Fatty Acid Metabolism

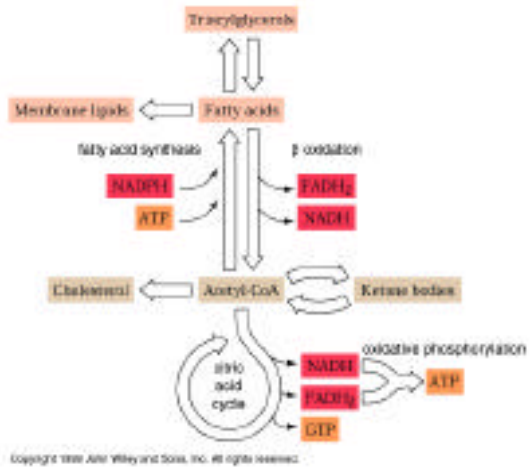
Introduction

Functions of fatty acids -

- membrane lipid starting material
- used in covalent modification of proteins
- fuel source
- biologically active molecules (messengers)
- stabilize membrane enzymes
- surface properties
- insulation for the cold MN winters (my function)

Sources of fatty acids

- diet - MacDonalds/plants
- *de novo* synthesis - we can make some kinds of fatty acids but not all



Stored in adipose tissues (super models are a disease state for this function)

- Esterified - TAG- triacyl glycerol (glycerol and 3 FAs) KNOW OW IT IS BONDED TO THE BACKBONE

- Stored in cells as globules in cytosol
- FA - in fluids carried by albumin - in cells free stored attached to fatty acid binding protein

- number of fat cells change very little mostly size -
- lipids are anhydrous compare to glycogen (more energy per weight)
  - fat has twice as oxidative (metabolic) energy than carbo and protein

Metabolic energy of a 70 kg person

	Dry weight	energy (kJ)
Fat	15,000	555,000
Muscle Protein	6,000	102,000
Muscle glycogen	120	1,920
Liver glycogen	70	1,120
Glucose	20	120

The primary ingested lipid is TAG (>> 90%)

Fatty acid composition of typical animal and plant fats %

	Saturated	Monounsaturatec	Polyunsaturated
Butter fat	60	36	4
Pork fat	59	39	2
Beef fat	53	44	2
Chicken fat	39	44	21
Corn oil	15	31	53
Soy bean oil	14	24	53
Soft margarine	23	22	52

Greasy spoon digestion and transport

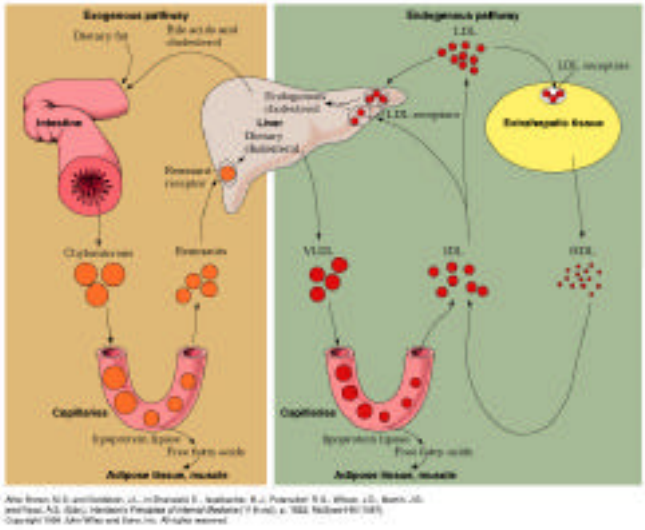
Initial absorption of dietary fats

- Digestion occurs at lipid water interface in intestine
- Transport & solubility in intestinal cells increased by Fatty acid-binding protein
- Lipid solubility aided by micelles composed of bile salts - cholesterol esters
- Pancreatic lipase hydrolyzes TAG into DAG then MAG
- PLA_2 - digests phospholipids to lysophospholipids and FFAs

Lipids are transported in bodily fluids as lipoprotein vesicles (chylomicrons, HDL, LDL, VLDL)

- Separated by centrifugation
- Density determined by total lipid content (low density) and protein content (high density)

View of a lipoprotein: **Atherosclerosis**



<u>Chylomicrons</u> (98-99% lipid 1-2% protein)

transport of dietary lipids into circulation

- mostly TAGs some phospholipid and cholerol esters
- Initially synthesized in intestine, 1/2 in rats min, in humans 30 mins
- transport FA from lymphatic system to blood stream
- Deliver to peripheral <u>extrahepatic</u> tissue (heart and skeletal muscle and adipose)
- transfer of TAGs catalyzed by lipoprotein lipase -> MAG and FFAs (not active in adult liver)
- lipoprotein lipase requires apoprotien C-II for activity
- remnants taken up by liver (high in dietary cholesterol. This requires apoprotein E gets it from HDL

VLDL (very low density lipoprotien)

- Serves similar role to chylomicrons except transports lipids from liver to extrahepatic tissue
- 90-93% lipid 7-10% protein
- ~ 50% lipid are TAGs. 20% P lipids 21% cholesterol and it's esters.
- apoprotein C and E
- As TAGs decrease cholesterol is enriched (formation of IDL ~ VLDL remnants)
- some IDL (with apoE) is taken up by liver by LDL receptors (apo B-100 and apoE)
- some IDL converted to LDL (no apoE)

LDL (low density lipoprotien) **THE BAD CHOLESTEROL**

- 70% lipid 21 % protein
- 13% TAG, 28% P lipids, 58% cholesterol esters and free cholesterol
- Serves as source of cholesterol for tissue
- 45% of plasma pool is degraded by liver and extrahepatic tissue each day
- Apo B-100 binds to LDL receptor - receptor level is regulated by cholesterol levels (more later)

HDL (high density lipoprotien) **THE GOOD CHOLESTEROL**

- 76% lipid 33 % protein
- 16% TAG, 43% P lipids, 41% cholesterol esters and free cholesterol
- Serves to remove cholesterol and it's esters from tissue to liver where cholesterol can then be lost as bile
- nascent HDL is devoid of cholesterol esters - picks up from tissue by LCAT (lecithin:cholesterol acyl transferase)- transfers FA from phosphatidyl choline onto unesterified cholesterol.
- LCAT activated by apoA
- cholesterol esters then transferred to VLDL and LDL
- High HDL levels are inversely proportional to coronary atherosclerosis

Release the grease

- Lipolysis - fatty acid (TAG) release from adipose storage
- PKA phosphorylates hormone sensitive lipase (active when phosphorylated)
- insulin inhibits fatty acid release by reducing cAMP levels - insulin deficiency causes increased FFA liberation and under utilization of chylomicrons and VLDL (hyperlipoproteinemia)
- once the first FA is liberated two additional unregulated lipases quickly act
- diacyl glycerol lipase and 2) monoacyl glycerol lipase
- end up with 3 FA and 1 glycerol (can enter carbo metabolism via dihydroxyacetone phosphate)
- free (unesterified) fatty acids move through blood to site of metabolism by protein carriers including albumin