

Pyruvate Dehydrogenase (PDH)

$\text{Pyruvate} + \text{CoASH} + \text{NAD}^+ \xrightarrow{\text{PDH}} \text{Acetyl-CoA} + \text{CO}_2 + \text{NADH} + \text{H}^+$

Lactate \rightleftharpoons Pyruvate \rightleftharpoons Alanine

PDH Gene Deficiency:
 Lactic Acidosis
 Neurological Defects

PDH Activity Low:
 Thiamine Deficiency
 Arsenic Poisoning

Treatment – ketogenic diet

Galactosemia

Galactokinase Deficiency

Elevated galactitol
Cataracts

Galactosemia

Galactosuria

Treatment:

Eliminate galactose/
Lactose MILK

Classical Galactosemia Galactose 1-P Uridyl- Transferase Deficiency

Elevated galactitol
Cataracts

Galactosemia

Galactosuria

Elevated Galactose 1-P

Hepatic Dysfunction
Brain Dysfunction
(Retardation)
Cataracts

Autosomal recessive

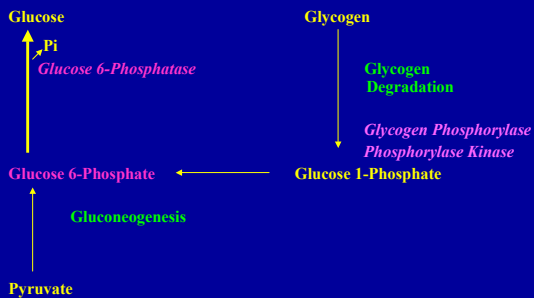
HEREDITARY FRUCTOSE INTOLERANCE A Deficiency of Aldolase B

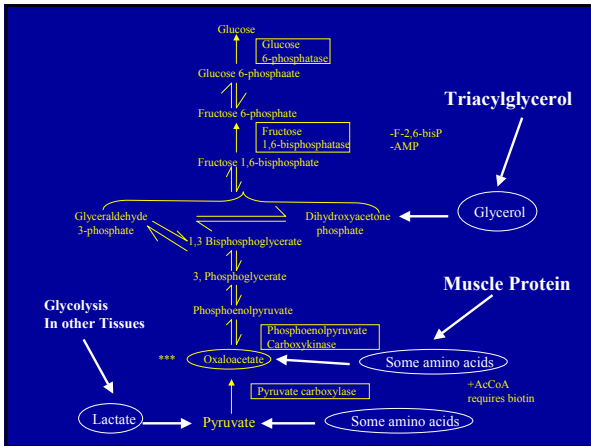
Symptoms

Hypoglycemia
Vomiting
Jaundice
Hepatic failure

Treatment: Decrease fructose/sucrose

Glucose Homeostasis is Required for Survival



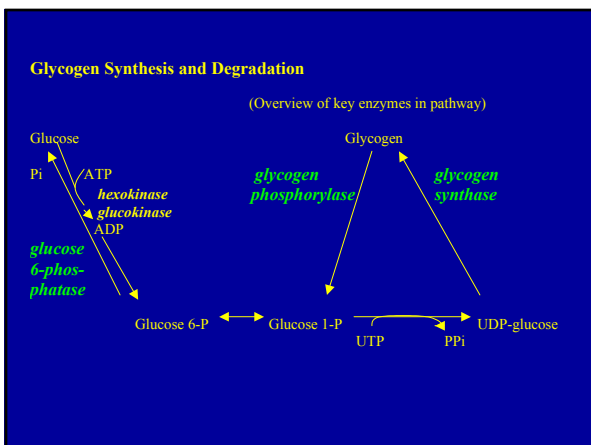


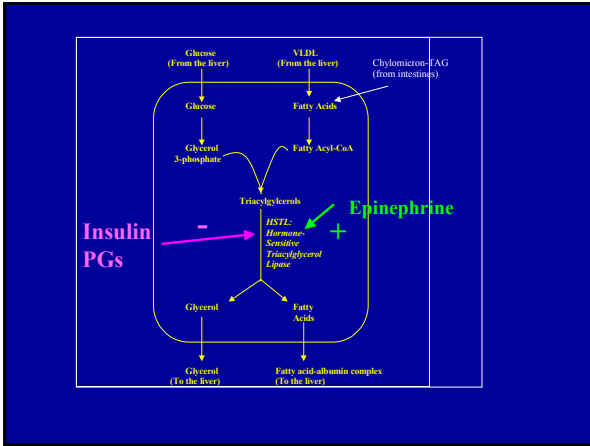
Ethanol metabolism can cause hypoglycemia; the high NADH opposes gluconeogenesis

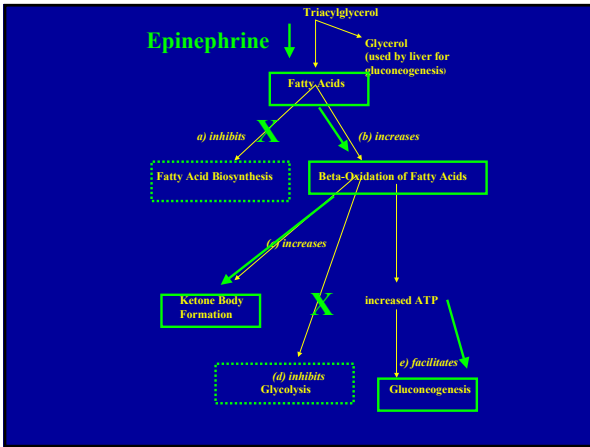
Ethanol metabolism increases NADH

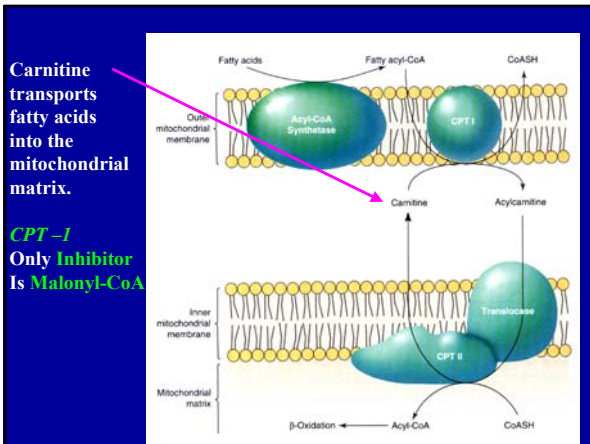
Increased NADH promotes the conversion of two glucogenic precursors (pyruvate and oxaloacetate) to lactate and malate.

This removes pyruvate and oxaloacetate from the pool of glucogenic precursors.



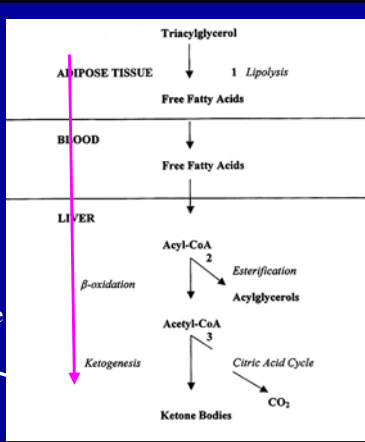






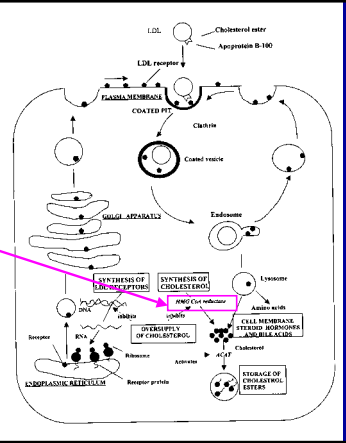
Ketone bodies:

Beta-hydroxybutyrate
Acetoacetate
acetone



LDL Metabolism

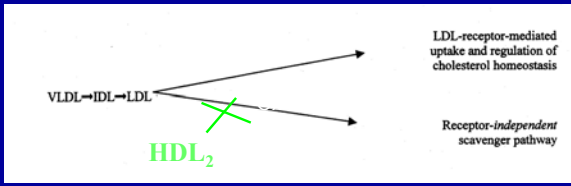
“Statins”
Inhibit
HMC-CoA
Reductase



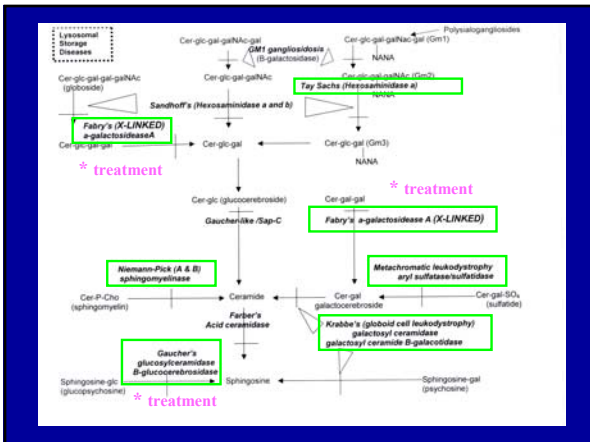
Chemical Composition of Plasma Lipoprotein Class

Lipoprotein Class	Function	Percent Composition of Lipid Fraction					
		% Protein	% Lipid	Phospho-lipids	Unesteri-fiedCh-olesterol	Choles-terol Esters	Triacyl-glycerols
HDL	Reverse Cholesterol Transport	40-55	50-55	20-35	12	3-4	3-5
LDL	Cholesterol Transport	20-25	75-80	15-20	35-40	7-10	7-10
IDL	LDL Precursor	15-20	80-85	22	22	8	30
VLDL	Transports Endogenous Fat	5-10	90-95	15-20	10-15	5-10	50-65
Chylo-microns	Transports Exogenous (Dietary) Fat	~2	97-99	7-9	3-5	1-3	84-89

Two Pathways of LDL Clearance



HDL is involved with reverse cholesterol transport



Type 1 Collagen

Triple-stranded
Gly-X-Y repeat
Glycine – smallest aa
Proline – polyproline
helix
OH-pro, OH-lys
H-bonding
Lysine aldehydes
cross-linking

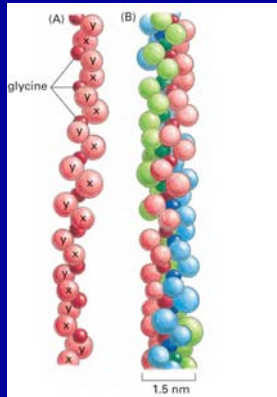


Figure 19-43. Molecular Biology of the Cell, 4th Edition

Selected Collagen Disorders

Disorder	Collagen synthesis	Clinical Manifestations
Osteogenesis Imperfecta 1	Decreased synthesis of type 1 collagen	susceptibility to fractures sometimes confused with child abuse blue sclerae - translucent connective tissue over choroid
Autosomal Dominant – may act like dominant negative		
Osteogenesis Imperfecta 2	Point mutations & re-arrangement of exons in triple helical regions	Perinatal death, soft, fragile & malformed bones
Autosomal Dominant		
Ehlers-Danlos	Faulty collagen synthesis	Hyperextensive skin, hypermobility of joints, tendency to bleed

Fibrillin is essential to the integrity of elastin

Marfan's Syndrome
mutation in the fibrillin gene

Regulation of Key Enzymes of Lipid Metabolism

Enzyme	Activator	Inhibitor	Hormonal Activator	Hormonal Inhibitor	Induces Enzyme Synthesis	Represses Enzyme Synthesis	Comments
Acetyl CoA-liver Carboxylase	Citrate	Long Chain FattyAcylCoA AMP	Insulin	Glucagon Epinephrine	HighCarb/Diet Fat Free Diet	Glucagon, (EP) High Fat Diet Fasting	Requires Biotin Synthesizes Malonyl-CoA, The inhibitor of CPT-1
Carnitine Palmitoyl Transferase - I - liver		Malonyl CoA					
Hormone Sensitive Triacylglycerol Lipase - Adipose Tissue			Epinephrine ACTH	Insulin PGE			
Mitochondrial HMG-CoA Synthase - Liver							
Acetoacetyl-CoA Synthase - Liver							
Transferrin - not liver							
HMG-CoA Reductase - liver		Cholesterol AMP Mevastatin	Insulin	Glucagon			Inhibited by drugs such as Lovastatin, mevastatin, etc. Effectiveness of drugs is Dependent on presence of Functional LDL receptors in the liver.
γ -alpha hydroxylase - liver	Cholesterol						
ACAT	Cholesterol						
Lipoprotein Lipase - endothelial	Apo CII						

Note: The regulation of these enzymes in specific tissues is noted. However, many of these pathways take place in several tissues (fatty acid synthesis, fatty acid oxidation, ketone utilization, cholesterol biosynthesis). Ketones are made only in the liver mitochondria and they are not utilized in the liver. Bile acids are made only in the liver. HSL Lipase is an adipose tissue enzyme. Lipoprotein lipase is found in the capillary endothelium and is activated by an apoprotein (C-II) found on several lipoproteins.
