Lipid metabolism.

ASSOC. PROF.
BILETS M.V.

Lecture plan

Lipoproteins.

Catabolism of triacylglycerols in adipocytes of adipose tissue.

Biosynthesis of triacylglycerols.

Hyperlipoproteinemias.

Oxidation of glycerol: enzyme reactions, bio-energetics.

Oxidation of fatty acids (β-oxidation).

Ketone bodies.

Biosynthesis of fatty acids.

Metabolism of complex lipids.

Biosynthesis of cholesterol.

Pathways of biotransformation of cholesterol.

Pathologies of lipid metabolism

Lipids are organic compounds, are nonpolar molecules, which are soluble only in nonpolar solvents and insoluble in water.

Types of Lipids:

Simple Lipids

Esters of fatty acids with various alcohols. **Fats:** Esters of fatty acids with glycerol. Oils are fats in the liquid state

Steroids (cholesterol)

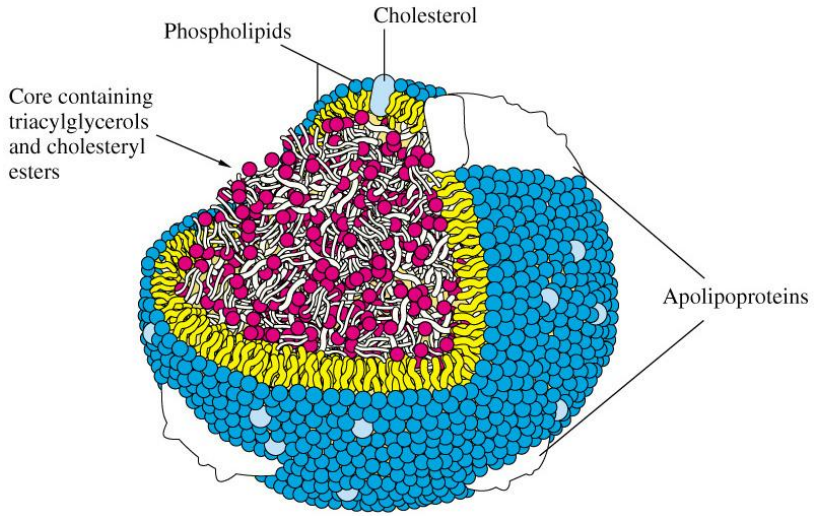
Complex Lipids

Esters of fatty acids containing groups in addition to alcohol and a fatty acid.

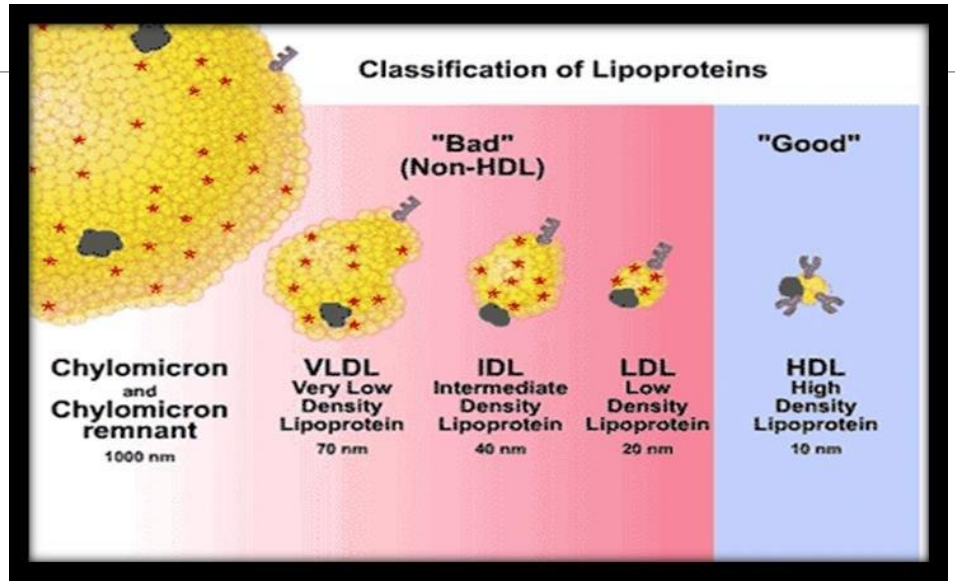
Phospholipids: These are lipids containing, in addition to fatty acids and alcohol, a phosphoric acid residue. They frequently have nitrogen-containing bases and other substituents, eg, in glycerophospholipids the alcohol is glycerol and in sphingophospholipids the alcohol is sphingosine.

Glycolipids (glycosphingolipids): Lipids containing a fatty acid, sphingosine, and carbohydrate.

Lipoproteins



https://www.apsubiology.org/anatomy/2020/2020_Exam_Reviews/Exam_1/CH18_Lipoproteins.htm



https://www.researchgate.net/figure/4-The-major-types-of-lipoproteins-are-chylomicrons-very-low-density-lipoprotein-VLDL_fig4_304525065

Classes of lipoproteins

oprotein	Functions
Chylomicrons	Transport dietary triacylglycerols and cholesterol from intestine to tissues
VLDL	Transports triacylglycerols from liver to tissues
IDL (VLDL remnants)	Picks up cholesterol from HDL to become LDL Picked up by the liver
LDL	Delivers cholesterol into cells
HDL	Picks up cholesterol accumulating in blood vessels Delivers cholesterol to liver and steroidogenic tissues Transfers apolipoproteins to other lipoproteins

https://schoolbag.info/chemistry/mcat_biochemistry/70.html#:~:text=Chylomicrons%20are%20the%20least%20dense,HDL%20(high-density).

Chylomicrons are highly soluble in both lymphatic fluid and blood and function in the transport of dietary triacylglycerol, cholesterol, and cholesteryl esters to other tissues. Assembly of chylomicrons occurs in the intestinal lining and results in a nascent chylomicron that contains lipids and apolipoproteins.

VLDL (VERY-LOW-DENSITY LIPOPROTEIN)

VLDL metabolism is similar to that of chylomicrons; however, VLDL is produced and assembled in liver cells. Like chylomicrons, the main function of VLDL is the transport of triacylglycerol to other tissues. VLDLs also contain fatty acids that are synthesized from excess glucose or retrieved from chylomicron remnants.

IDL (INTERMEDIATE-DENSITY LIPOPROTEIN)

Once triacylglycerol is removed from VLDL, the resulting particle is referred to as either a **VLDL remnant** or **IDL**. Some IDL is reabsorbed by the liver by apolipoproteins on its exterior, and some is further processed in the bloodstream. For example, some IDL picks up cholesteryl esters from HDL to become LDL. IDL thus exists as a transition particle between triacylglycerol transport (associated with chylomicrons and VLDL) and cholesterol transport (associated with LDL and HDL).

LDL (LOW-DENSITY LIPOPROTEIN)

Although both LDL and HDL are primarily cholesterol particles, the majority of the cholesterol measured in blood is associated with **LDL**. The normal role of LDL is to deliver cholesterol to tissues for biosynthesis. However, cholesterol also plays an important role in cell membranes. In addition, bile acids and salts are made from cholesterol in the liver, and many other tissues require cholesterol for steroid hormone synthesis (steroidogenesis).

HDL (HIGH-DENSITY LIPOPROTEIN)

HDL is synthesized in the liver and intestines and released as dense, protein-rich particles into the blood. HDL contains apolipoproteins used for cholesterol recovery—that is, the cleaning up of excess cholesterol from blood vessels for excretion. HDL also delivers some cholesterol to steroidogenic tissues and transfers necessary apolipoproteins to some of the other lipoproteins.

Apolipoproteins

Apolipoproteins, also referred to as **apoproteins**, form the protein component of the lipoproteins described above. Apolipoproteins are receptor molecules and are involved in signaling. While it is highly unlikely that specific functions of each apolipoprotein will be tested on the MCAT, they are briefly summarized below to illustrate their diverse purposes:

- **apoA-I**: activates LCAT, an enzyme that catalyzes cholesterol esterification
- **apoB-48**: mediates chylomicron secretion
- **apoB-100**: permits uptake of LDL by the liver
- **apoC-II**: activates lipoprotein lipase
- **apoE**: permits uptake of chylomicron remnants and VLDL by the liver

Hyperlipoproteinemia

Fredrickson Classification

Type	Synonyms	Lipoprotein Elevation
I (rare)	''Primary hyperlipoproteinemia'', or ''Familial hyperchylomicronemia''	Chylomicrons
IIa	''Polygenic or Familial hypercholesterolemia''	LDL
IIb	''Combined hyperlipidemia''	LDL+VLDL
III (rare)	''Familial dysbetalipoproteinemia''	Chylomicrons+ IDL
IV	''Familial hyperlipemia''	VLDL
V (rare)	''Endogenous hypertriglyceridemia''	VLDL+ Chylomicrons

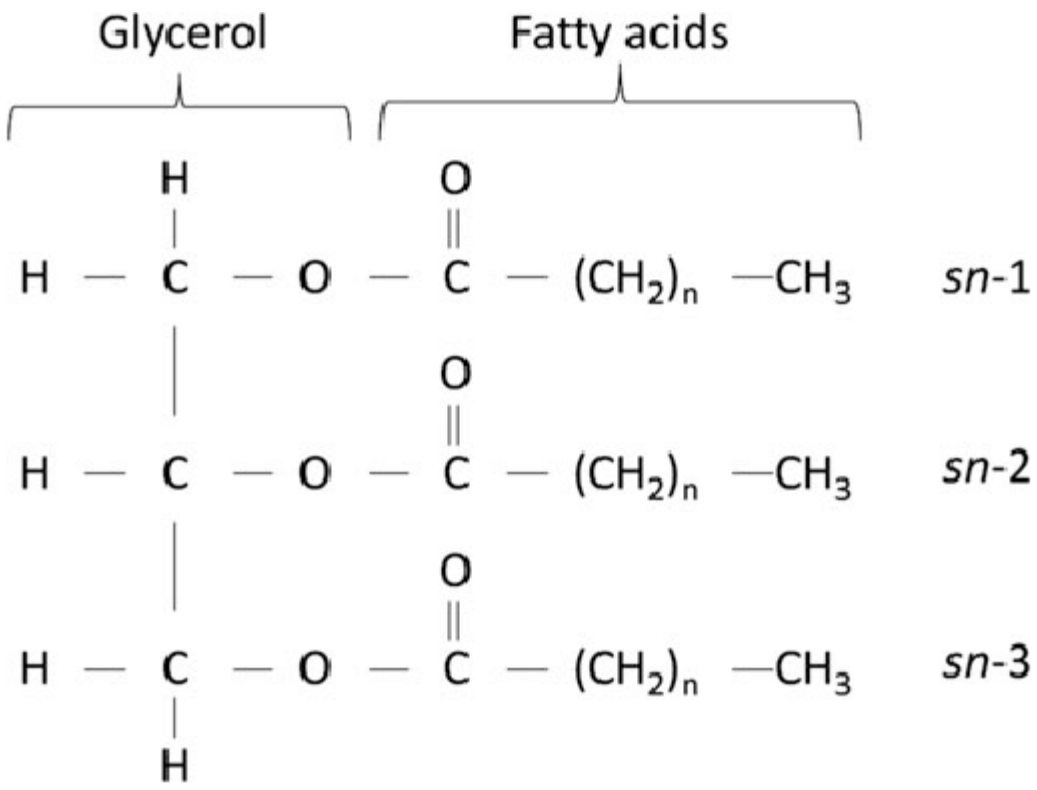
Hereditary Causes of Hyperlipidemia Caused by Known Single Gene Mutations

- Familial Hypercholesterolemia:
  - Occurs in 1 in 500 individuals/ AD.
  - Mutation in LDL receptor, resulting in elevated levels of LDL at birth and throughout life.
  - High risk for atherosclerosis, tendon xanthomas and xanthelasmas of eyes, CHD
- Familial Combined Hyperlipidemia:
  - Autosomal dominant.
  - Increased secretions of LDL& VLDLs.
  - High risk for atherosclerosis, no xanthomas.
- Dysbetalipoproteinemia:
  - Affects 1 in 10,000
  - A binding-defective form of apoE (which usually plays important role in catabolism of chylomicron and VLDL).
  - Increased risk for atherosclerosis, palmar xanthomas, CHD, PVD.

Secondary Causes of Hyperlipidemia

- Hypothyroidism (high LDL)
- NS (high LDL)
- Cholestasis (high LDL)
- Obesity (high TG)
- DM type 2 (high TG & chylomicrons)
- Pregnancy (high TG)
- Sepsis (high TG)
- Stress
- Reduced HDL: smoking, DM2, obesity, malnutrition, B- blockers
- Acute hepatitis (high TG)
- Drugs (thiazide, steroids, B- blockers, cyclosporine, protease inhibitors).
- MM, lymphoma (high TG)
- Glycogen storage disease (high TG).
- Alcohol, interferon, estrogen, thiazide, steroid (high TG).
- Acromegaly, renal failure (high TG).

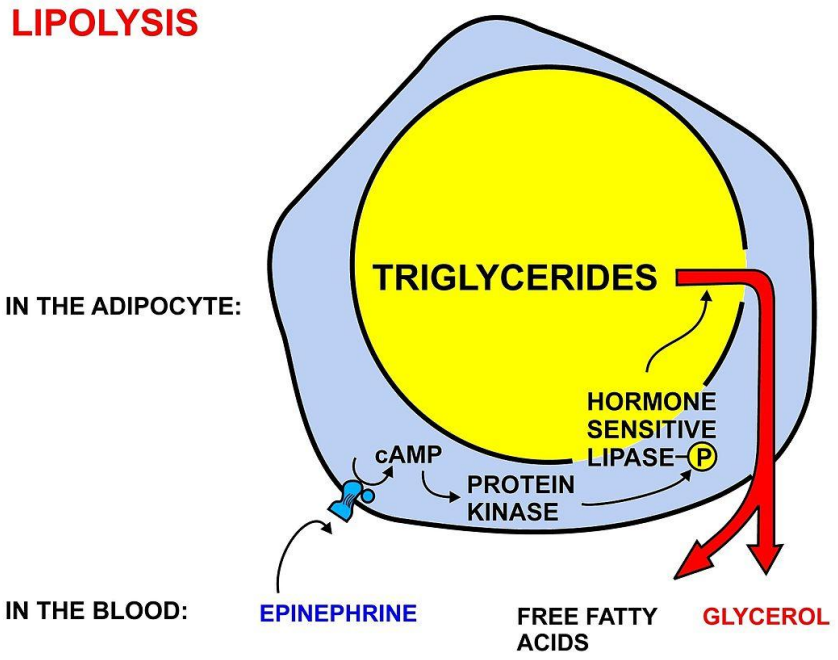
Structure of triacylglycerol



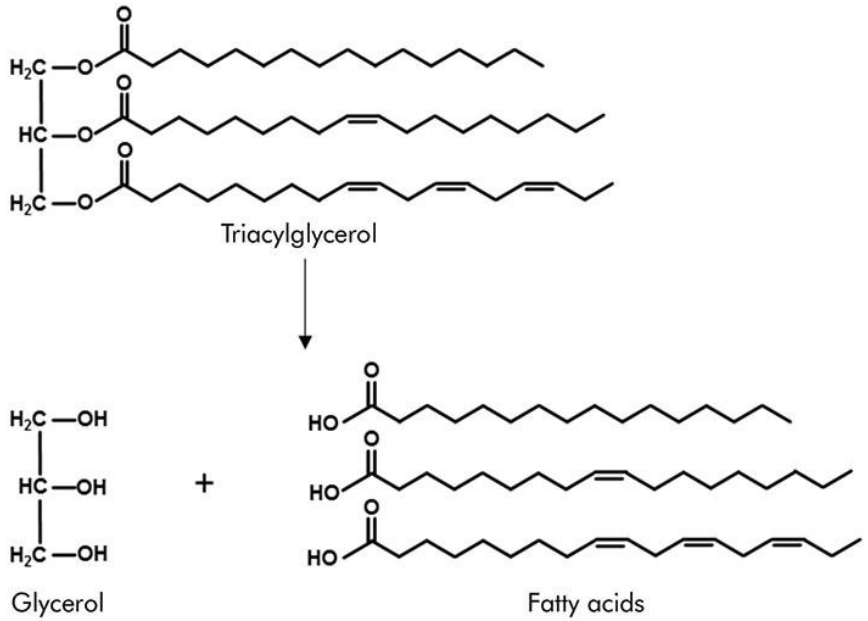
https://www.researchgate.net/figure/Triacylglycerol-TAG-structure-showing-glycerol-with-three-fatty-acids_fig1_316787887

Lipolysis is the metabolic pathway through which lipid triacylglycerols are hydrolyzed into a glycerol and three fatty acids.

Occurs in adipocytes. Lipolysis is induced by glucagon,[1] epinephrine, norepinephrine, growth hormone, cortisol. Lipolysis is activated when: under normal physiological stressful situations - emotional stress, muscle work, fasting,
in pathological conditions - type I diabetes mellitus, other hormonal diseases (hypercortisolism, hyperthyroidism).

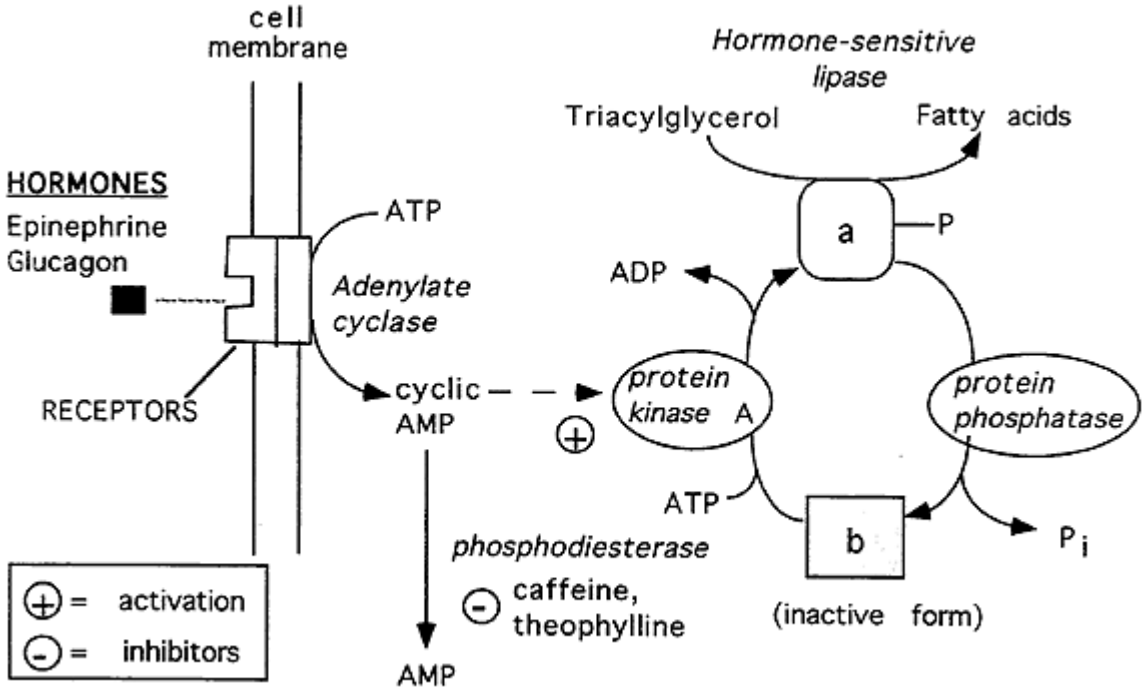


https://en.wikipedia.org/wiki/Lipolysis



https://www.researchgate.net/figure/Triacylglycerol-TAG-structure-showing-glycerol-with-three-fatty-acids_fig1_316787887

Lipolysis regulation



http://www2.csudh.edu/nsturm/CHE452/09_Fat%20Met-RegIntegr.htm

Lipogenesis

Fats not only obtained from the diet but also obtained from lipogenesis in the body. **Lipogenesis** means synthesis of neutral fats (TAG) from CHO and proteins present in excess of body need.

Lipogenesis requires: 1- Synthesis of fatty acids (FA) and glycerol
2- Activation of fatty acids by CoA and glycerol by glycerokinase,
3- the combination of activated fatty acids and activated glycerol

De *no vo* synthesis of fatty acid (cytoplasmic synthesis):

Occur mainly for the synthesis of palmitic acid

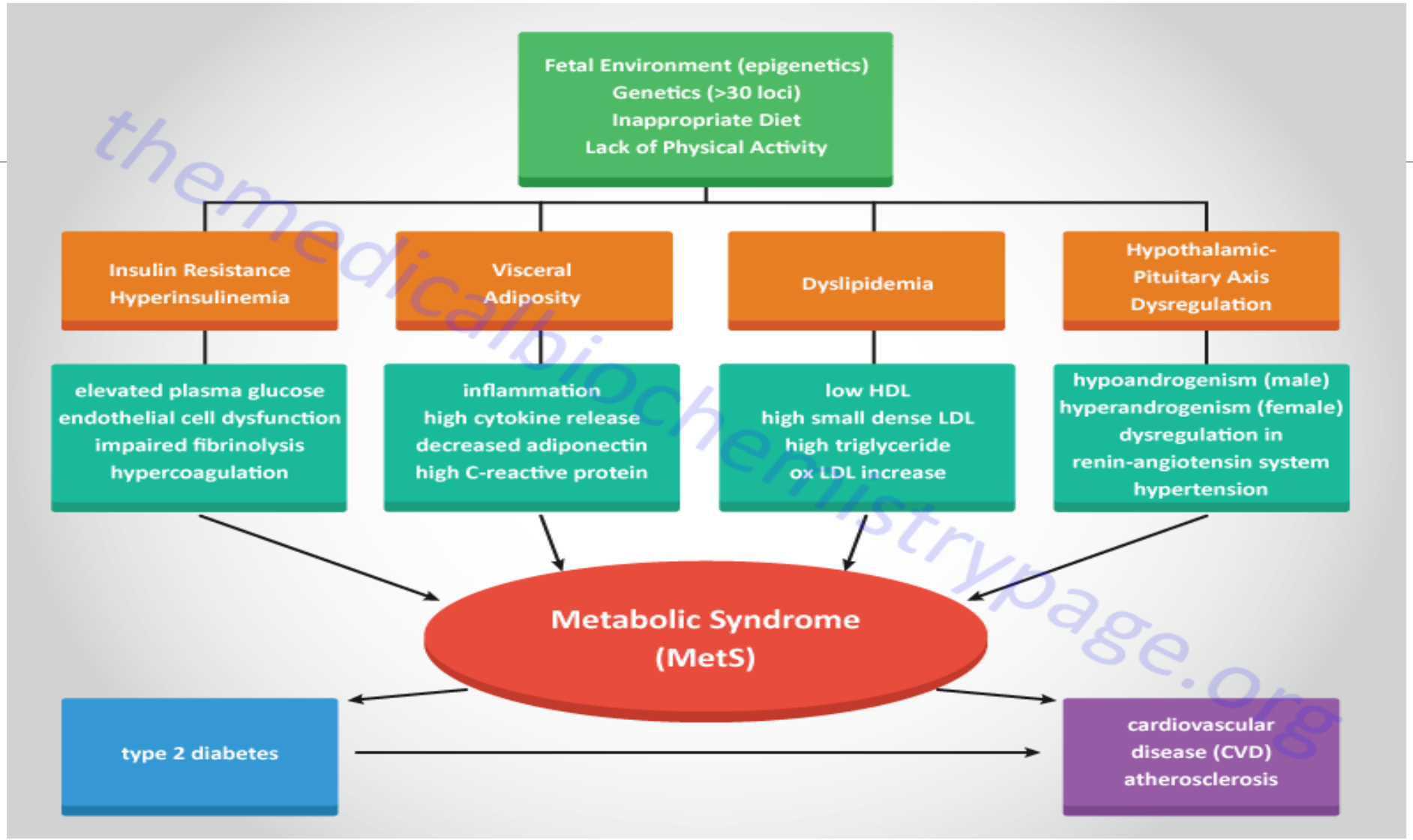
Site: ***Cytoplasm*** of liver, mammary glands and adipose tissues.

https://www.slideserve.com/castor-mills/lipogenesis

Obesity

Obesity is essentially an excessive accumulation of triacylglycerols in fatty tissue that is the net result of excessive energy intake compared to energy usage.
Obesity is diagnosed when your body mass index (BMI) is 30 or higher.
To determine your body mass index, divide your weight in pounds by your height in inches squared and multiply by 703.
Or divide your weight in kilograms by your height in meters squared.

BMI	Weight status
Below 18.5	Underweight
18.5-24.9	Normal
25.0-29.9	Overweight
30.0 and higher	Obesity



http://themedicalbiochemistrypage.org/the-metabolic-syndrome-mets/

Glycerol Oxidation

95% of the energy in a fatty acid is derived from the oxidation of acetyl-CoA

5% from glycerol

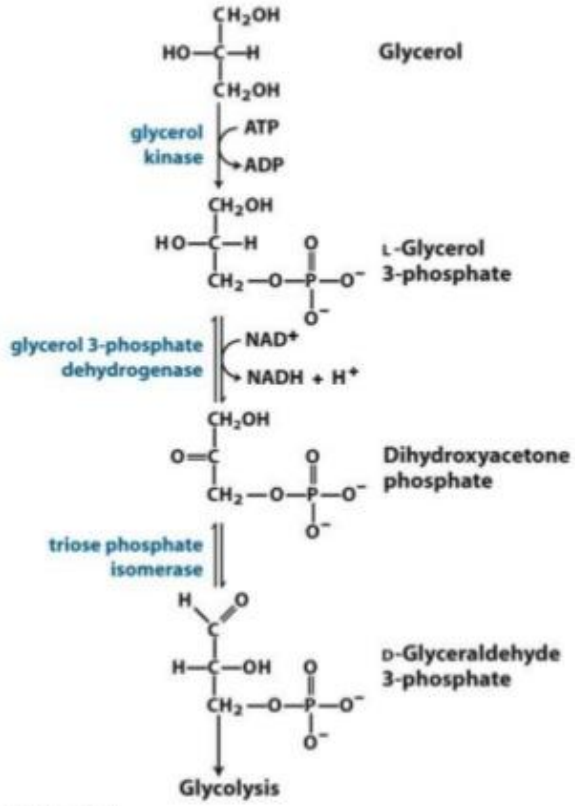


Figure 17-4
Lehninger Principles of Biochemistry, Fifth Edition

https://www.slideshare.net/obanbrahma/beta-oxidation-protein-catabolism-57804497

β oxidation of fatty acids

The **β oxidation** of long-chain fatty acids to acetyl-CoA is a central energy-yielding pathway. The electrons removed during fatty acid oxidation pass through the mitochondrial respiratory chain, driving ATP synthesis, and the acetyl-CoA

produced from the fatty acids may be completely oxidized to CO_2 via the citric acid cycle, resulting in further energy conservation. **β oxidation**, by which fatty acids are converted into acetyl-CoA.

The enzymes of fatty acid oxidation are located in the mitochondrial matrix.

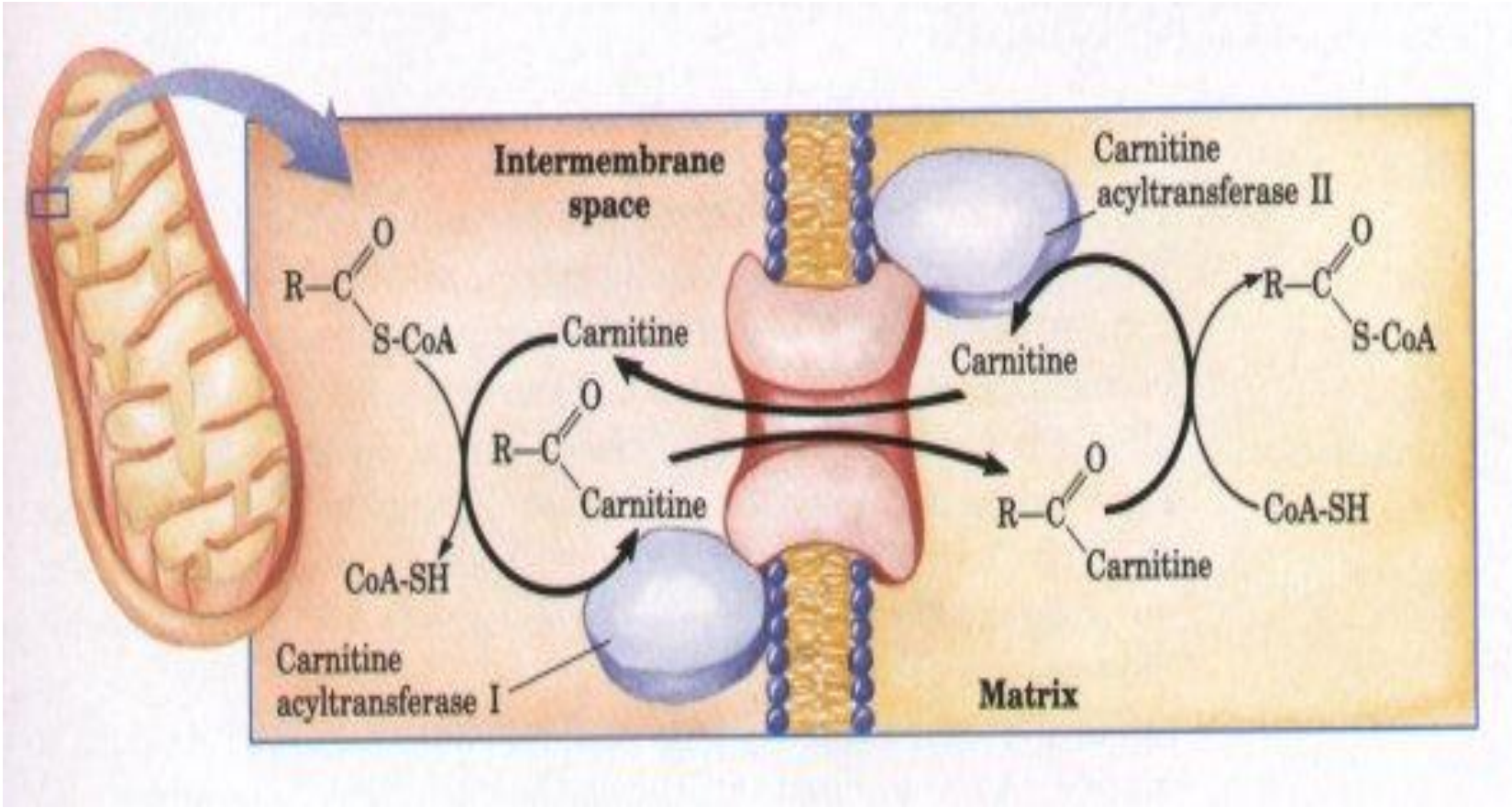
The free fatty acids that enter the cytosol from the blood cannot pass directly through the mitochondrial membranes, but must first undergo a series of three enzymatic reactions. The first is catalyzed by a family of isozymes present in the outer mitochondrial membrane, acyl-CoA synthetases, which promote the general reaction:

Fatty acid + CoA + ATP fatty acyl-CoA + AMP + PPi

acyl-CoA

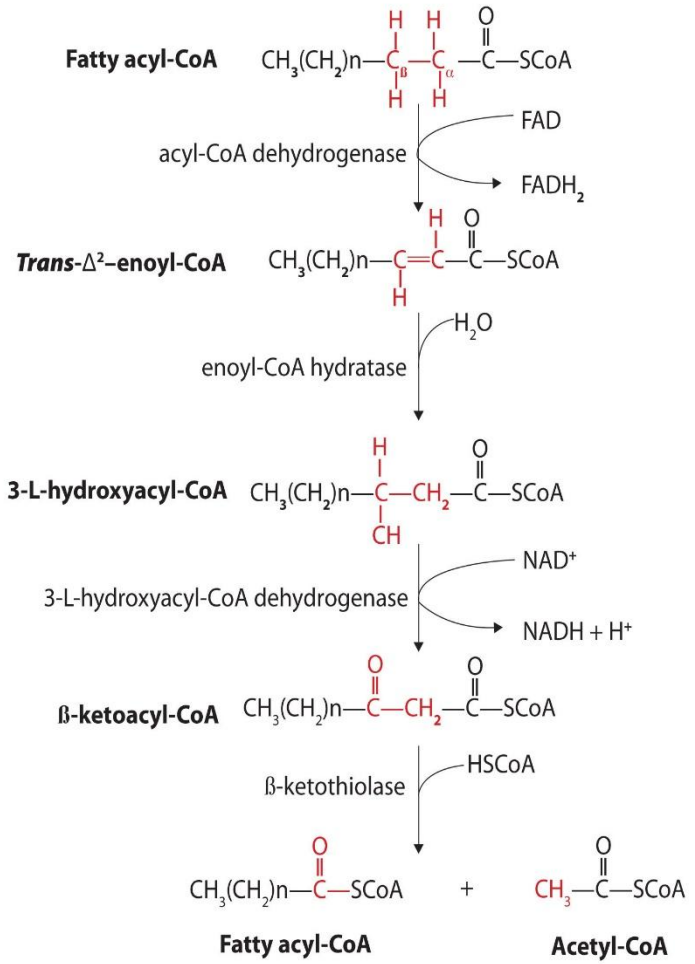
Fatty acyl-CoA esters formed in the outer mitochondrial membrane do not cross the inner mitochondrial membrane intact. Instead, the fatty acyl group is transiently attached to the hydroxyl group of **carnitine** and the fatty acyl-carnitine is carried across the inner mitochondrial membrane by a specific transporter In this second enzymatic reaction required for fatty acid movement into mitochondria, **carnitine acyltransferase I**, present on the outer face of the inner membrane, catalyzes transesterification of the fatty acyl group from coenzyme A to carnitine. The fatty acyl-carnitine ester crosses the inner mitochondrial membrane into the matrix by facilitated diffusion through the **acyl-carnitine/carnitine transporter**.

Fatty acyl-CoA esters formed in the outer mitochondrial membrane do not cross the inner mitochondrial membrane intact. Instead, the fatty acyl group is transiently attached to the hydroxyl group of **carnitine** and the fatty acyl-carnitine is carried across the inner mitochondrial membrane by a specific transporter In this second enzymatic reaction required for fatty acid movement into mitochondria, **carnitine acyltransferase I**, present on the outer face of the inner membrane, catalyzes transesterification of the fatty acyl group from coenzyme A to carnitine. The fatty acyl-carnitine ester crosses the inner mitochondrial membrane into the matrix by facilitated diffusion through the **acyl-carnitine/carnitine transporter**.



http://www.bioinfo.org.cn/book/biochemistry/chapt16/bio1.htm

Steps of β-oxidation



https://saylordotorg.github.io/text_the-basics-of-general-organic-and-biological-chemistry/s23-06-stage-ii-of-lipid-catabolism.html

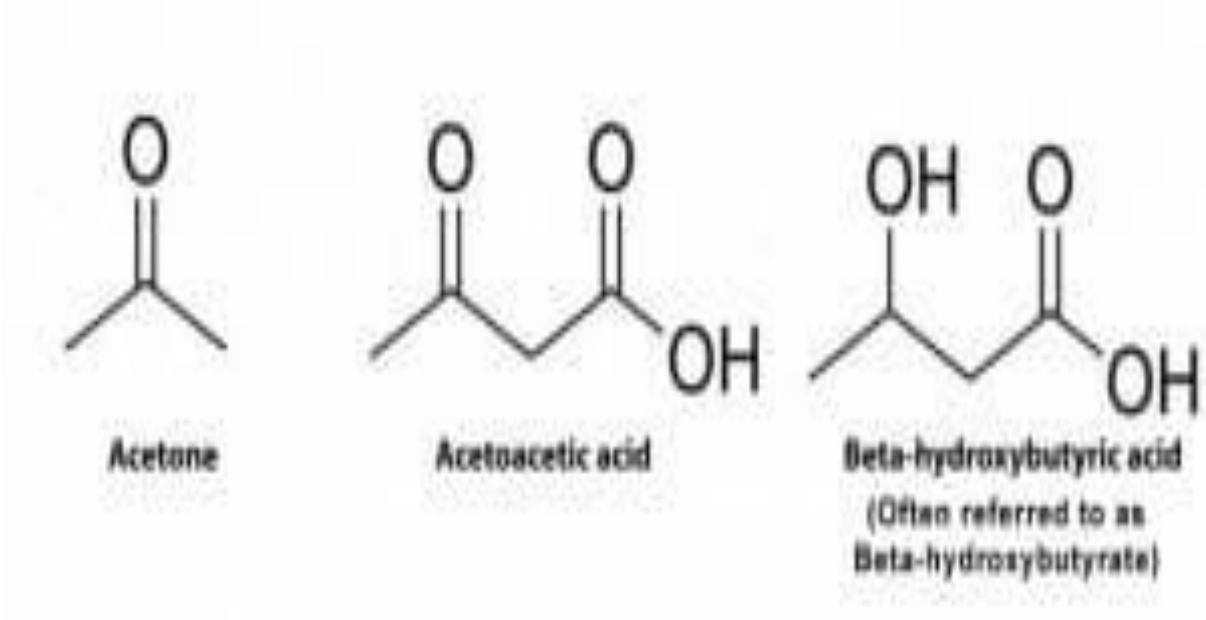
Energy Yield from β-Oxidation

- Yield of ATP per mole of stearic acid (C_{18}).

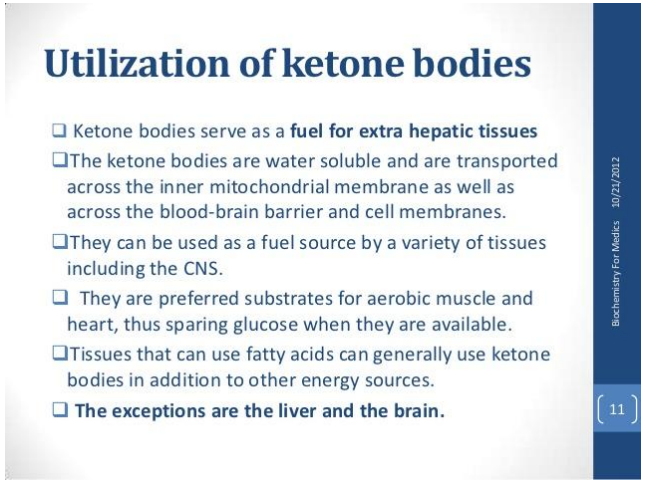
Step	Chemical Step	Happens	ATP
1	Activation (stearic acid -> stearyl CoA)	Once	-2
2	Oxidation (acyl CoA -> trans-enoyl CoA) produces $FADH_2$	8 times	16
4	Oxidation (hydroxy-acyl CoA to ketoacyl CoA) produces $NADH + H^+$	8 times	24
	Oxidation of acetyl CoA by the common metabolic pathway, etc.	9 times	108
		TOTAL	146

https://www.slideshare.net/obanbrahma/beta-oxidation-protein-catabolism-57804497

Ketone bodies



Ketone bodies, or simply *ketones* are substances produced by the liver from acetyl-CoA. There are three ketone bodies: *acetoacetate*, *beta-hydroxybutyrate*, and *acetone*. These compounds are used to provide energy to the cells of the body. There are important source of energy for cardiac muscle and neurons (when glucose is low or absent in the diet).
Concentration of ketone bodies increased in times of fasting and starvation, insulin dependent diabetes mellitus, intake of high in lipids and low in carbohydrates.



https://www.slideshare.net/namarta28/ketosis

Ketonemia

- **Ketonemia - increased concentration of ketone bodies in blood**
- **It is due to increased production of ketone bodies** by the liver rather than to a deficiency in their utilization by extra hepatic tissues.
- The production of ketone bodies occurs at a relatively low rate during normal feeding and under conditions of normal physiological status.
- Normal physiological responses to carbohydrate shortages cause the liver to increase the production of ketone bodies from the acetyl-CoA generated from fatty acid oxidation.

Causes of Ketosis

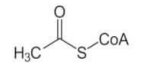
- ❑ Uncontrolled diabetes mellitus
- ❑ Starvation
- ❑ Chronic alcoholism
- ❑ Von- Gierke's disease
- ❑ Heavy exercise
- ❑ Low carbohydrate diet- For weight loss
- ❑ Glycogen storage disease type 6(Due to phosphorylase kinase deficiency)
- ❑ Pyruvate carboxylase deficiency

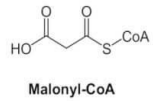
https://www.slideshare.net/namarta28/ketosis

Enzymes:
1.Fatty acid synthase (6 enzymes and 1 Acyl carrier protein molecule)
2.Acetyl-CoA carboxylase (rate-limiting enzyme)

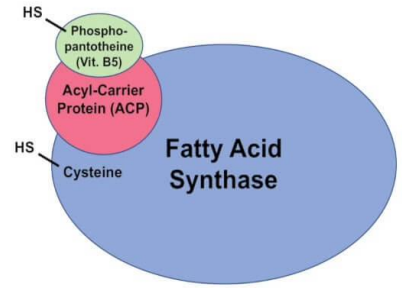
Starting material:
1.For palmitate synthesis: Acetyl-CoA
2.For odd number carbon long chain fatty acid synthesis: Propionyl-CoA
2 Carbon donor: Malonyl-CoA (donates 2 C and 1 C is thrown out as CO2)

Site: Cytosol
Citrate shuttle transfers acetyl-CoA from mitochondria to cytosol.
•OAA + **Acetyl-CoA** = Citrate (Mitochondria)
•Citrate (Mitochondria) = Citrate (Cytosol)
•Citrate = OAA + **Acetyl-CoA** (Cytosol)





Malonyl-CoA



Formation of **Malonyl-CoA** (3C) from Acetyl-CoA (2C) by **Acetyl-CoA carboxylase**.
•**1 ATP** used
•Requires **Biotin and Bicarbonate** (source of CO2)
•**Stimulated by:** Insulin, Citrate, ChREBP (induced by high carbohydrate diet/caloric intake)
•**Inhibited by:** Glucagon, Epinephrine (AMP dependent kinase), Palmitoyl-CoA
Malonyl-CoA inhibits carnitine acyltransferase to prevent fatty acids from being taken into the mitochondrial matrix to be beta oxidized at times when fatty acids are being synthesized, thus preventing a futile cycle.

It is a multimeric complex, but the 2 important domains are:
1. Ketoacyl synthase (KAS) end:
•has **Cysteine**-SH active site
•accepts **Acetyl-CoA and Acyl chain extended by 2 C on each cycle**
2. Acyl carrier protein (ACP) end:
•has **Pantothenic**-SH active site
•accepts **Malonyl-CoA**

https://epomedicine.com/wp-content/uploads/2018/07/FA-synthase.jpg

NADPH donors:
1.HMP shunt pathway
2.Isocitrate dehydrogenase
3.Malic enzyme
Mnemonic: HIM donates NADPH.

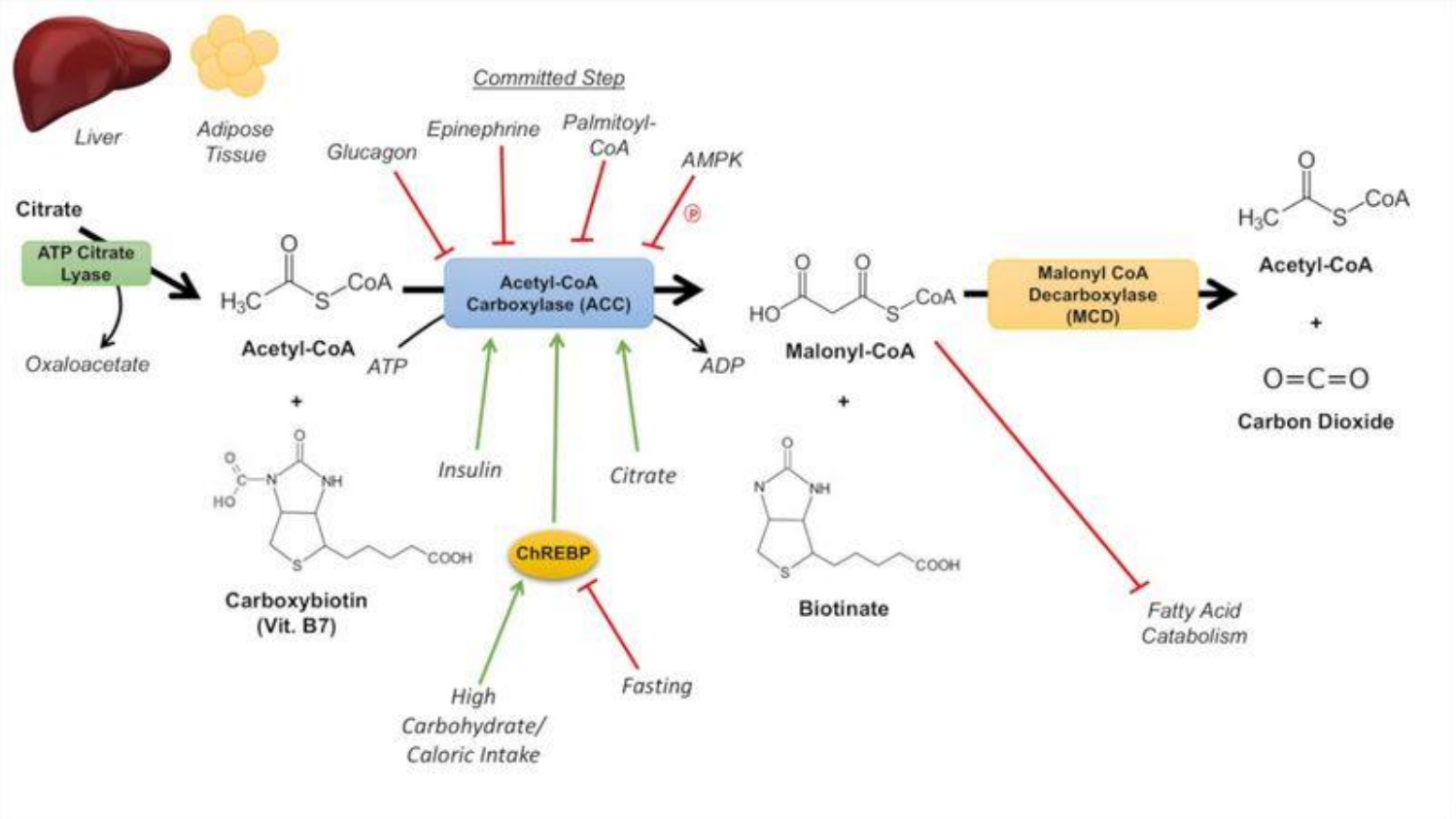
1. Loading of precursors to KAS and ACP end of FA synthase.
2. Condensation: Addition of 2 C atoms derived from Malonyl-CoA (Malonyl-CoA at ACP end takes precursor at KAS end and KAS end is free)
3. Reduction: **1 NADPH used**
4. Dehydration
5. Reduction: **1 NADPH used**
6. Acyl chain extended by 2 C atom (donated by Malonyl-CoA) is transferred to KAS end and ACP end is free to receive Malonyl-C0A.

Precursor loaded on KAS end is transferred to ACP end with Malonyl-CoA (KAS end is free).
Acyl chain elongated with 2 C atom is transferred from ACP end to KAS end (ACP end is free).
Malonyl-CoA is loaded on ACP end.
Cycle repeats.

7. **Cycle of precursor loading, condensation, reduction, dehydration and reduction** (Chain elongation) occurs unless **16 C Palmitate** is formed which is released from FA synthase enzyme complex by **Thioesterase**.

Humans make palmitic acid (16:0) as stored fat (only de novo fat possible).
•End-product: Palmitate (C16:0)
•Total of 7 cycles:
- •Starts with 2 carbon acetyl-CoA
- •Malonyl-CoA acts as a 2 carbon donor
- •7 Malonyl-CoA utilized (14 carbons)
- •2 NADPH (2 reduction reactions) X 7 cycles = 14 NADPH utilized
- •1 ATP (acetyl-CoA carboxylase reaction) X 7 cycles = 7 ATP utilized (+1 ATP to transport acetyl-CoA from mitochondria to cytosol)
- •1 CO_2 (released when malonyl-CoA donates 2 C acyl chain) X 7 cycles = 7 CO_2 released
- •1 Acetyl-CoA (to make malonyl-CoA) X 7 cylces + 1 Acetyl-CoA (precursor in KAS end) = 8 Acetyl-CoA utilized

Fatty acids synthesis



https://epomedicine.com/wp-content/uploads/2018/07/FA-synthase.jpg

Complex lipids

2. Complex lipids:

Esters of fatty acids with alcohols and molecules with other groups.

Phospholipids:

Lipids containing:

- Fatty acids
- Alcohol
- Phosphoric acid residue.

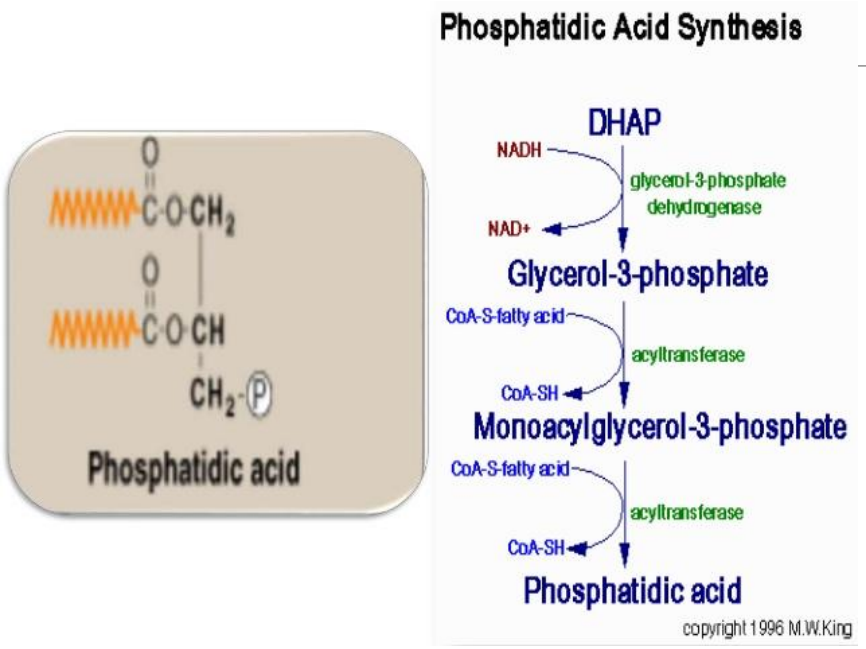
Glycolipids (glycosphingolipids):

Lipids containing:

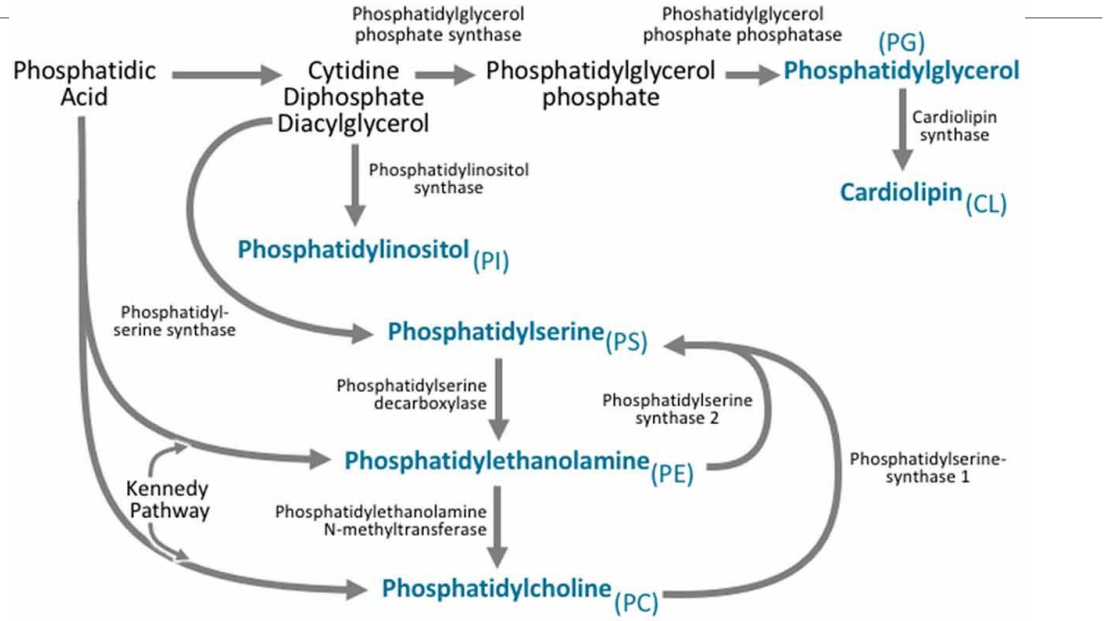
- Fatty acid
- Sphingosine
- Carbohydrate.

https://www.slideshare.net/Dr-HAMDAN/simple-lipids

Phospholipids synthesis



https://www.slideshare.net/YESANNA/synthesis-of-phospholipids



https://www.frontiersin.org/articles/10.3389/fnmol.2018.00010/full

Lipotropic factors

Lipotropic Factors

- These are the substances required for the normal mobilisation of fat from liver.
- The deficiency of these factors may result in fatty liver.
- Important lipotropic factors:
- Choline, Betaine, Methionine & Inositol.
- Folic acid, vitamin B_{12}, glycine & serine also serve as lipotropic factors.

https://www.slideshare.net/YESANNA/fatty-liver-43649058

Lipotropic factors

- Substances which facilitate mobilisation of fat and prevent accumulation of fat in liver are called LIPO TROPIC FACTORS / AGENTS / LIPOTROPINS

Lipotropic factors

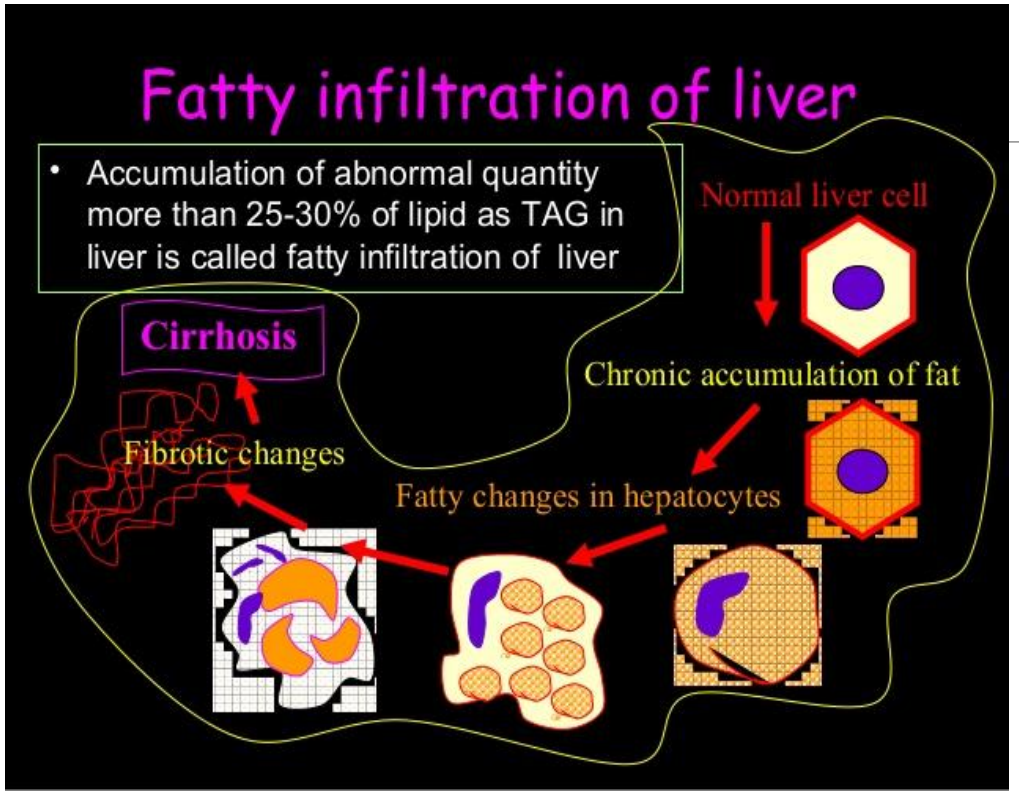
- **Choline** – ↓ oxidation of FA ↓phospholipid synthesis,
  – Impair lipoprotein syntheisis
- **Betain**-- ↓ choline synthesis,
  methyl gr. Donor for choline
- **Methionine**-- ↓ choline synthesis
- **Essential Fatty acids**– required for VLDL and lipoprotein synthesis
- **Inositol** -- ↓phospholipid synthesis

Lipotropic factors

- **Casein**
- **Heparin**
- **Vit. E, Selenium, Pantothenic acid**
- **ω3 Fatty acids** have protective role

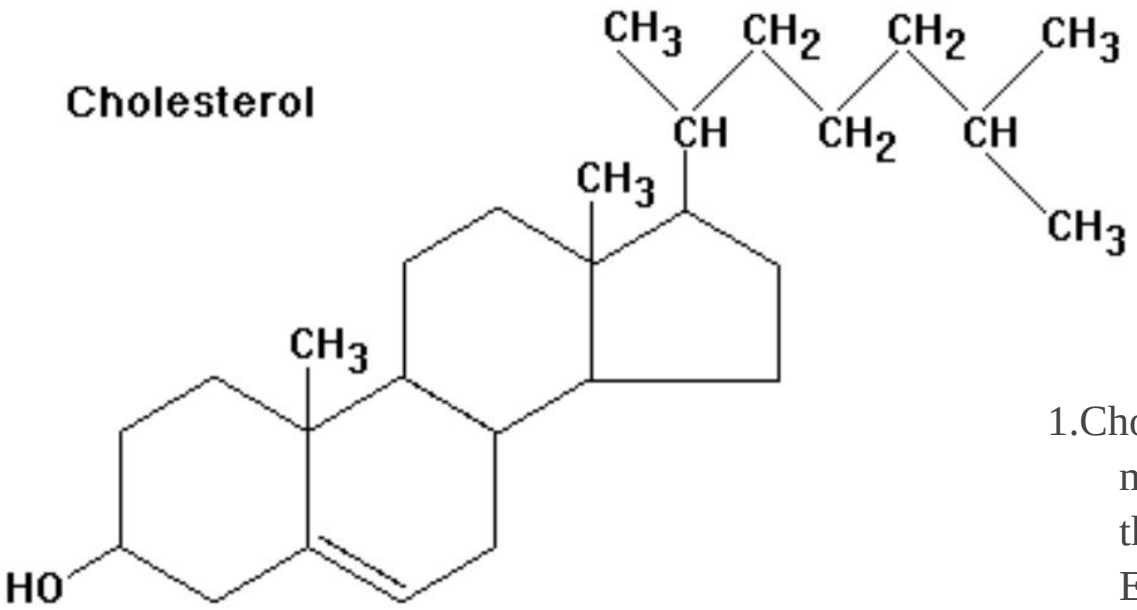
- Lipotropic factors prevents fatty liver but cannot reverse the condition

https://pt.slideshare.net/DJ4SDM/fatty-liver-and-lipotropic-factors/4?smtNoRedir=1



https://pt.slideshare.net/DJ4SDM/fatty-liver-and-lipotropic-factors/4?smtNoRedir=1

Cholesterol



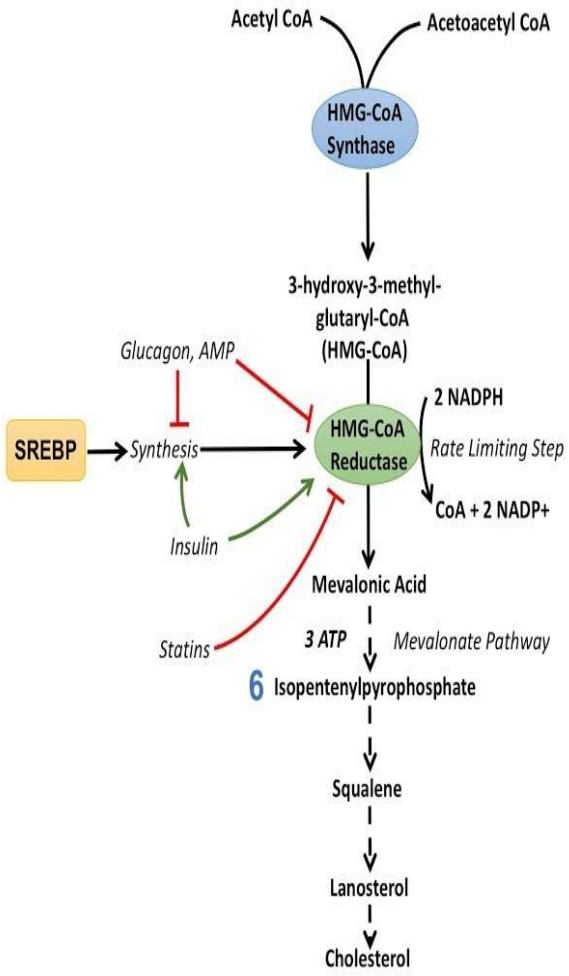
1.Cholesterol is a major constituent of the cell membranes. Cholesterol modulates physical properties of these membranes that in turn affect the function of membrane proteins such as receptors and transporters. Experimental depletion of membrane cholesterol cripples many cellular functions.

2.Cholesterol is the biosynthetic precursor of bile acids, which are essential for fat digestion.

3.Cholesterol is the precursor of all steroid hormones, namely, androgens, estrogens, progestins, glucocorticoids, and mineralocorticoids, as well as of calciferol (vitamin D).

https://www.precisionnutrition.com/all-about-cholesterol

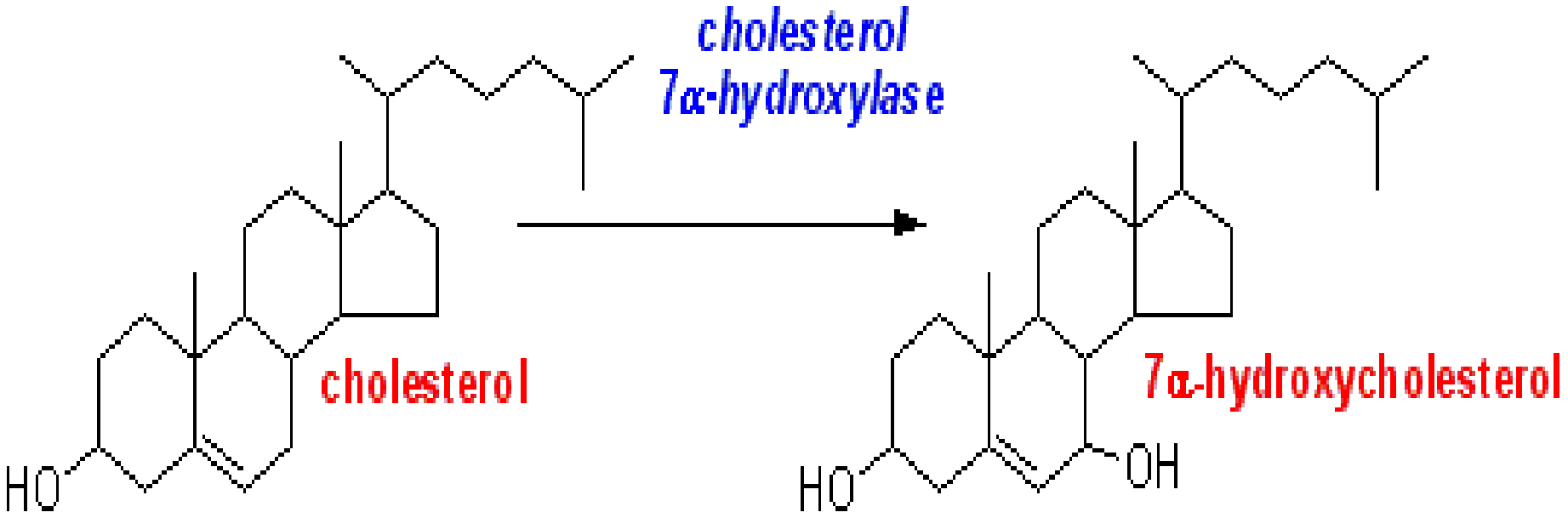
Cholesterol biosynthesis



The process of cholesterol synthesis can be considered to be composed of five major steps where the reactions that culminate in the synthesis of isopentenyl pyrophosphate, and its isomeric form dimethylallyl pyrophosphate, are commonly referred to as the mevlonate pathway:

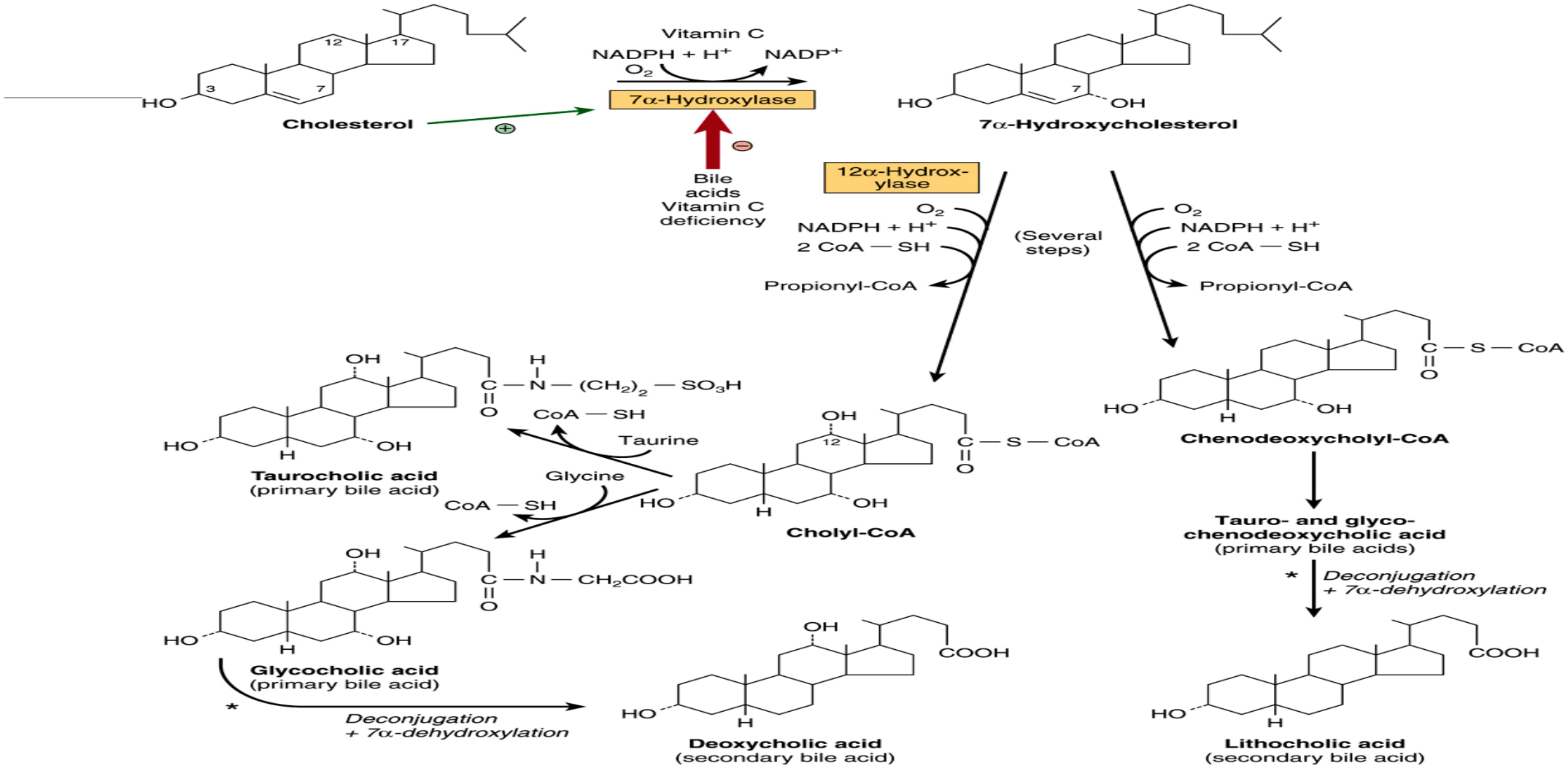
1.Acetyl-CoAs are converted to 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA)
2.HMG-CoA is converted to mevalonate
3.Mevalonate is converted to the isoprene based molecule, isopentenyl pyrophosphate (IPP)
4.IPP molecules are converted to squalene
5.Squalene is converted to cholesterol

Cholesterol hydroxylation



https://www.david-bender.co.uk/metabonline/lipids/bile/bile16.html

Bile acids metabolism

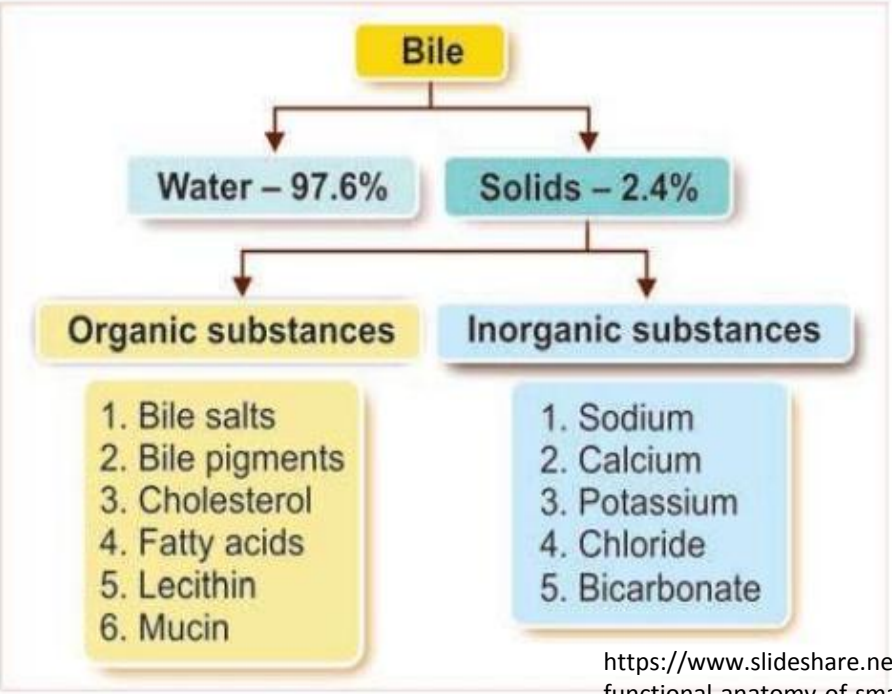


https://basicmedicalkey.com/cholesterol-synthesis-transport-excretion/

Bile

COMPOSITION OF BILE

- Bile contains 97.6% of water and 2.4% of solids. Solids include organic and inorganic substances.



FUNCTIONS OF BILE

- Most of the functions of bile are due to the bile salts.

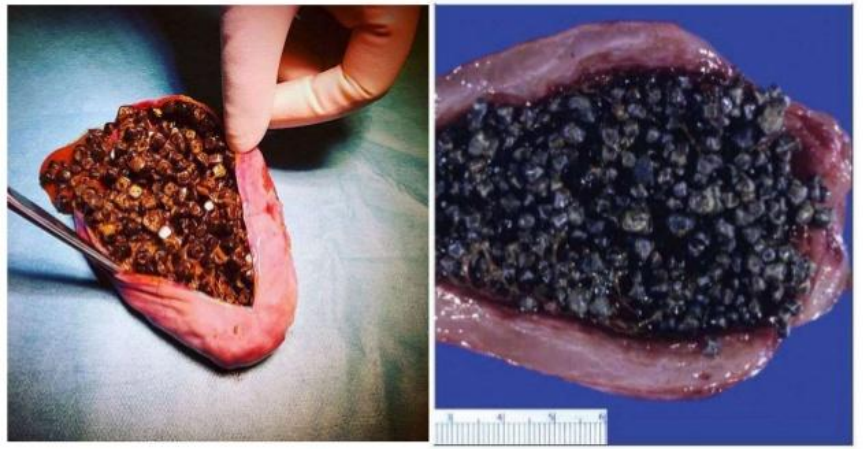
1. DIGESTIVE FUNCTION
2. ABSORPTIVE FUNCTIONS
3. EXCRETORY FUNCTIONS
4. LAXATIVE ACTION
5. ANTISEPTIC ACTION
6. CHOLERETIC ACTION
7. MAINTENANCE OF pH IN GASTROINTESTINAL TRACT
8. PREVENTION OF GALLSTONE FORMATION
9. LUBRICATION FUNCTION
10. CHOLAGOGUE ACTION

https://www.slideshare.net/VamsiIntellectual/physiology-properties-of-bile-composition-of-bile-functions-of-bile-functional-anatomy-of-small-intestine-functional-anatomy-of-si-functional-anatomy-of-li-functions-of-li

Gallstones

Composition of Gall stones

- Gallstones -composed mainly of cholesterol, bilirubin, and calcium salts, with smaller amounts of protein and other materials
- Three types of gallstones
  - (i) Pure cholesterol stones-contain at least 90% cholesterol,
  - (ii) pigment stones (brown or black)-contain at least 90% bilirubin
- Brown pigment stones are mainly composed of **calcium bilirubinate** and **Black pigment** stones contain **bilirubin**, calcium and/or tribasic phosphate
- **Brown pigment stones** are soft and greasy, consisting of bilirubinate and fatty acids (Ca palmitate or stearate). They form during infection, inflammation, and parasitic infestation
  - (iii) mixed composition stones, which contain varying proportions of cholesterol, bilirubin and other substances such as $CaCO_3$, $Ca_3(PO_4)_2$ and calcium palmitate



- Cholesterol gallstone formation begins with the secretion of bile supersaturated with cholesterol from the liver. Initiated by nucleating factors such as mucin, microscopic crystals then precipitate in the gallbladder
- Excessive cholesterol biosynthesis, -main lithogenic mechanism in obese persons.
- In the non-obese, defective conversion of cholesterol to bile acids, due to a relatively low activity of cholesterol 7α hydroxylase, the rate limiting enzyme for bile acid biosynthesis and cholesterol elimination could result in excessive cholesterol secretion.
- Interruption of the enterohepatic circulation of bile acids could increase bile saturation.
- Pigment stones occur when RBCs are destroyed, leading to excessive bilirubin in the bile.
- Gallbladder sludge, i.e., **Thickened gallbladder mucoprotein with tiny entrapped cholesterol crystals is thought to be the usual precursor of gallstones**

https://www.slideshare.net/akashmahadev/steatorrhea-chyluria-gallstone-cholelithiasis-pancreatitis-chronic-and-

Analyte	Range	Classification
Total Cholesterol[1] (mmol/L)	< 5.2	Desirable
	5.2 - 6.1	Borderline high
	> 6.1	High
HDL[1,2] (mmol/L)	> 1.53	Less than avgerage risk
	1.03 - 1.53	Average risk (male)
	1.29 - 1.53	Average risk (female)
	< 1.03	Increased risk (male)
	< 1.29	Increased risk (female)
LDL[1] (mmol/L)	< 2.6	Optimal
	2.6 - 3.3	Near optimal
	3.4 - 4.1	Borderline high
	4.2 - 4.9	High
	> 4.9	Very high
CHOL/HDL[3,4] (mmol/L)	< 3.5	Optimal (male)
	< 3.4	Optimal (female)
	> 5.0	Above average risk (male)
	> 4.4	Above average risk (female)
Non-HDL[1,2] (mmol/L)	< 3.4	Optimal
	3.4 - 4.1	Near optimal
	4.2 - 4.9	Borderline high
	5.0 - 5.7	High
	> 5.7	Very high
Triglycerides[1] (mmol/L)	< 1.69	Desirable
	1.69 - 2.25	Borderline high
	2.26 - 5.63	High
	> 5.63	Very high

Sources

1. National Cholesterol Education Program ATP III
2. Lab Tests Online - Lipid Panel
3. Harvard Medical Health Guide
4. American Heart Association

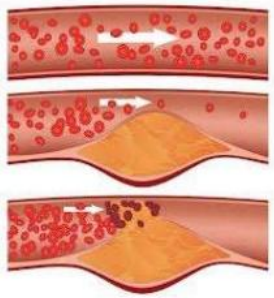
Contributing causes of polygenic hypercholesterolemia

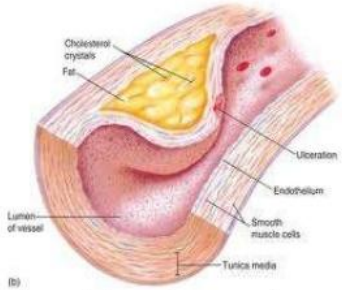
Diet	High saturated fat intake
	High trans fat intake
	High cholesterol intake
Lifestyle	Sedentary lifestyle
	Obesity
Diseases	Cushing syndrome
	Diabetes mellitus
	HIV-infection
	Hypothyroidism
	Insulin resistance
	Metabolic syndrome
	Nonalcoholic fatty liver disease
Medication	Amiodarone, betablockers, corticosteroids, cyclosporine, estrogens, thiazide diuretics
Genetics	> 30 SNPs

Atherosclerosis

- Atherosclerosis is a disease of large and medium-sized muscular arteries and is characterized by –
- endothelial dysfunction,
- vascular inflammation, and
- the buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall.

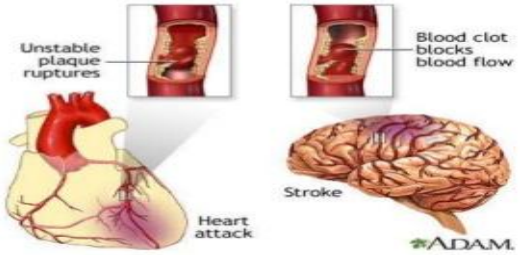
Atheromatous plaque

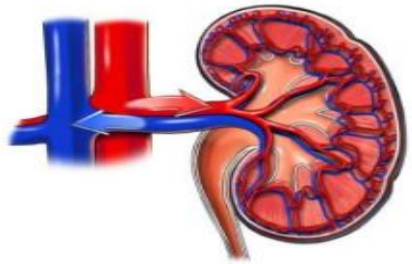




Atherosclerosis or Arteriosclerosis is a slow and progressive building up of plaque, fatty substances, cholesterol, cellular waste products, calcium and fibrin in the inner lining of

Atherosclerosis





- Atherosclerosis also takes a toll through other consequences of acutely or chronically diminished arterial perfusion, *such as mesenteric occlusion, sudden cardiac death, chronic IHD, and ischemic encephalopathy.*

https://www.slideshare.net/mpattani/atherosclerosis-59199971

Major Risk Factors

Unhealthy blood cholesterol levels. This includes high LDL cholesterol (sometimes called "bad" cholesterol) and low HDL cholesterol (sometimes called "good" cholesterol).

High blood pressure. Blood pressure is considered high if it stays at or above 140/90 mmHg over time. If you have diabetes or chronic kidney disease, high blood pressure is defined as 130/80 mmHg or higher. (The mmHg is millimeters of mercury—the units used to measure blood pressure.)

Smoking. Smoking can damage and tighten blood vessels, raise cholesterol levels, and raise blood pressure. Smoking also doesn't allow enough oxygen to reach the body's tissues.

Insulin resistance. This condition occurs if the body can't use its insulin properly. Insulin is a hormone that helps move blood sugar into cells where it's used as an energy source. Insulin resistance may lead to diabetes.

Diabetes. With this disease, the body's blood sugar level is too high because the body doesn't make enough insulin or doesn't use its insulin properly.

Overweight or obesity. The terms "overweight" and "obesity" refer to body weight that's greater than what is considered healthy for a certain height.

Lack of physical activity. A lack of physical activity can worsen other risk factors for atherosclerosis, such as unhealthy blood cholesterol levels, high blood pressure, diabetes, and overweight and obesity.

Unhealthy diet. An unhealthy diet can raise your risk for atherosclerosis. Foods that are high in saturated and trans fats, cholesterol, sodium (salt), and sugar can worsen other atherosclerosis risk factors.

Older age. As you get older, your risk for atherosclerosis increases. Genetic or lifestyle factors cause plaque to build up in your arteries as you age. By the time you're middle-aged or older, enough plaque has built up to cause signs or symptoms. In men, the risk increases after age 45. In women, the risk increases after age 55.

Family history of early heart disease. Your risk for atherosclerosis increases if your father or a brother was diagnosed with heart disease before 55 years of age, or if your mother or a sister was diagnosed with heart disease before 65 years of age.

Sources of information

Halkerston I.D.K. Biochemistry: 2nd edition. The National medical series for independent study / Halkerston I.D.K. - 1988. - 522 p.

Harper`s Biochemistry. R.K.Murray, D.K.Granner, P.A.Mayes, V.W.Rodwell. Prentice-Hall International Inc., 2010. – 1134 p.

Koolman J. Color Atlas of Biochemistry / J.Koolman, K.-H. Rom. – Stuttgart. New York. – Thieme Verlag. — 1996. – 435 p.

Lehninger A. Principles of Biochemistry / Lehninger A. – New York. – W.H.Freeman and Company. – 2005. – 1010 p.

Pamela C.Champe Lippincott's Illustrated Reviews: Biochemistry, 3rd Edition / Pamela C.Champe and Richard A.Harvey. – Baltimore, Lippincott Williams & Wilkins, MD ©, 2005. – 534p.

https://www.apsubiology.org/anatomy/2020/2020_Exam

_Reviews/Exam_1/CH18_Lipoproteins.htm

https://www.researchgate.net/figure/4-The-major-types-of-lipoproteins-are-chylomicrons-very-low-density-lipoprotein-VLDL_fig4_304525065

https://schoolbag.info/chemistry/mcat_biochemistry/70.html#:~:text=

Chylomicrons%20are%20the%20least%20dense,HDL%20(high-density)

https://slideplayer.com/slide/13652465/

https://www.researchgate.net/figure/Triacylglycerol-TAG-structure-showing-glycerol-with-three-fatty-acids_fig1_316787887

https://en.wikipedia.org/wiki/Lipolysis

https://www.researchgate.net/figure/Triacylglycerol-TAG-structure-showing-glycerol-with-three-fatty-acids_fig1_316787887

https://www.slideserve.com/castor-mills/lipogenesis

https://www.slideserve.com/castor-mills/lipogenesis

http://themedicalbiochemistrypage.org/the-metabolic-syndrome-mets/

http://www.bioinfo.org.cn/book/biochemistry/chapt16/bio1.htm

https://saylordotorg.github.io/text_the-basics-of-general-organic-and-biological-chemistry/s23-06-stage-ii-of-lipid-catabolism.html

https://www.slideshare.net/obanbrahma/beta-oxidation-protein-catabolism-57804497

https://www.slideshare.net/namarta28/ketosis

https://epomedicine.com/wp-content/uploads/201

https://epomedicine.com/wp-content/uploads/2018/07/FA-synthase.jpg

https://www.slideshare.net/Dr-HAMDAN/simple-lipids

https://www.slideshare.net/YESANNA/synthesis-of-phospholipids

https://www.frontiersin.org/articles/10.3389/fnmol.2018.00010/full

https://pt.slideshare.net/DJ4SDM/fatty-liver-and-lipotropic-factors/4?smtNoRedir=1

https://www.precisionnutrition.com/all-about-cholesterol

https://www.david-bender.co.uk/metabonline/lipids/bile/bile16.html

https://www.slideshare.net/VamsiIntellectual/physiology-properties-of-bile-composition-of-bile-functions-of-bile-functional-anatomy-of-small-intestine-functional-anatomy-of-si-functional-anatomy-of-li-functions-of-li

https://www.slideshare.net/mpattani/atherosclerosis-59199971