

Lipid Biosynthesis

- Regulation
- Elongation
- Unsaturation



Chapter 22 Opener part 1
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Pathway integration

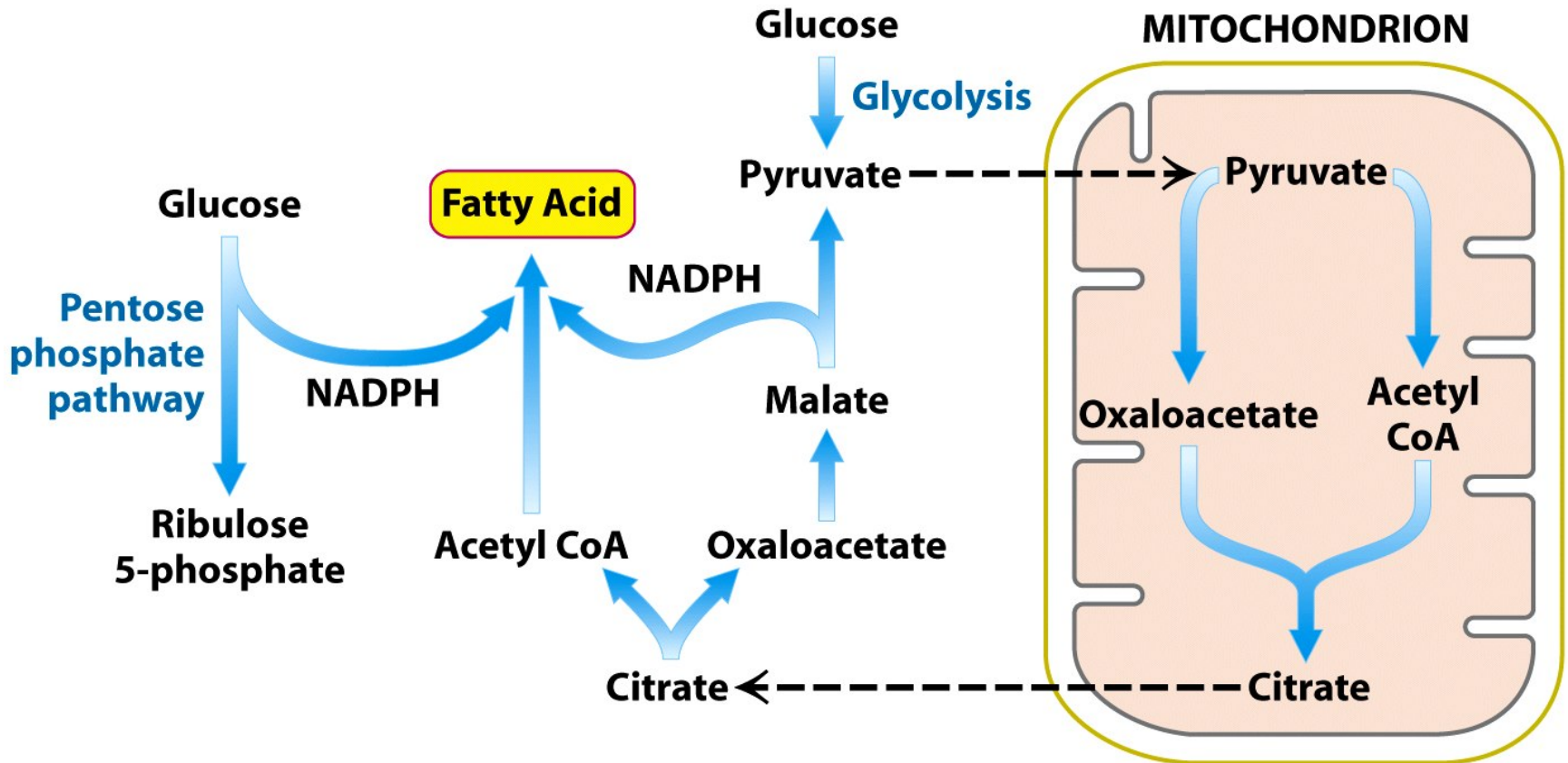


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FA synthesis regulation via acetyl CoA carboxylase

- Acetyl CoA carboxylase is inhibited by fatty acyl CoA (increased FA concentrations lead to decreased FA synthesis)
- Acetyl CoA carboxylase is under hormonal control: glucagon and epinephrine (fasted state) stimulate phosphorylation (inactivation) of the enzyme

Regulation

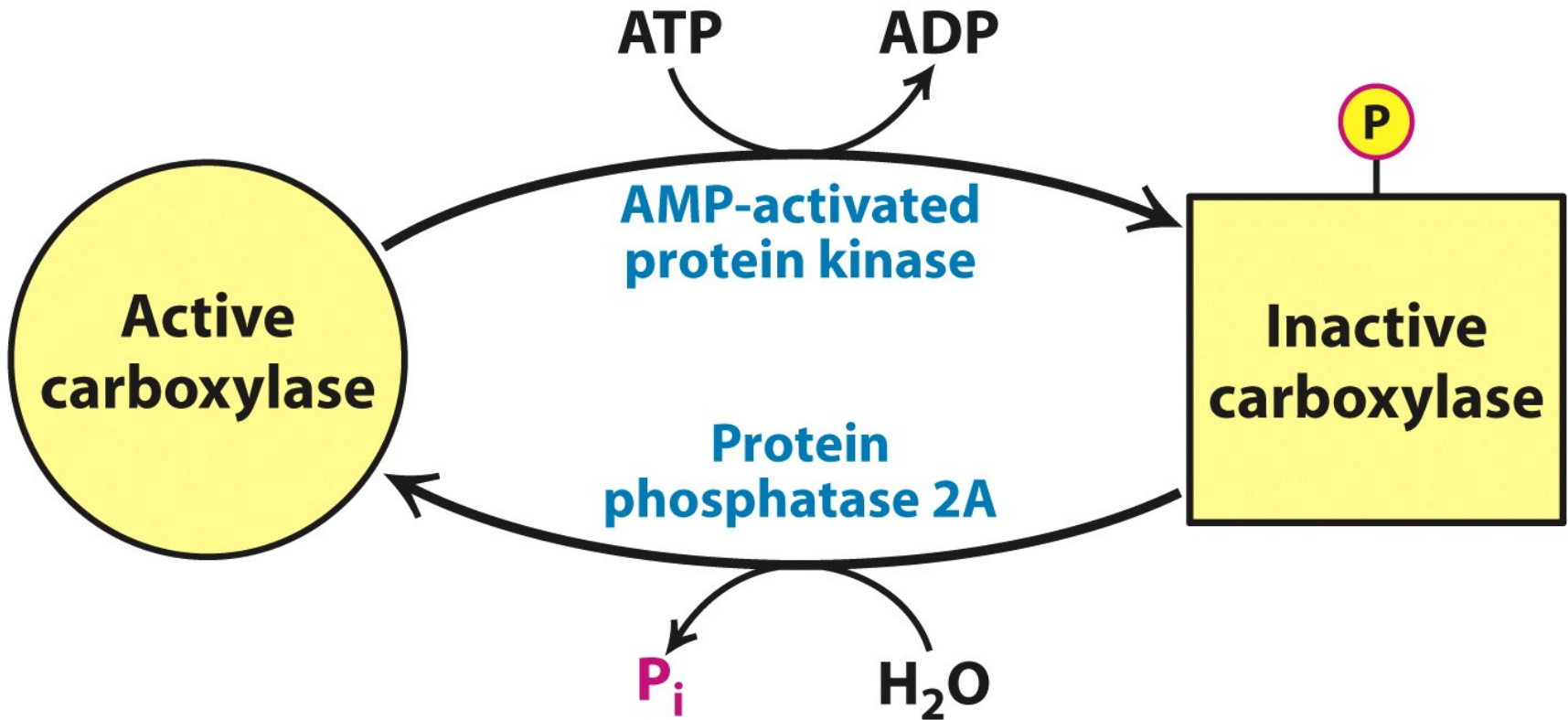


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Citrate dependence

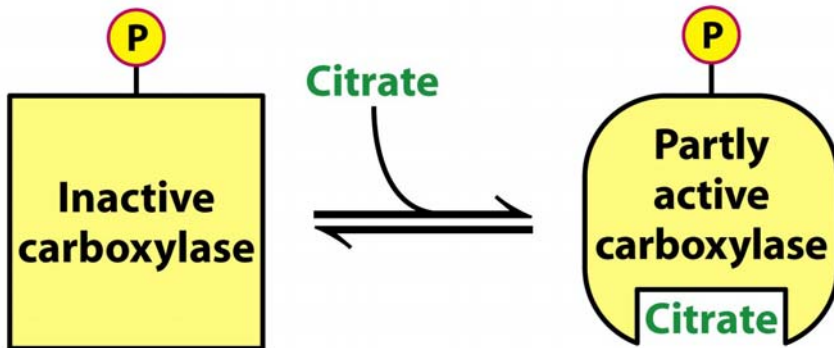


Figure 22-31a
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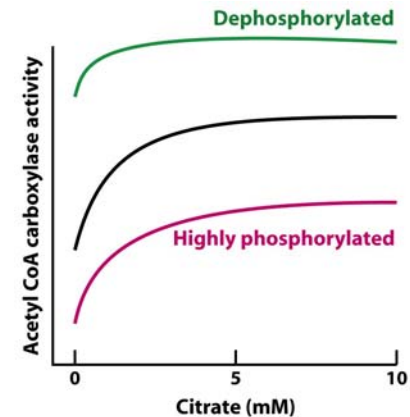


Figure 22-31b
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- Activated by citrate, inhibited by Palmitoyl CoA
- Malonyl CoA inhibits: Carnitine acyl transferase I
- Glucagon/Epinephrine: Inhibit FA synthesis
- Insulin: stimulates the activity of protein phosphatase

Fatty Acid Desaturation

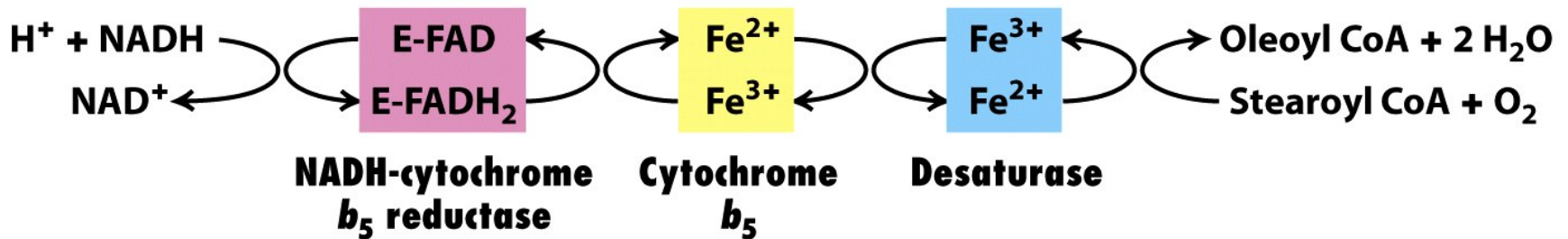
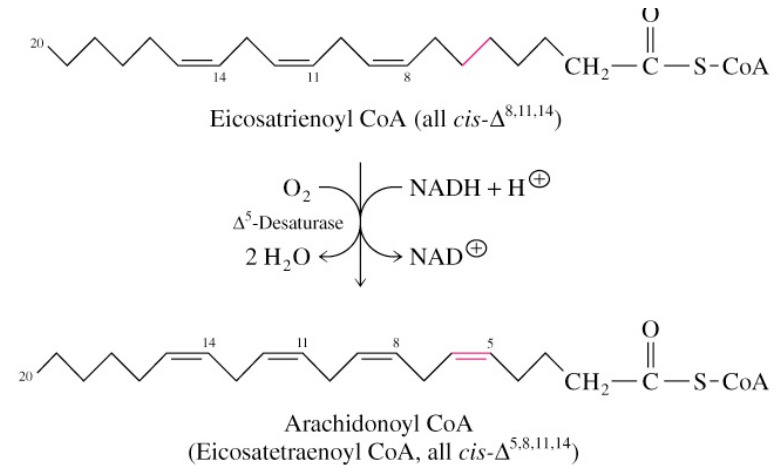
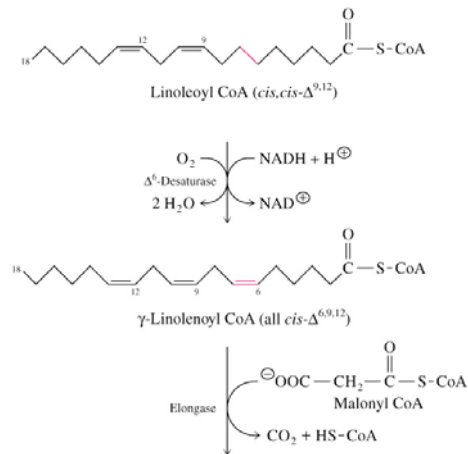


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- Endoplasmic reticulum
- Two electrons come from NADH and two from FA substrate
- Mammals lack the enzyme to introduce double bonds beyond C-9
- Mammals need linoleate and linolenate in the diet

Fatty Acid Elongation and Desaturation



- Cytoplasmic face of endoplasmic reticulum
- Uses saturated and unsaturated fatty acids
- Malonyl CoA is the two carbon donor

Arachidonate

- Arachidonate (20:4) derived from linoleate
- Used to synthesize to prostaglandins
- Prostaglandins stimulate inflammation, regulate blood flow to particular organs, ion transport, modulate synaptic transmission, induce sleep
- Aspirin blocks access to the active site of prostaglandin synthase by blocking the hydrophobic channel and inhibiting cyclooxygenase activity

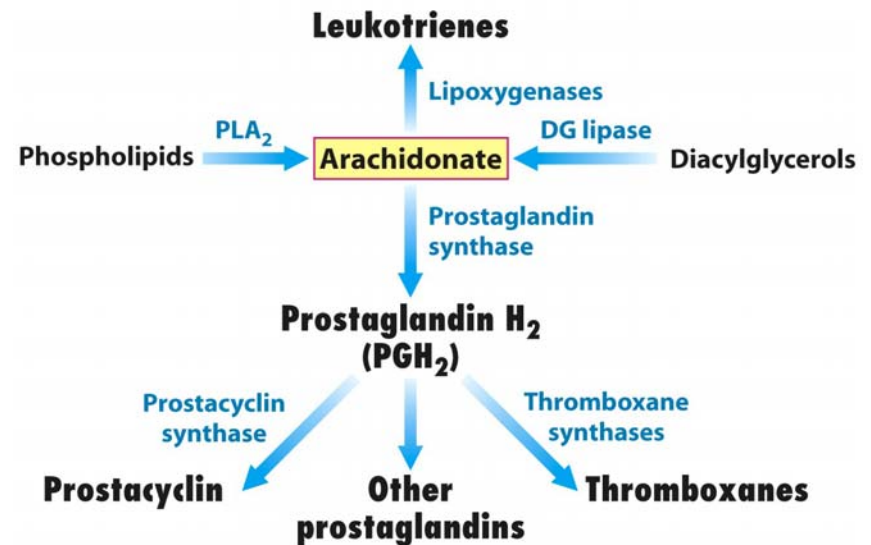


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Synthesis of Triacylglycerols (TGs) and Glycerophospholipids (GPLs)

- Most fatty acids in cells are found in esterified forms as TGs or GPLs
- Phosphatidic acid (phosphatidate) is an intermediate in the synthesis of TGs and GPLs
- Glycerol 3-phosphate is acylated by fatty acyl CoA molecules

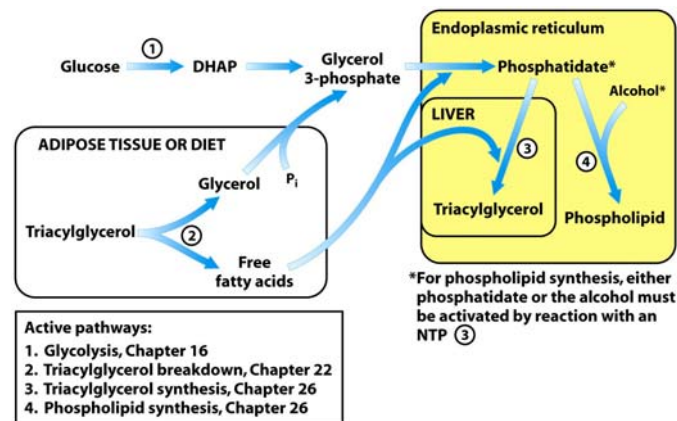
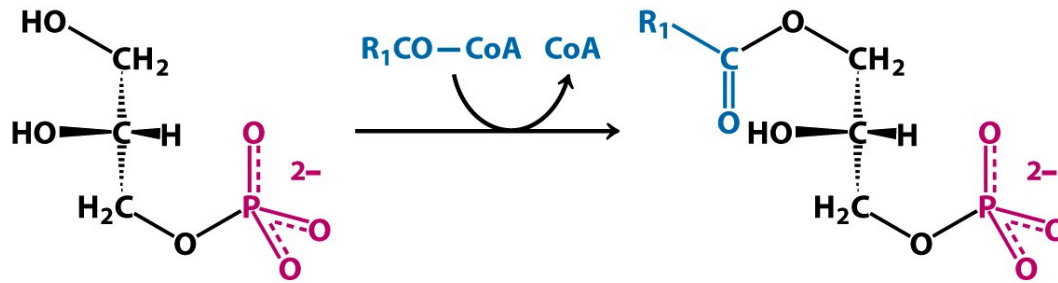


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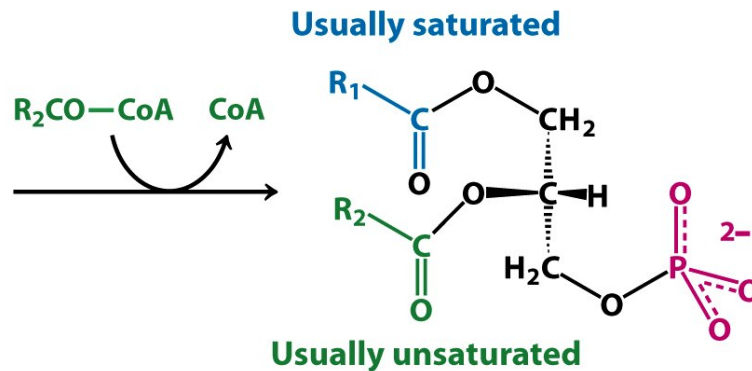
Formation of phosphatidate



Glycerol 3-phosphate

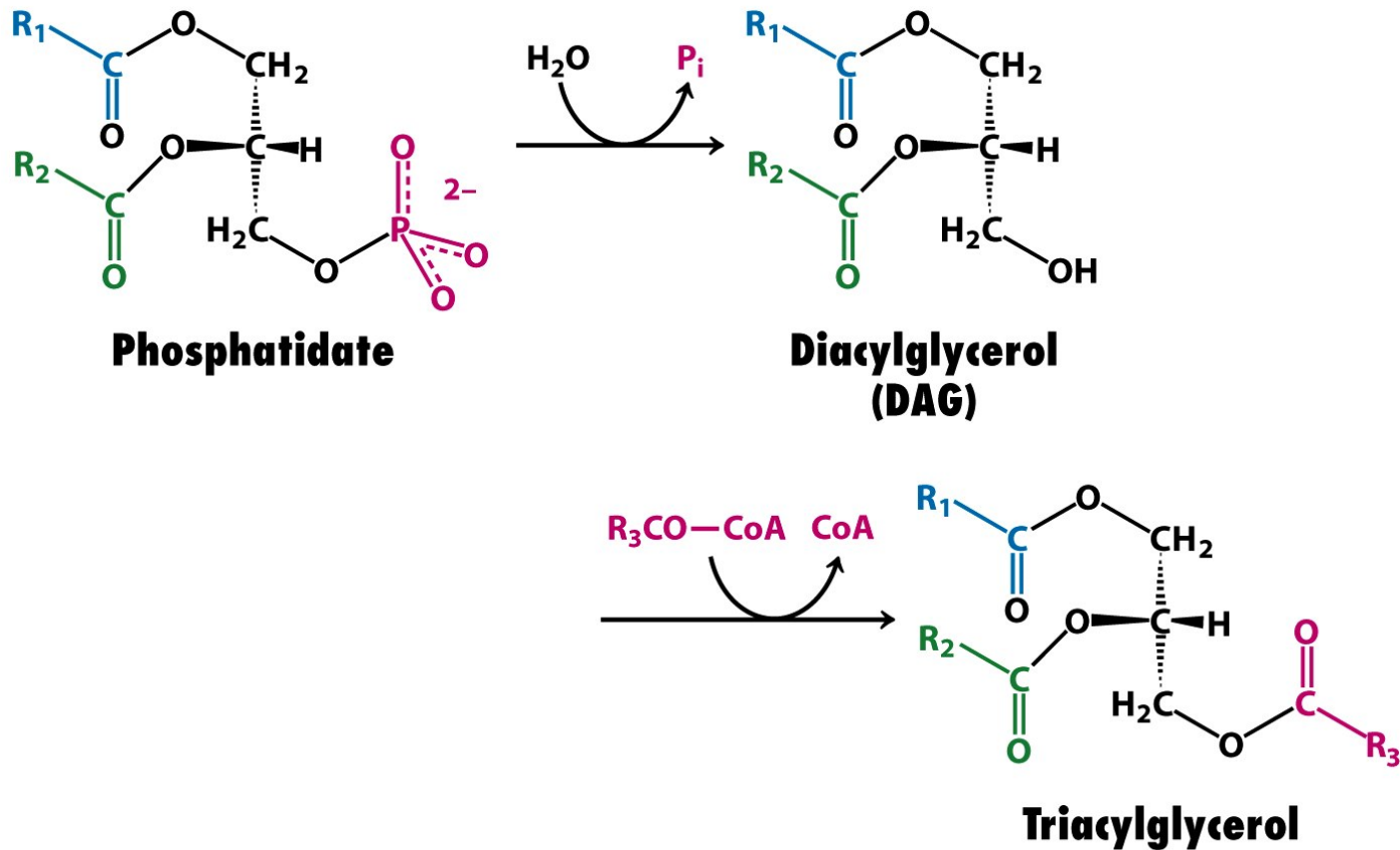
Lysophosphatidate

Catalyzed by glycerol phosphate
Acyltransferase
C-1 saturated FA
C-2 unsaturated FA

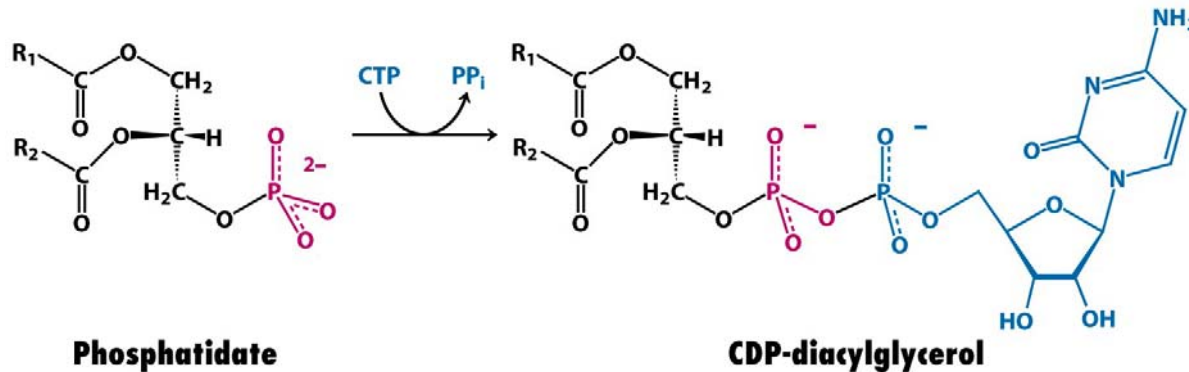


Phosphatidate

Synthesis of Triacylglycerols



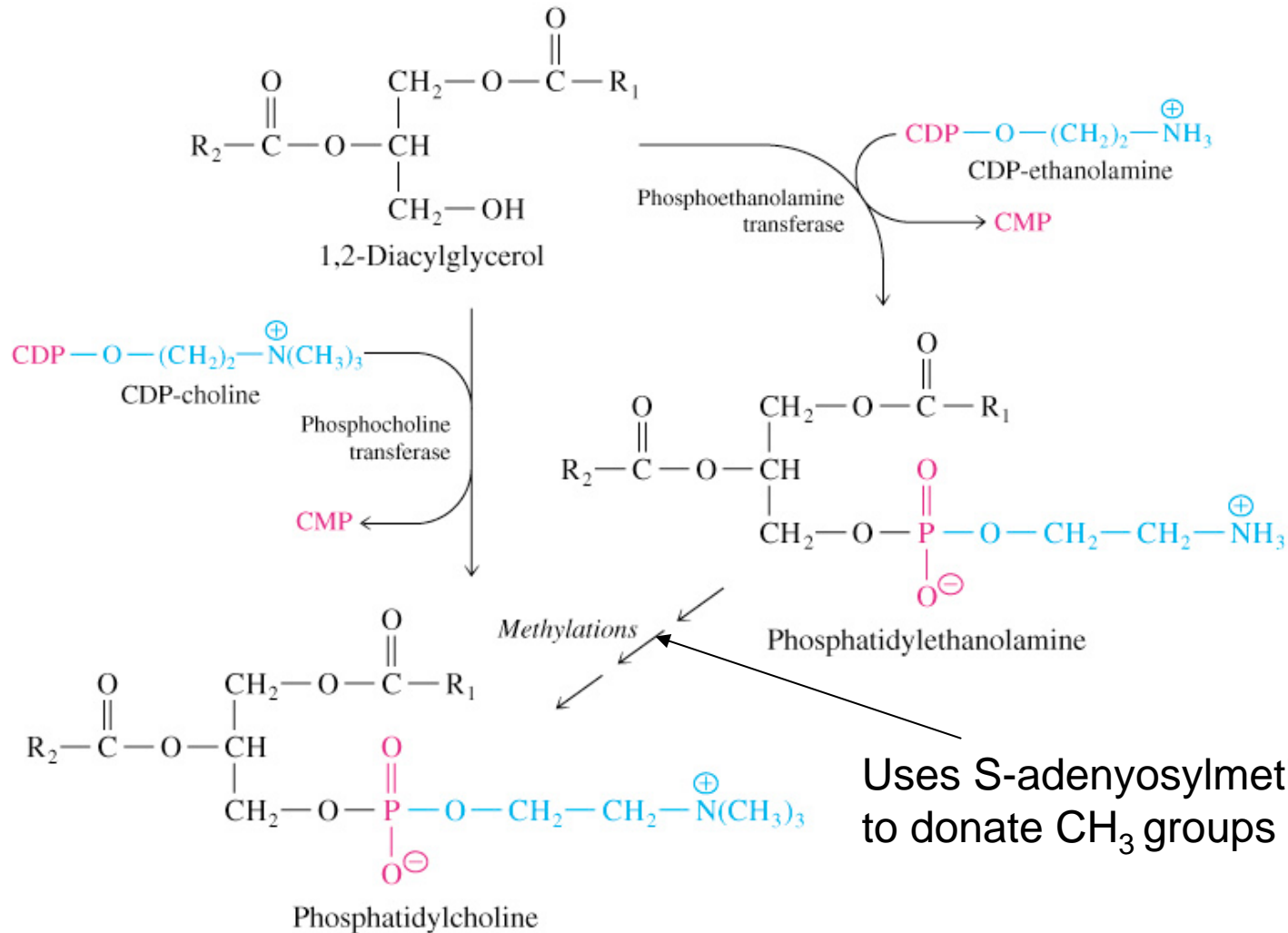
Synthesis of neutral phospholipids



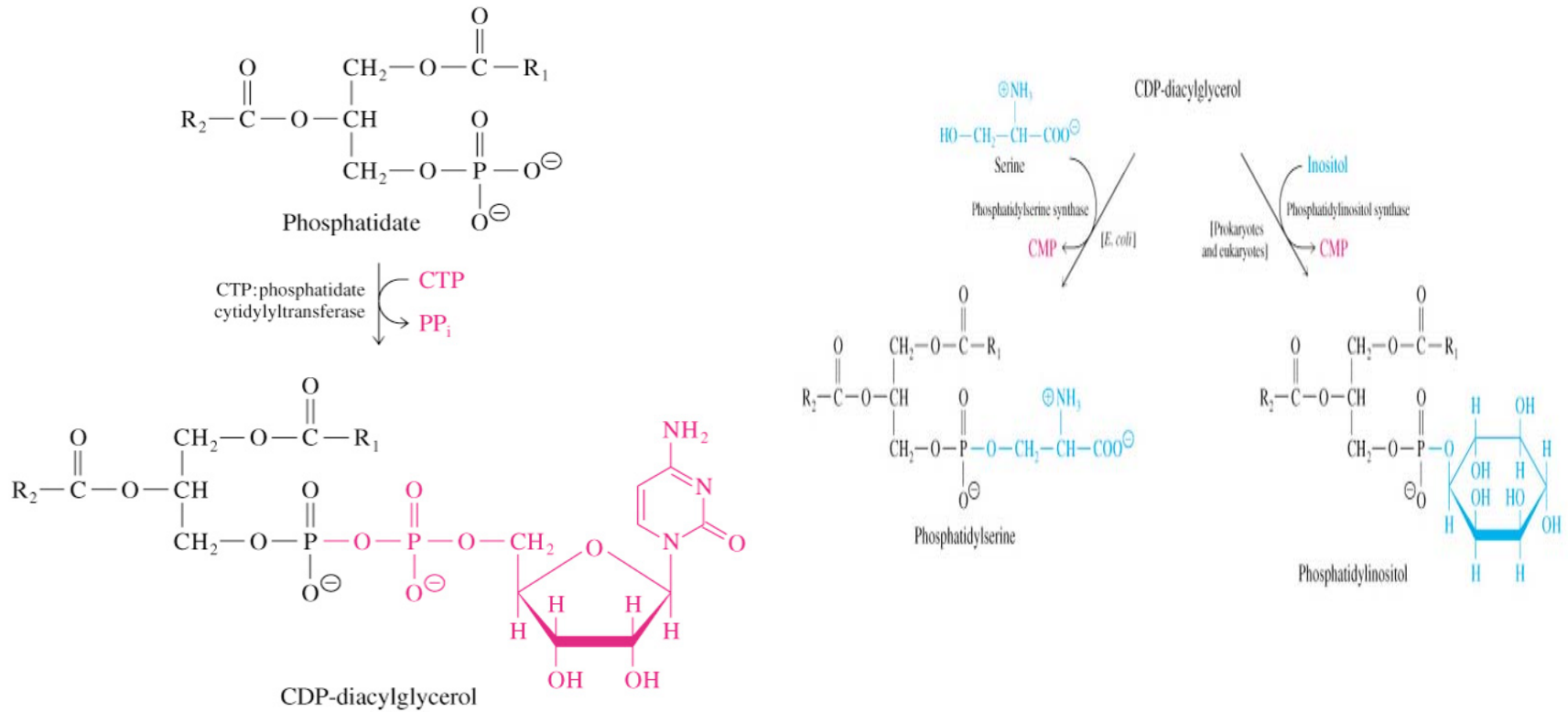
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- Uses CTP for energy
- Activated diacylglycerol
- CDP-diacylglycerol activated intermediate for synthesis

Synthesis of phospholipids



Synthesis of acidic phospholipids



(Continued next slide)

Respiratory distress and Tay-Sachs

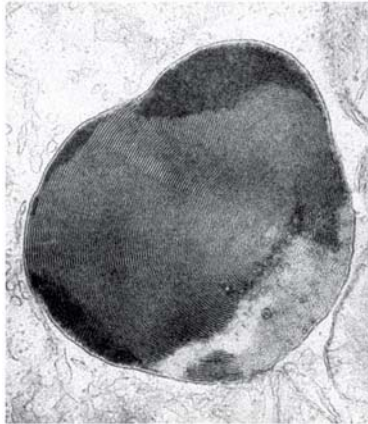
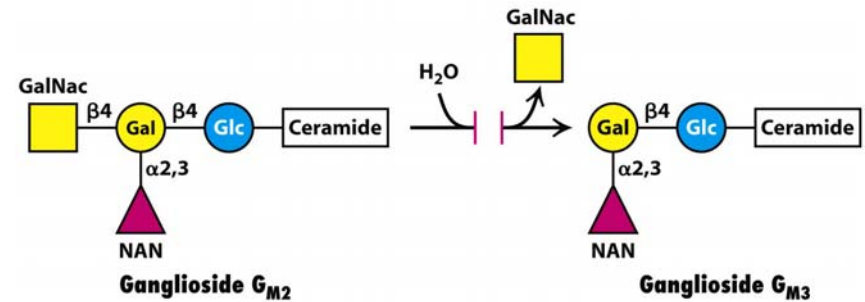


Figure 26-5
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- Respiratory distress: lack of dipalmitoyl phosphatidylcholine found in extracellular fluid in aveoli. Function to decrease surface tension to prevent lung collapse.
- Tay-Sachs: lack of hexoseaminidase A, slows lipid degradation inside lysosomes. Neurons are affected.