

Review of the Midterm
(and associated problems)

Themes for this time:

Molecules with more than their share of power
Molecules that regulate the actions and fates of others.

Hormones alter the **balance of energy storage and release**, in response to availability of more (glucose).

Peptide hormones, amino acid-derivatives, steroids.

Effects are diverse and far-reaching. Mutations in enzymes that make them, or administration, profoundly affects one's metabolism (and life).

Hormones:

Molecules that transmit messages via the blood.

Small proteins, amino acid derivatives, steroids.

Epinephrine (adrenalin) = Tyrosine (Tyr) derivative: muscle activity, fatty acid release

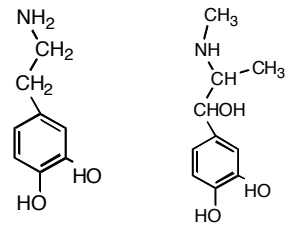
Melatonin = N-acetyl-5-methoxytryptamine circadian rhythms.

Oxytocin = 9-residue polypeptide (mini-protein) uterine contraction, milk release.

Estrogens and androgens = steroids

1,25-dihydroxy vitamin D3 = steroid, Ca uptake

Tyrosine oxidation and decarboxylation produces the neurotransmitter DOPA

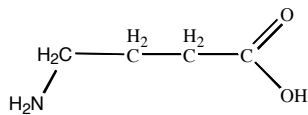


Ephedrine:
A stimulant that acts by binding to neuronal receptors that would normally bind DOPA.

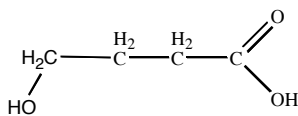
DOPA (dihydroxyphenylalanine)

Ephedrine

GABA, gamma amino butyric acid.



GBH, Gamma hydroxybutyric acid, binds to GABA receptors.

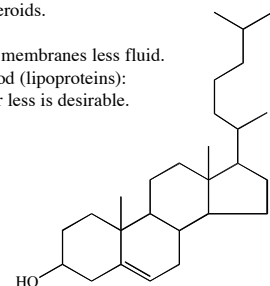


Cholesterol and fats

Cholesterol: the mother of all steroids.

Lipid soluble, inflexible: makes membranes less fluid.

Carried on proteins when in blood (lipoproteins):
200 mg cholesterol /dl or less is desirable.



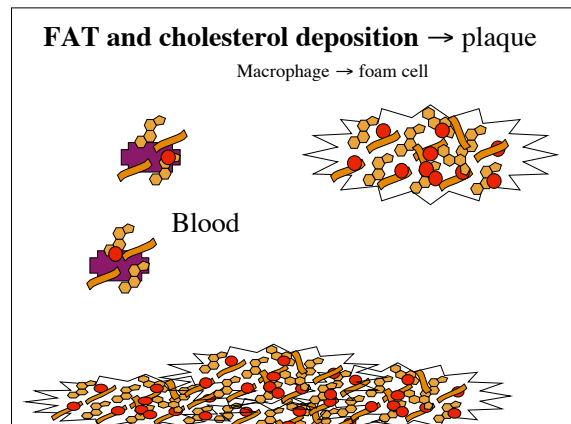
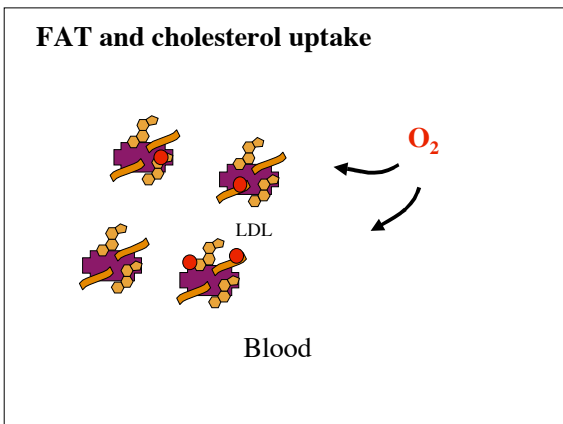
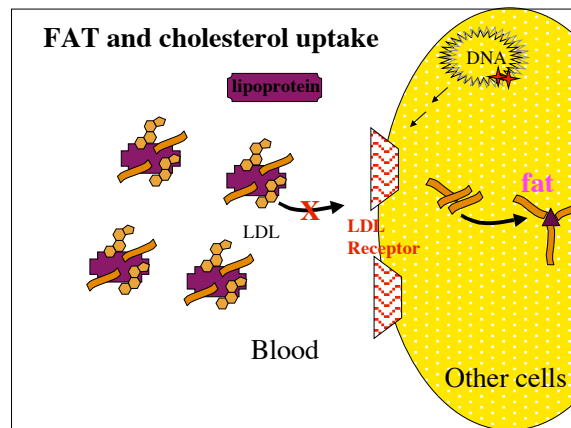
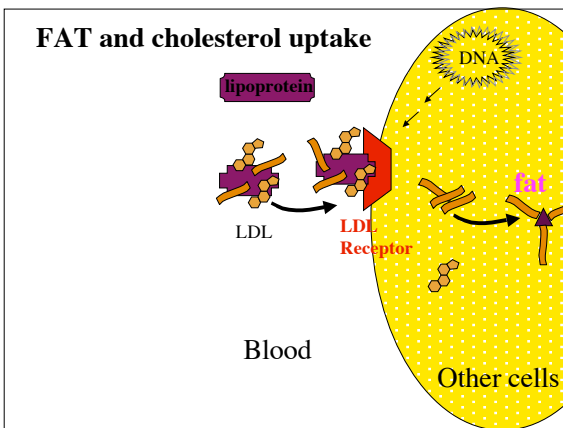
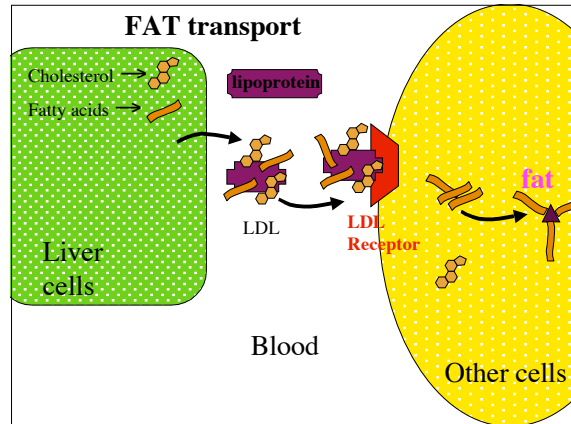
Low Density Lipoprotein (LDL) is normally taken up by cells.

Faulty LDL uptake leads to accumulation of cholesterol in blood, and high levels of LDL. This is BAD.

When LDL gets oxidized, it excites immune cells (macrophages).

Local inflammation response results (with more oxidative damage).

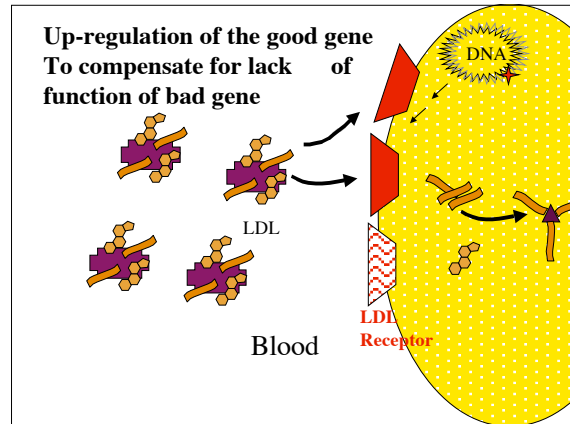
Engorged macrophages (foam cells) accumulate to form plaques, which block arteries.



Strategy: stimulate LDL uptake by cells
 reduce levels of cholesterol production
 reduce levels of cholesterol absorption from food.

LDL receptor: ≈ 1000 amino acid protein, if ONE is wrong:
 cholesterol ≈ 300 mg/dl if one copy of gene is affected
 cholesterol ≈ 700 mg/dl if both copies are affected.

People with two defective copies of the gene typically die of coronary heart disease in childhood. A liver transplant is needed.



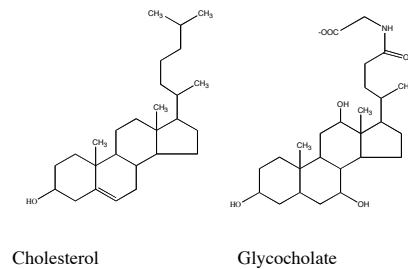
People with one normal copy of the gene are treated by stimulating that gene to make extra LDL receptor.

Trick the cells into behaving as if they were starving for cholesterol.

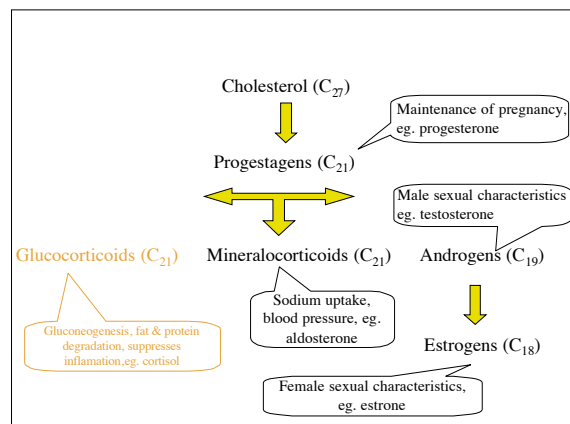
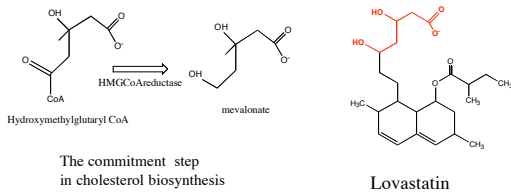
Prevent uptake of cholesterol in food (tie up bile acids with positively charged 'fatty bases', eg. cholestyramine).

Block cholesterol synthesis (statins inhibit key enzyme in cholesterol biosynthesis).

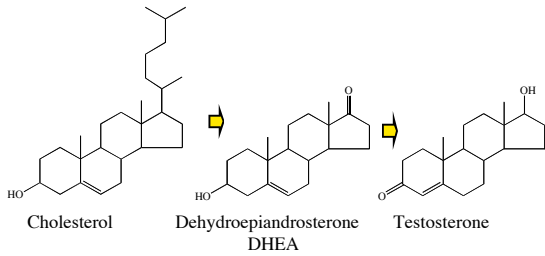
Bile salts: detergents, produced in liver and stored in gall bladder, permit absorption of dietary lipids.



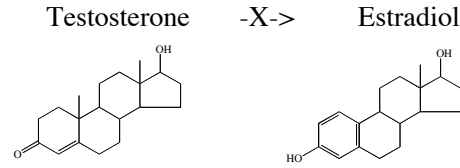
Cholesterol is also synthesized in our bodies, by the enzyme HMG-CoA reductase, a control point in cholesterol biosynthesis. Drugs that inhibit HMG-CoA reductase are very effective at decreasing blood cholesterol (with diet and exercise). A class of these are called 'statins'.



Steroid hormones are derived from cholesterol



Mutations in enzymes that convert testosterone to estrogens



Masculinization

A person with two X chromosomes
Can nonetheless appear male.

Anabolic-Androgenic Steroids, biochemistry

These support development of male sexual characteristics and anabolic effects such as growth of muscle, bone, red blood cells.

The balance between these two sets of activities varies for different AA_steroids. However the most potent anabolic steroids are the most androgenic too.

Protein synthesis is enhanced and protein degradation is inhibited. Muscle mass gain still requires weight training, but more intense training is supported.

AA steroids effect feedback inhibition of testosterone production, leading to feminization of males. However they lead to masculinization of females.

The actions of cortisol are blocked: blockage of tissue breakdown (for fuel), but absence of cortisol reduces protection vs. inflammation injury. Also, adaptation to less cortisol means that when AA-steroid use ceases and cortisol rebounds, tissue degradation is more rapid than normal. Also, cortisol's suppression of the immune system causes the ceasing user to be susceptible to disease.

Claims include 30 % increases in strength, weight gains of 30-40 pounds. One is referred to articles on sports medicine from the former Soviet Union.

Anabolic Androgenic Steroids, cultural aspects

Increased risk of heart attack, stroke, severe liver problems including cancer. Stunted growth (adolescents). Possible psychological effects. Many of the effects are not evident on a short-term basis. IV use has additional risks.

Illicit use is relatively high in certain subcultures. Motivated by image concerns, competitive forces, desire to prevent recurrence of physical attacks.

In general: 2.9 % 12th graders, 2.7 % of 10th and 2.7 % of 8th graders have tried AA steroids.

Doses are up to 100 mg / day (vs. < 10 mg daily natural production of testosterone).

No benefit to agility, cardiovascular fitness or skill.

Information from web sites of NIDA (165.112.78.61/Steroidalert.html), espn.go.com/special/drugsandsports/steroids.html

Diet tricks

Pyruvate

Citrate

Atkins

South Beach

Web sites of interest:

http://dietary-supplements.info.nih.gov/Health_Information/IBIDS.aspx

<http://www.bodybuilding.com/store/infopages.html>

<http://www.worldzone.net/health/supplementinfo/>

<http://content.nhiondemand.com/dse/consumer/dsmain.asp?ctype=ds>

<http://www.quackwatch.org/>