Energetics:
During synthesis of complex lipids, compounds with a high group-transfer potential donate their activated groups to a substrate, yielding products with a low group-transfer potential. Energy-rich donors in lipid metabolism include acyl-CoA and CDP-derivatives. In lipid metabolism, the products are low-energy oxygen esters, amides, or phosphodiesters.

Synthesis of Glycerolipids: phosphatidate, phosphatidylinositol, phosphatidylglycerol & cardiolipin

Glycerophospholipid Biosynthesis

Consider a generic glycerophospholipid:

If "X" is
- choline
- ethanolamine
- serine
- inositol
- inositol-P
- inositol bis-P
- glycerol-phosphatidic acid

Phospholipid is
- Phosphatidylcholine (PC)
- Phosphatidylethanolamine (PE)
- Phosphatidylserine (PS)
- Phosphatidylinositol (PI)
- Phosphatidylinositol- P (PIP)
- Phosphatidylinositol bis-P (PIP2)
- Diphosphatidylglycerol (Cardiolipin)
A. Phosphatidate and cytidine nucleotide derivatives are key precursors in the biosynthesis of glycerolipids. (Minor exceptions are plasmalogens and platelet activating factor, where precursor is 1-O-alkyl, 2-acyl-glycerol-P instead of 1,2 diacyl-glycerol-P.)

B. Conversion of PA to other phospholipids involves "activation" of various intermediates by CTP. (See Fig 12-1, p 175; 12-2, p 176; 12-3, p 178 (salvage)) Other de novo pathways include synthesis of PC from PE in liver (Fig 12-4, p 179), the interconversion of PE and PS in the ER via "base exchange" (Fig 12-5), and the mitochondrial decarboxylation of PS to form PE (Fig 12-5).

C. The fatty acid at position 2 on the glycerol moiety is usually unsaturated, often a C20, polyunsaturated F.A. (e.g., arachidonate) removed by Phospholipase A2, leaving a glycerophospholipid. In platelet activating factor, the position 2 substituent is an acetyl group.

D. The fatty acid at position 1 on glycerol is replaced by an O-alkyl group in platelet activating factor and by an O-alkenyl group in plasmalogens.

E. Carbons in the glycerol moiety are denoted by sn (stereochemical numbering) notation. P—X is attached at sn3.

F. Phospholipases hydrolyze bonds as follows:
   A1 ...... ester linkage at sn1
   A2 ...... ester linkage at sn2
   C ...... ester bond between glycerol and phosphate (at sn3)
   D ...... ester bond between phosphate and "X"

A1 and A2 are important in "remodeling" phospholipids, allowing replacement of fatty acids with others having different properties (e.g., fluidity); they work in concert with acyltransferases. Cleavage of PIP2 by phospholipase C (Fig 12-6, p 180) leads to mobilization of intracellular Ca** by IP3 (inositol trisphosphate) and to activation of Protein kinase C by diglyceride. Release of C20 polyunsaturated fatty acids by A2 leads to formation of prostaglandins and thromboxanes (via cyclooxygenase) and of leukotrienes (via lipooxygenase).

Phosphatidate and cytidine nucleotide derivatives are key precursors in the biosynthesis of glycerolipids. Phosphatidate reacts with CTP to form CDP-diglyceride and PPI. CDP-diglyceride is the activated form of phosphatidate. CDP-diglyceride is a prominent intermediate in the biosynthesis of phosphatidylinositol, phosphatidylglycerol, and cardiolipin.

CDP-ethanolamine and CDP-choline are activated phosphate esters that participate in the biosynthesis of complex lipids. When phosphatidyl-choline is made from phosphatidyl-ethanolamine and/or phosphatidylethanolamine is made from phosphatidylserine, the pathway is a de novo pathway. When ethanolamine and choline are the starting compounds of the metabolic pathways, the pathways are called salvage pathways.
Metabolism of ethanolamine, choline and serine derivatives: Phosphatidylethanolamine is a minor constituent of membranes but an important precursor of phosphatidylethanolamine. Phosphatidylethanolamine can be converted to phosphatidylcholine (in liver) by three successive methylation reactions. The activated methyl donor is S-adenosylmethionine (AdoMet). AdoMet is synthesized from methionine and ATP (type iv reaction of ATP). During this synthesis, the amino group of phosphatidylethanolamine reacts in succession with three molecules of AdoMet to form the mono-, di- and tri-methyl (choline) derivatives. Phosphatidylserine is made in an exchange reaction involving phosphatidylethanolamine. Phosphatidylserine can undergo a decarboxylation reaction to produce phosphatidylethanolamine. This decarboxylation reaction is exergonic and unidirectional.

Metabolism of Phosphatidylinositol Bisphosphate (PIP$_2$): Phosphatidylinositol derivatives play an important role in metabolic regulation and signal transduction (when extracellular substances influence intracellular processes). Phosphatidylinositol 4,5-bisphosphate is a key metabolite in signal transduction. It is converted into 2 other second messengers, diglyceride and inositol 1,4,5-trisphosphate, through the action of phospholipase C. Text p 180 Fig. 12-6

Synthesis of PIP$_2$ is cyclic. The synthesis pathway is divided into a lipid cycle and an inositol phosphate cycle. In the lipid cycle, diglyceride is converted to CDP-diglyceride in two reactions. CDP-diglyceride reacts with inositol to form phosphatidylinositol and CMP. In the inositol phosphate portion of the cycle, phosphatidylinositol undergoes two successive phosphorylation reactions with ATP as the phosphoryl donor and to regenerate PIP$_2$. Text p181, Fig. 12-7.

SPHINGOLIPIDS-SYNTHESIS: There are three general classes of sphingolipids: sphingomyelin, cerebrosides and gangliosides. These three classes have different substituents attached to the C$^1$-hydroxyl group of sphingosine. Sphingomyelin contains phosphocholine. Cerebrosides contain a monosaccharide and gangliosides contain an oligosaccharide. Ceramide is an important precursor or intermediate in the formation of sphingolipids.
Ceramide is synthesized from palmitoyl-CoA and serine (p.182, Fig. 12-8). The 1st step is catalyzed by 3-ketosphinganine synthase (PLP). This is a unidirectional exergonic reaction forming 3-ketosphinganine from serine and palmitoyl-CoA. In the 2nd step, 3-ketosphinganine reductase catalyzes the reduction of 3-ketosphinganine to sphinganine. In the 3rd step, a transferase adds a fatty acid to the amino group of sphinganine to form N-acylshinganine. The 4th step, catalyzed by a dehydrogenase, produces ceramide from N-acylshinganine.

Sphingomyelin synthesis: Conversion of ceramide to sphingomyelin is isoergonic. Choline from phosphatidylcholine is transferred to the C1-hydroxy group of ceramide to form sphingomyelin.

Cerebroside synthesis: Cerebrosides and gangliosides contain carbohydrate linked to the terminal alcohol group of ceramide via a glycosidic bond. The donors of the carbohydrates are UDP-sugars. The reaction is exergonic and unidirectional (p. 183, Fig. 12-10). The pathway for the biosynthesis of some gangliosides is similar. Activated sugars are sequentially transferred to the carbohydrate portion of the cerebroside forming gangliosides.

Phosphoadenosylphosphosulfate (PAPS): PAPS undergoes reaction with substrates that yield low-energy sulfate esters. The loss of the high-energy bond makes these processes exergonic. The product of the sulfuryl transfer reactions (3’-phosphoadenylylate) undergoes an exergonic hydrolysis to give AMP. The role of PAPS in the sulfation of sphingolipids is illustrated (p 185, Fig. 12-13).

Active sulfate: Sulfate esters formed from alcohol and sulfate occur in sphingolipids. The donor of sulfate in the biosynthetic reactions is 3’-phosphoadenosine-5’-phosphosulfate (PAPS). PAPS has an extraordinarily high energy bond between the sulfate and phosphate groups. PAPS is synthesized in 2 steps. In step one, ATP and sulfate combine to form the mixed anhydride, adenosylphosphosulfate. Adenosylphosphosulfate reacts with ATP to form PAPS and ADP in an exergonic kinase reaction.

N-acetylhexosamine synthesis: The precursor for N-acetylhexosamines is fructose 6-phosphate with an amido group transferred from glutamine to form glucosamine 6-phosphate. Glucosamine 6-phosphate is acetylated by acetyl-CoA to form N-acetylglucosamine 6-phosphate. N-acetylglucosamine 6-phosphate undergoes an isomerization to form N-acetylglucosamine 1-phosphate. N-acetylglucosamine 1-phosphate is uridylated by UTP to form UDP-GlcNAc. UDP-GlcNAc undergoes epimerization to form UDP-ManNAc which is hydrated and finally phosphorylated to form N-acetylmannosamine 6-phosphate.

N-acetylneuraminate is an acetylated 9-carbon carbohydrate derivative common to sphingolipids and glycoproteins. It is synthesized from N-acetylmannosamine 6-phosphate and phosphoenolpyruvate which react together to form N-acetylneuraminic 9-phosphate. This compound is dephosphorylated to form N-acetylneuraminic. N-acetylneuraminic combines with CTP to form an activated compound, CMP-N-acetylneuraminic. CMP-N-acetylneuraminic is the universal donor of N-acetylneuraminic with a high energy bond sufficient to promote group transfer.

Sphingolipidoses: These diseases are typically due to enzyme deficiencies in the pathways needed for the breakdown of gangliosides. The accumulation of these metabolic intermediates can cause severe disease. Page 188, Fig. 12-16.
Cholesterol synthesis: Cholesterol is made from acetyl-CoA. The first step in synthesis is the condensation of 3 acetate units to form mevalonate. The synthesis of mevalonate is catalyzed by 3 enzymes:

1. Thiolase
2. HMG-CoA synthase
3. HMG-CoA reductase

The rate-limiting reaction in cholesterol biosynthesis is catalyzed by HMG-CoA reductase. Mevalonate, formed by the HMG-CoA reductase reaction undergoes 2 successive phosphorylation reaction involving ATP. The products include 5-phophomevalonate then 5-pyrophosphomevalonate and two ADP molecules. Condensation of isoprenoid precursors yields geranyl pyrophosphate which condenses with isopentenyl pyrophosphate to yield farnesyl pyrophosphate. Two molecules of farnesyl pyrophosphate condense to form squalene. Squalene reacts with molecular oxygen and undergoes an epoxidation and ring closures to form lanosterol. Lanosterol is converted to cholesterol by removal of three methyl groups, reduction of a double bond and isomerization. Three molecules of ATP are required to make each isoprenoid unit. Six isoprenoid units are used to synthesize cholesterol, so 6 x 3 = 18 ATP/cholesterol molecule.

Cholesterol is the precursor of steroid hormones, bile salts, and neutral sterols. Humans are unable to degrade completely the steroid ring to carbon dioxide and water. Animals lack enzymes that catalyze break down of steroid rings. Because of this, cholesterol cannot be degraded to produce metabolic energy and excessive cholesterol results in disease. The only way to rid the body of excess cholesterol is via excretion of cholesterol, neutral sterols, and bile salts in the feces.

Cholesterol is synthesized by liver & secreted in bile in one of three forms: biliary cholesterol, bile acids, or cholesteryl esters.

Bile acids and their salts are relatively hydrophilic cholesterol derivatives. Humans synthesize primary bile salts. Secondary bile salts result from intestinal bacterial metabolism of primary bile salts. Cholesteryl esters are formed in the liver through the action of acyl-CoA-cholesterol acyl transferase. This enzyme catalyzes the transfer of a fatty acid for coenzyme A to the hydroxyl group of cholesterol. Cholesteryl ester is more hydrophobic. It is transported in lipoprotein particles to other tissues that use cholesterol or stored in the liver. Cholesterol, bile & cholesteryl ester emulsify dietary fat. See Fig. 12-21 & 12-22, pp. 192 & 193.
LIPOPROTEIN- SYNTHESIS & TRANSPORT: Because lipid is not soluble in aqueous solution, it must be transported through the bloodstream. An elaborate protein transport system has evolved to complete this important function. These proteins can be separated in two groups: 1. proteins that physically complex with lipid to form one of 5 types of transport particles, and 2. enzymes that breakdown the lipoprotein transport particles.

Lipoprotein particles perform three major functions: 1. Transport dietary fat from the intestinal mucosal to other tissues (exogenous lipid transport); 2. Transfer triglyceride and cholesterol from liver to other tissues (endogenous lipid transport); and 3. Transfer cholesterol from extrahepatic tissues to the liver (reverse cholesterol transport). Lipoprotein particles form 5 major classes:

<table>
<thead>
<tr>
<th>Major Classes of Human Plasma Lipoproteins:</th>
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<tbody>
<tr>
<td>Lipoprotein</td>
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<tr>
<td>--------------</td>
</tr>
<tr>
<td>Chylomicron</td>
</tr>
<tr>
<td>LDL</td>
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<tr>
<td>HDL</td>
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The proteins incorporated into the particles have a variety of functions-see Table 12-3, p195.
Enzymes that breakdown the lipoprotein transport particles—
1. **Lipoprotein lipase** (heparin-sensitive lipase): catalyzes the hydrolysis of triglyceride in VLDL and chylomicrons. This enzyme is on the surface of the capillary lumen. It generates fatty acids and glycerol.
2. **Hepatic lipase**: catalyzes the hydrolysis of triglyceride and phospholipids in HDL and IDL. It is found in liver sinusoids.
3. **Acid lipase**: catalyzes the hydrolysis of triglyceride and cholesteryl ester in lysosomes. Acid lipase participates in the catabolism of lipoproteins that are taken up by receptor-mediated endocytosis.
4. **LCAT** catalyzes the transfer of the C-2 fatty acyl group of phosphatidylcholine (lecithin is a common name for phosphatidylcholine) to cholesterol to produce cholesteryl ester and lysolecithin. This reaction converts cholesterol from a polar molecule to a non-polar, very hydrophobic ester.

Properties of lipoprotein particles:
**Chylomicrons** are large complexes that are formed in the mucosal epithelial cells of the small intestine. They enter the blood from the lymphatics through the thoracic duct. Their main function is to transport dietary fat (mostly triglyceride, some cholesterol and cholesteryl ester). The triglyceride is hydrolyzed by lipoprotein lipase and fatty acids enter cells. Glycerol liberated in the extracellular space can be metabolized in cells that contain glycerol kinase (liver & kidney). As triglyceride is hydrolyzed, chylomicrons grow smaller, becoming remnants that contain cholesterol, cholesteryl ester, apo-B-48 and apo-E. The remnants are removed from blood by the liver in an apoE-receptor driven process. In the liver the remnants are digested by lysosomal lipase to yield cholesterol and fatty acids.

**VLDL**: The major function of VLDL is to transport large amounts of triglyceride and small amounts of cholesterol from the liver to other tissues. When the diet contains more fatty acids than are needed immediately as fuel, they are converted into triacylglycerols in the liver and packaged into VLDL particles. Excess dietary carbohydrate can also be converted into triacylglycerols in the liver and exported as VLDLs. VLDLs contain some cholesterol, cholesteryl esters, apoB-100, apoC-I, apoC-II, ApoC-III, and apo-E. They are transported from the liver to muscle and adipose tissue where activation of lipoprotein lipase by apoC-II causes the release of free fatty acids from triglycerols. Most VLDL remnants are removed from blood by hepatocytes in an apoE-receptor driven process.

**IDL & LDL**: The major function of IDL & LDL is to transport large amounts of triglyceride and small amounts of cholesterol from the liver to other tissues. The loss of triglycerides from VLDL particles converts the particles into remnants of intermediate density called IDL. IDL particles typically lack apo-C protein. The amount of triglyceride and cholesterol in IDL is intermediate between VLDL & LDL. Further removal of triglyceride converts the lipoprotein particles to LDL. LDL particles typically lack apoE. LDL contains most of the cholesterol in the plasma after an overnight fast and 75% is in the form of cholesteryl ester. ~1/2 of LDL
is taken up by the liver and the remainder by extrahepatic tissues. LDL particles are taken up by apoB-100 receptors or by apoE receptors.

**HDL:** is synthesized in the liver and small intestine as protein-rich particles that contain relatively little cholesterol and no cholesteryl esters. HDLs contain apoA-1, apoC-1, apoC-II, LCAT, and more. LCAT on the surface of newly formed HDL particles converts the cholesterol and phosphatidyl choline of chylomicron and VLDL remnants to cholesteryl esters. These more hydrophobic molecules migrate to the core of the HDL particle from a disk to a spherical shape. These cholesteryl-rich HDL particles are taken up by the liver where the cholesterol is unloaded. HDL may be taken up in the liver by receptor-mediated endocytosis. A second receptor mediated process, HDL takes up cholesterol and selectively transfers it to hepatocytes.

**Lipoprotein Receptors:**

**LDL receptor:** recognizes both apo-B-100 and apo-E. The LDL receptor binds and removes LDL & IDL but NOT VLDL from plasma. Binding of LDL or IDL particles to the receptor protein causes localization within coated-pits and subsequent endocytosis. The coated-vesicles fuse with lysosomes. The receptor is recycled to the cell surface and cholesteryl ester is hydrolyzed to form cholesterol that is released into the cytosol. Intracellular cholesterol causes lower levels of LDL receptor and reduced synthesis of HMG-CoA reductase. These lead to reduced uptake and synthesis of cholesterol.

**The Chylomicron Remnant Receptor:** This receptor is only expressed by liver cells and recognizes apo-E. This receptor transports the dietary triglycerides and cholesterol remaining in the chylomicron remnants into hepatocytes.

Hypercholesterolemias/hyperlipoproteinemia cause premature atherosclerotic disease. Primary hyperlipoproteinemia is due to one of several defects in the LDL receptor. It is autosomal dominant and affects 1/500 people. Secondary hyperlipoproteinemia results from other disorders such as diabetes mellitus.

**Plasma lipoproteins and lipid transport details** *(Figs 12-25 & 12-26, p 196; Fig 12-27, p 197; Fig 12-29, p 200)*

- **Chylomicrons:** carry triglyceride from intestinal mucosa to extrahepatic cells (& remnants to liver). Main apoprotein: B48, acquires CII from HDL to allow activation of lipoprotein lipase.
- **VLDL (very low density lipoproteins):** carry triglyceride from liver to extrahepatic cells; converted to LDL (intermediate density lipoprotein) by unloading some TG cargo. Main apoprotein: B100, longer version of B48 (due to alternative splicing of mRNA).
- **LDL (low density lipoprotein) (= "bad" cholesterol):** delivers cholesterol to extrahepatic tissues; formed from LDL following unloading of more TG cargo; main apoprotein: B100, necessary for binding to LDL receptor at both liver and extrahepatic cells.
- **HDL (high density lipoproteins) (= "good" cholesterol):** originates from both liver and intestine, carries extrahepatic cholesterol to liver for disposal via conversion to bile salts; main apoprotein: A1, necessary for activation of LCAT (lecithin: cholesterol acyltransferase), used in formation of cholesteryl esters.

**STEROID BIOSYNTHESIS:**

All steroid hormones are synthesized from pregnenolone. Pregnenolone is first converted to progesterone and subsequently to cortisol, corticosterone & testosterone. A second synthesis pathway can make testosterone without a progesterone intermediate.

The conversion of cholesterol to pregnenolone is rate-limiting in steroid hormone biosynthesis. Hydroxylation reactions play a very important role in the synthesis of cholesterol from squalene and in the conversion of cholesterol into steroid hormones and bile salts. All these hydroxylations require NADPH and O2. One oxygen atom from O2 goes to the substrate and the second is reduced to H2O. The enzymes catalyzing these reactions are monoxygenases. All hydroxylation reactions during steroid biosynthesis are catalyzed by mixed-function oxidases that use NADPH, O2, and mitochondrial cytochrome P-450.

The second synthetic step in the synthesis of pregnenolone is catalyzed by the enzyme, desmolase.

**Structures:**

- Estradiol: 18 carbon atoms and aromatic A ring.
- Testosterone: 19 carbon atoms
Progesterone, aldosterone, and cortisol contain 21 carbon atoms. Aldosterone contains an aldehyde group on C\textsuperscript{18}. Glucocorticoids contain a hydroxyl group on C\textsuperscript{11}.

Synthesis of progesterone, aldosterone and cortisol:

**Progesterone** - 2 steps: 1. a 3\textbeta-alcohol dehydrogenase catalyzed the NAD\textsuperscript{+}-dependent oxidation of alcohol to a ketone& 2. double bond migration (Fig. 12-31).

**Aldosterone** - 4 steps: catalyzed by ER enzyme 21-hydroxylase and mitochondrial enzymes: 11\beta-hydroxylase, 18-hydroxylase, and 18-hydroxysteroid oxidase. All 4 reactions require NADPH, O\textsubscript{2}, and cytochrome P-450.

**Cortisol** - 3 steps: Catalyzed by 17\alpha- and 21-hydroxylases and a mitochondrial 11\beta-hydroxylase. All 3 reactions require NADPH, O\textsubscript{2}, and cytochrome P-450.

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**EICOSANOIDs**

Eicosanoids (Greek eikosi, "twenty"): derived from the 20-carbon saturated fatty acid, arachidonic acid, & synthesized in almost all cells. The following are different types of eicosanoids: prostaglandins (5-carbon ring), thromboxanes (6-membered ring containing an ether), and leukotrienes (3-conjugated double bonds). Eicosanoids are paracrine hormones, meaning that they act only on cells near the point of synthesis instead of being transported in the blood to act on cells in other tissues or organs. They are involved in reproductive function, inflammation, fever, blood clot formation, regulation of blood pressure, gastric secretion, smooth muscle contraction and more. Eicosanoids are not stored in cells but synthesized on demand with lifetimes of ~1 minute.

Eicosanoids can be placed in one of 2 divisions: 1.) cyclic prostainglandins and their derivatives, protacyclins and thromboxanes and 2.) linear leukotrienes. The cyclic and linear pathways for biosynthesis are in Fig. 12-33 (p 205).

Synthesis: The first step in the metabolism of prostaglandins is the generation of arachidonate from phospholipids. This is catalyzed by phospholipase A2 and is the rate-limiting reaction in the pathway of eicosanoid biosynthesis. This hydrolysis is unidirectional and exergonic.
Prostaglandin biosynthesis: In a reaction catalyzed by cyclooxygenase, arachidonate reacts with 2 molecules of oxygen to form PGH$_2$. PGH$_2$ is a precursor that can be used to synthesize the other prostaglandins, protacyclins, and thromboxanes.

**NSAIDS inhibit synthesis of prostaglandins, protacyclins, & thromboxanes by inhibiting the enzyme, cyclooxygenase.** Cyclooxygenase is bound to the membranes of the endoplasmic reticulum.

Conversion of PGH$_2$ to PGE$_2$ involves an isomerization reaction in which the hydrogen linked to C$^9$ adds to the oxygen on C$^{11}$ to form an alcohol and the other oxygen of the peroxide forms a double bond with carbon to make a ketone.

PGF$_{2\alpha}$ synthesis involves a reduction of the two peroxide oxygen atoms to 2 alcohol groups.

Arterial walls contain prostacyclin synthase, an enzyme that catalyzes the conversion of PGH$_2$ to prostacyclin with a new 5-membered oxygen-containing ring. This reaction involves the formation of an ether bond linking C$^9$ and C$^6$.

The Linear Lipoxygenase Pathway—synthesis of leukotrienes—Lipoxygenases catalyze the insertion of oxygen in the 5, 12, or 15 position of the various eicosanoids. The products are hydroperoxyeicosatetraenoates or HPETEs. 5-HPETE is the precursor of leukotrienes. It undergoes sequential hydrolysis reactions to form many leukotrienes. Dehydration of 5-HPETE yields leukotriene C$_4$. Leukotriene C$_4$ undergoes hydrolysis to form D$_4$. These hydrolysis reactions are exergonic and unidirectional.

**PLASMALOGENS & PLATELET ACTIVATING FACTOR SYNTHESIS:** Plasmalogens are phosphoglycerolipids that contain an ether bond at sn-1 and phosphoethanolamine or phosphocholine at sn-3. Plasmalogens are in the membranes of brain, heart, erythrocytes, and other tissues. Plasmalogens make up about 20% of the phospholipid in human nervous tissue. The pathway for biosynthesis begins with the exergonic acylation of dihydroxyacetone phosphate (Fig. 12-37) to form 1-acyl-dihydroxy-acetone phosphate. An ether is then formed when a long chain alcohol replaces the acyl group. Four additional steps catalyzed the addition of a fatty acid to sn-2 and formation of a phosphoethanolamine or phosphocholine ester bond at sn-3.

**PLATELET ACTIVATING FACTOR (PAF)** is an ether-containing phospholipid that causes platelet degranulation. It also acts on muscle, liver, kidney and brain. PAF is released during inflammatory and allergic responses. PAF is unusual in that it has an acetyl ester at sn-2 rather than a FA. It is synthesized from a plasmalogen intermediate, 1-alkyl-2-acylglycerol-3-phosphocholine. Phospholipase A2 catalyzes the hydrolysis of this compound to form 1-alkyl-2-acylglycerol-3-phosphocholine. Subsequent acylation forms PAF.