “START HERE” announcement in Laulima for updates and instructions.
3. Review the Powerpoints and listen to the audio from the face-to-face lecture. You may opt to watch the appropriate videos for this lecture. Review any handouts available for this lecture in the Course Index.
4. Complete the SLO practice set for CV3 in Tasks, Tests and Surveys.
5. Use “Chat,” “Discussions and Private Messages” or the lecture “Forum” to ask questions and find answers or to seek assistance.
6. Complete the online quiz in Laulima, Tasks, Tests and Surveys.

If you have any questions, email me at abeale@hawaii.edu