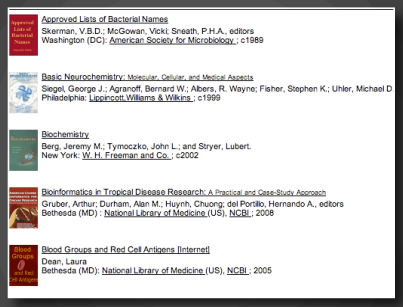

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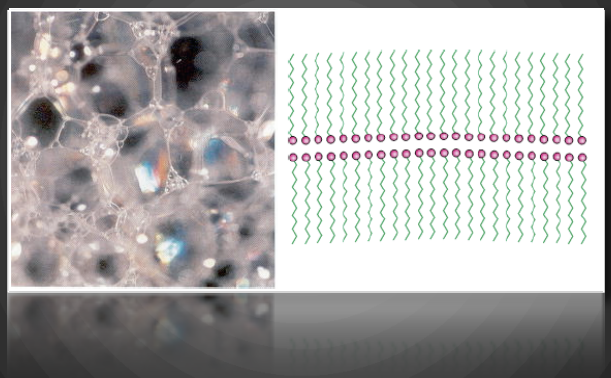
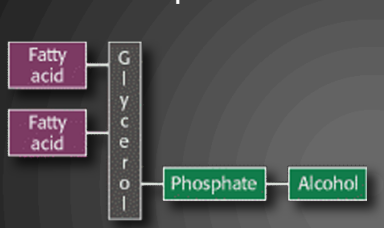


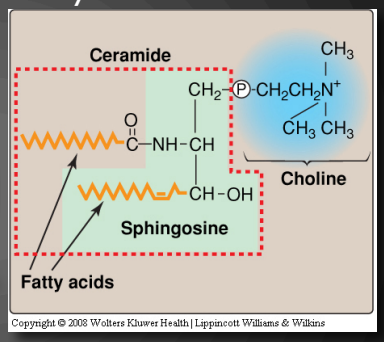
The surface of a soap bubble is a bilayer formed by detergent molecules

2

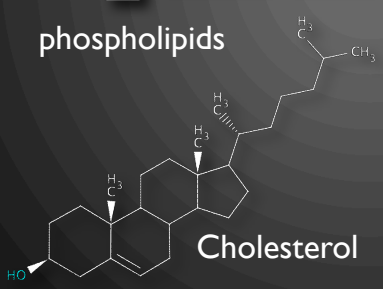
Chapter 26 Biochemistry 5th edition



phospholipids



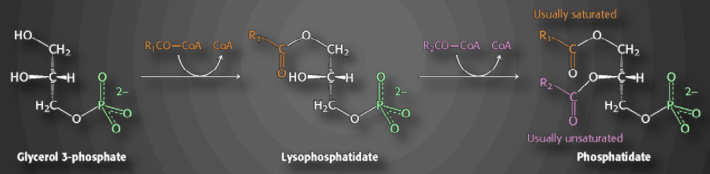
Sphingolipids



Cholesterol

3

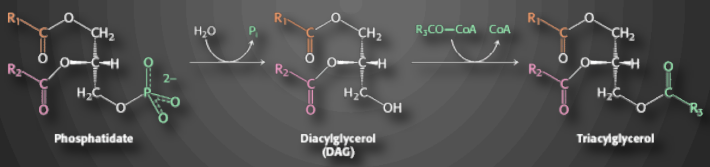
Phospholipids are synthesized in the ER



- The first step involves the synthesis of phosphatidate
- Glycerol 3-phosphate is acylated by acyl-CoA to form lysophophatidate, and acylated again by acyl-CoA to form phasphatidate

4

1) Phosphatidate can form triacylglycerol via *triacylglycerol synthetase* on the ER membrane



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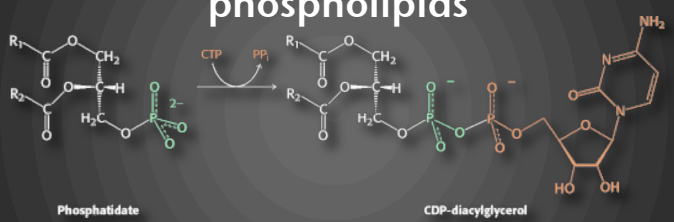
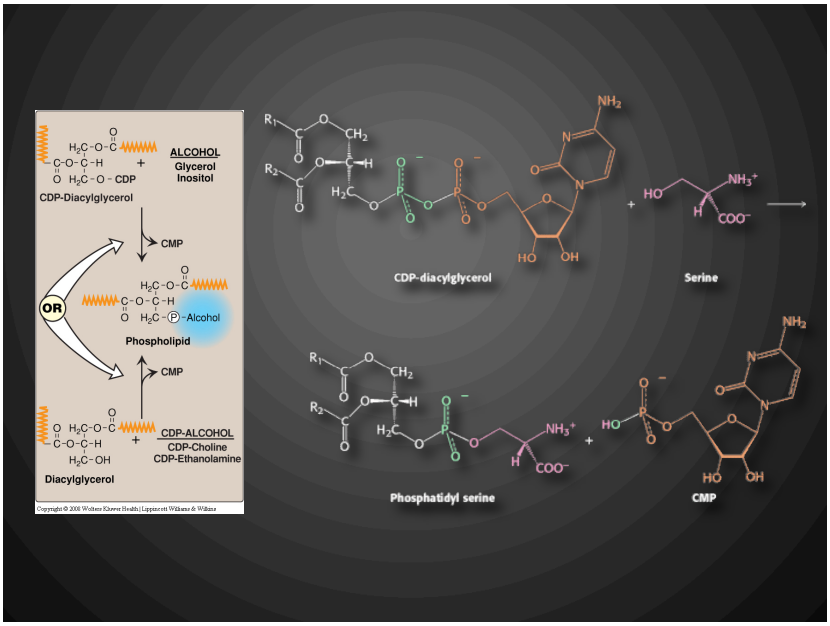
2) Phosphatidate can instead form phospholipids



- The synthesis of phospholipids requires an activated intermediate (in this case, CTP is key).
- Many different alcohol-bearing compounds can react with CDP-diacylglycerol to form different types of phospholipids.

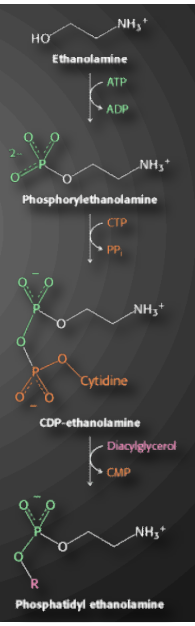
6



7

Serine	+ PA →	phosphatidylserine
Ethanolamine	+ PA →	phosphatidylethanolamine (cephalin)
Choline	+ PA →	phosphatidylcholine (lecithin)
Inositol	+ PA →	phosphatidylinositol
Glycerol	+ PA →	phosphatidylglycerol

- The activation of either the phosphatidate or the alcohol partner by CTP represents the committed /rate-limiting step in phospholipid synthesis
- Once again, the hydrolysis of PPi to inorganic phosphate makes the activation of these components irreversible.



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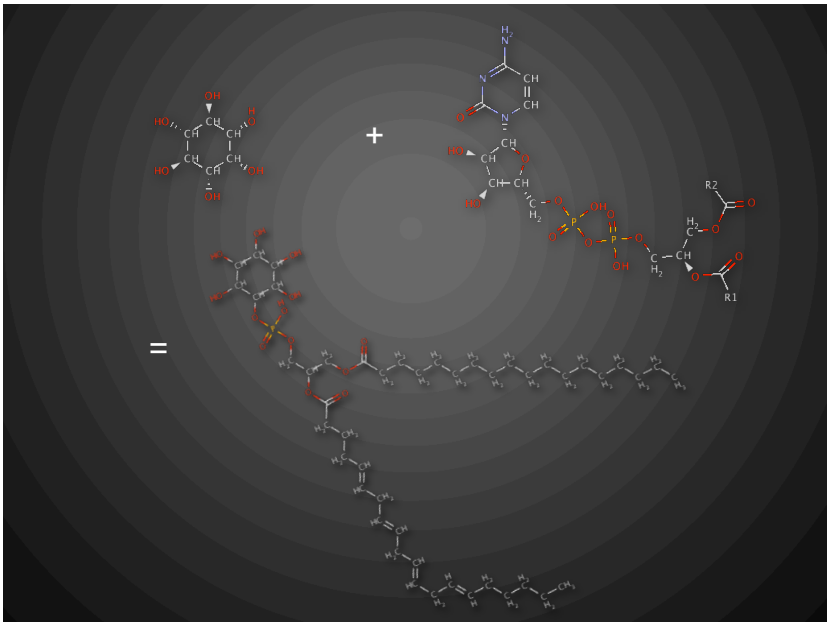

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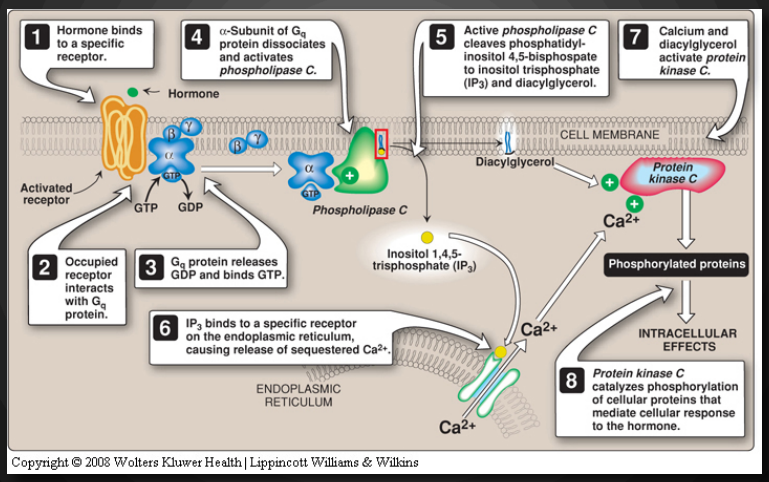

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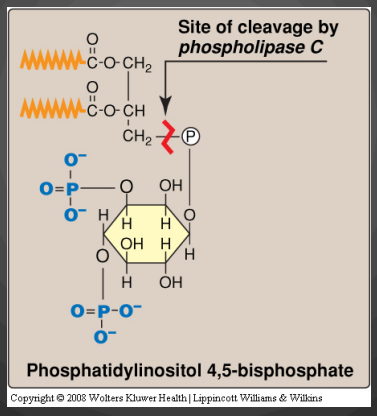
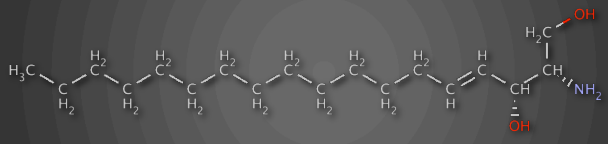
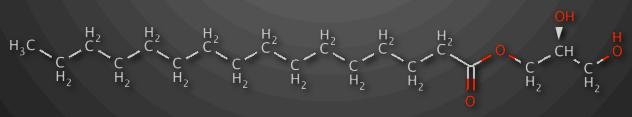


11

The backbone of sphingolipids is sphingosine rather than glycerol

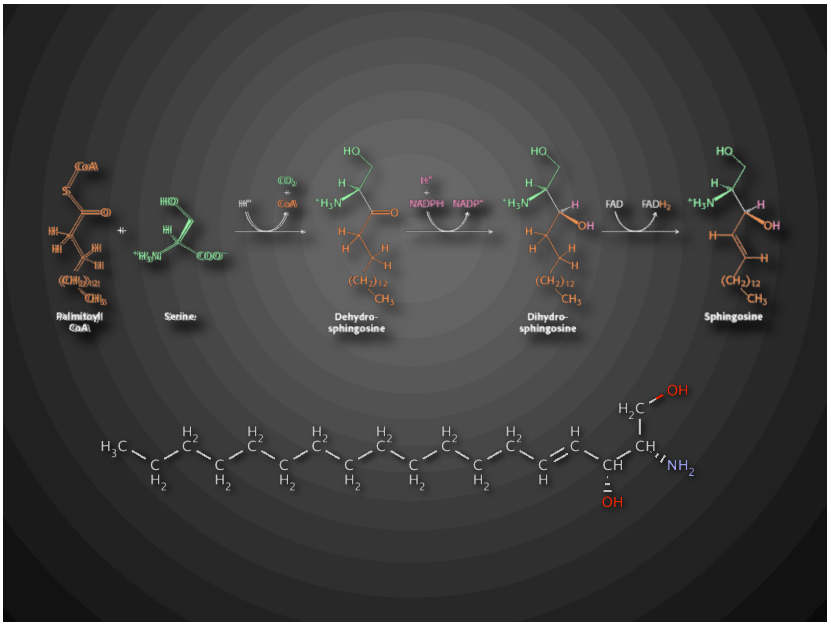


sphingosine



glycerol palmitate

12



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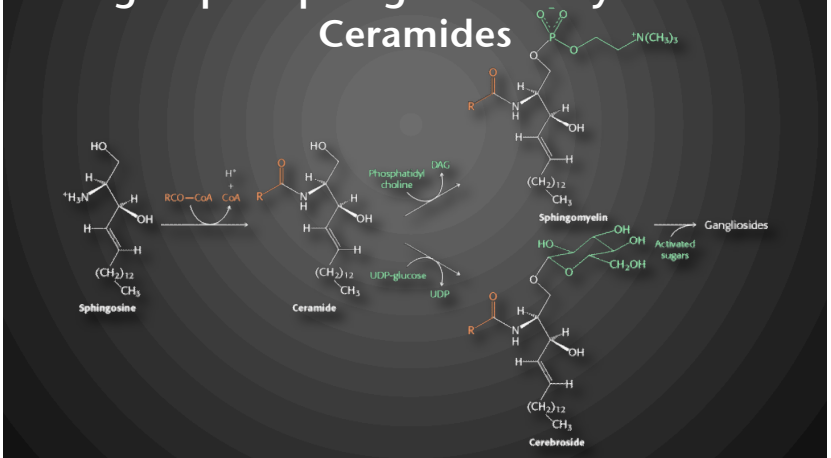
In all sphingolipids, the amino group of sphingosine is acylated: Ceramides



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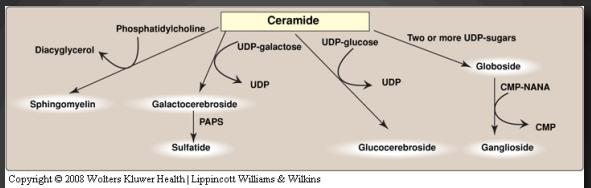

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Eicosanoids are derived from long-chain fatty acids

- Eicosanoids are specialized signaling molecules derived from polyunsaturated fatty acids with twenty carbons: e.g. arachidonate (from linoleate)
- They are not secreted by a gland and do not circulate. Rather, they act locally at or near their site of synthesis.
  - Prostaglandins
  - Thromboxanes
  - Leukotrienes

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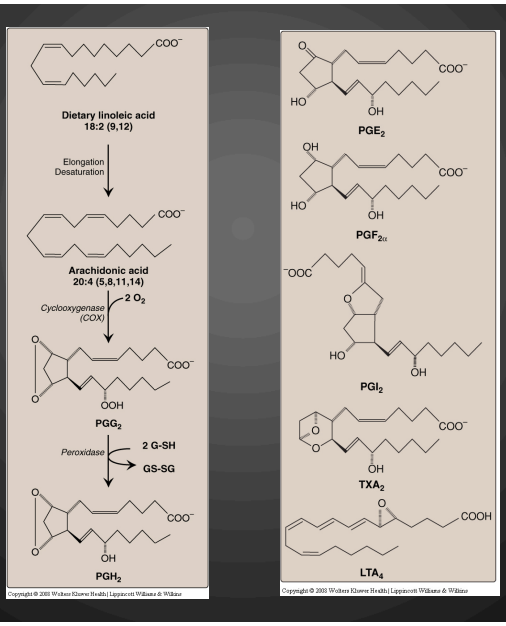

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Prostaglandins

- Generated by COX1 (constitutive) and mediates gastric function, renal homeostasis, and platelet aggregation
- COX2 (inducible) mediates pain, swelling, inflamation and fever.
- Aspirin is an irreversible inhibitor of both COX1 and COX2, while celecoxib (Celebrex or Vioxx) only inhibits COX2.

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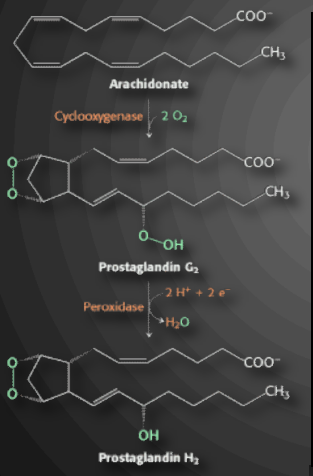
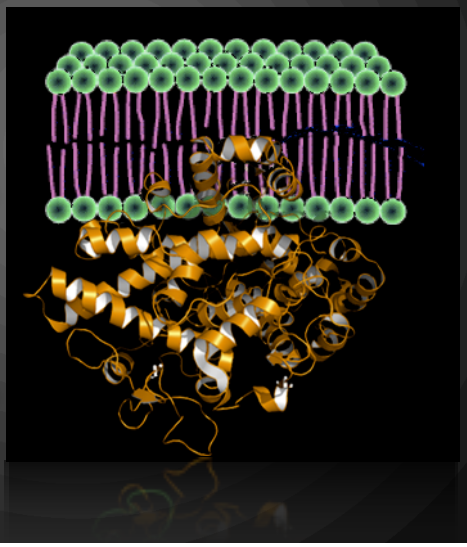
Prostaglandin H_2 synthase-1 (COX1)





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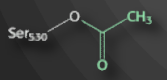
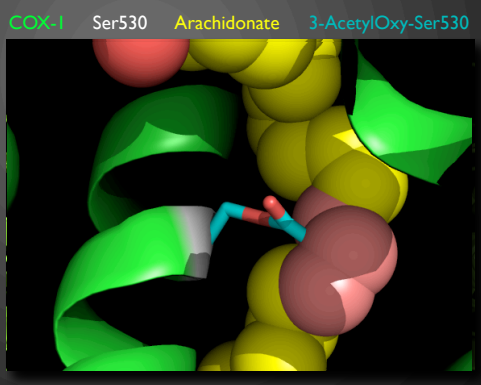
Aspirin's effects on prostaglandin H_2 synthase-1 (COX-1)





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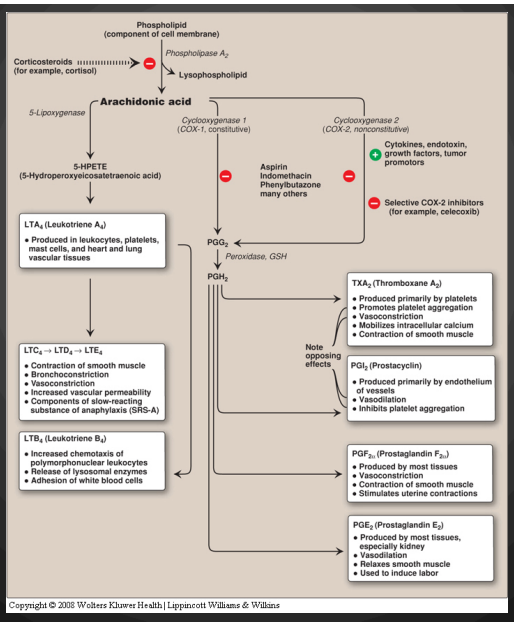

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Cholesterol (chapter 18)

- Cholesterol is synthesized by all tissues in humans, although liver, intestine, adrenal cortex, and reproductive tissues make the most.
- All the carbon atoms in cholesterol come from acetate, with reducing equivalents from NADPH.
- Energy for synthesis comes from hydrolysis of thioester bonds of acetyl CoA and terminal phosphate bond of ATP.
- Synthesis occurs in the cytoplasm, with some enzymes found in the membrane of the ER.

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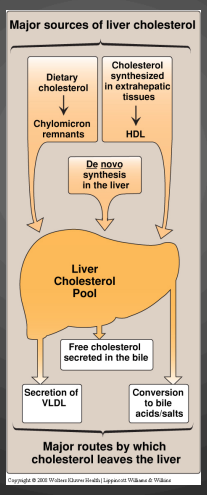

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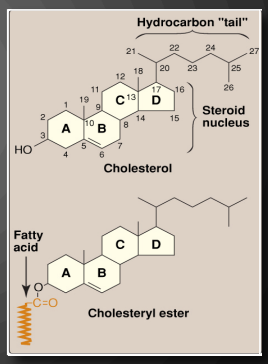
cholesterol structure

- most plasma cholesterol is in the esterified form (not found in cells or membranes)
- cholesterol functions in all membranes (drives formation of lipid microdomains)
- cholesterol is the precursor for steroid hormones
- note 4 fused rings, single dbl bond, single hydroxyl, acyl chain at C17



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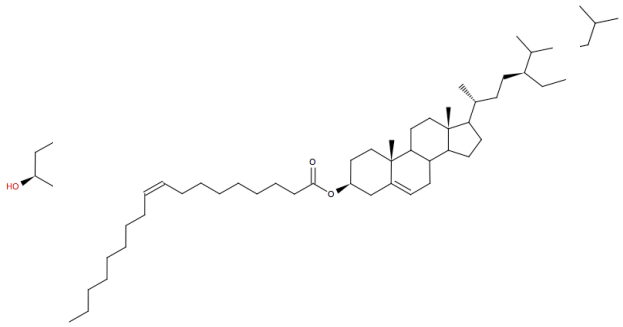
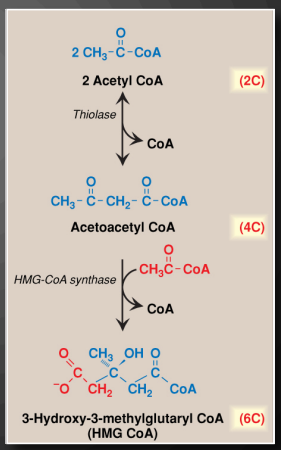
plant sterol margarines (Benecol, sitosterol) lower LDL cholesterol by inhibiting intestinal absorption of cholesterol



26

Cholesterol synthesis initially follows that of ketone bodies

3 cytoplasmic acetyl CoA molecules are sequentially condensed to form HMG CoA (6 carbons)



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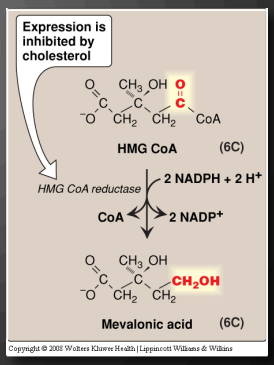
The rate-limiting step of de novo cholesterol biosynthesis is catalyzed by HMG CoA reductase

- The reduction of HMG CoA by HMG CoA reductase results in the oxidation of two NADPH and results in mevalonate.
- HMG CoA reductase is a membrane protein of the ER: catalytic domain projects into the cytoplasm.
- Target of statin drugs



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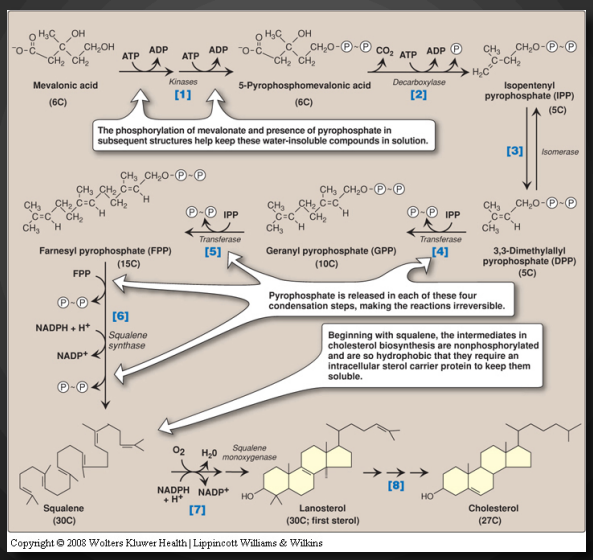

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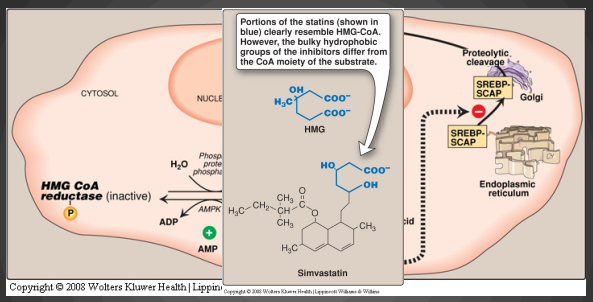

Regulation of HMG CoA reductase

1. regulation of gene expression by SREBP
2. phosphorylation state
3. regulation by hormones (insulin, glucagon)
4. inhibition by statin drugs

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Degradation of Cholesterol

- The ring structure of cholesterol cannot be metabolized to CO_2 and H_2O in humans.
- The sterol ring nucleus is eliminated from the body by conversion to bile acids and bile salts.

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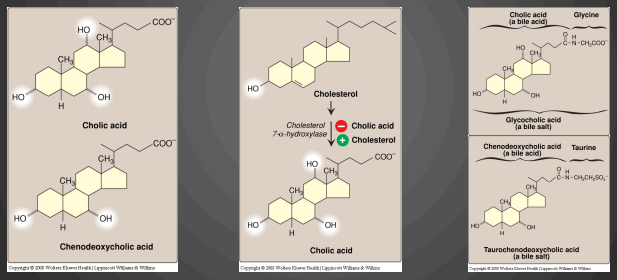
Degradation of Cholesterol



- The theme is for cholesterol to be converted to a relatively soluble amphipathic molecule.
- As a bonus, these molecules are used as emulsifying agents during digestion.

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