ANSC/NUTR 618
Lipids and Lipid Metabolism
Exercise, Starvation, and Lipid Metabolism

I. Overview of adipose tissue metabolism

A. Fatty acids synthesized in liver and/or adipose tissue, stored as triacylglycerols in adipose tissue.

B. Stimulation of triacylglycerol hydrolysis (i.e., lipolysis) causes release of fatty acids from adipose tissue to the circulatory system.

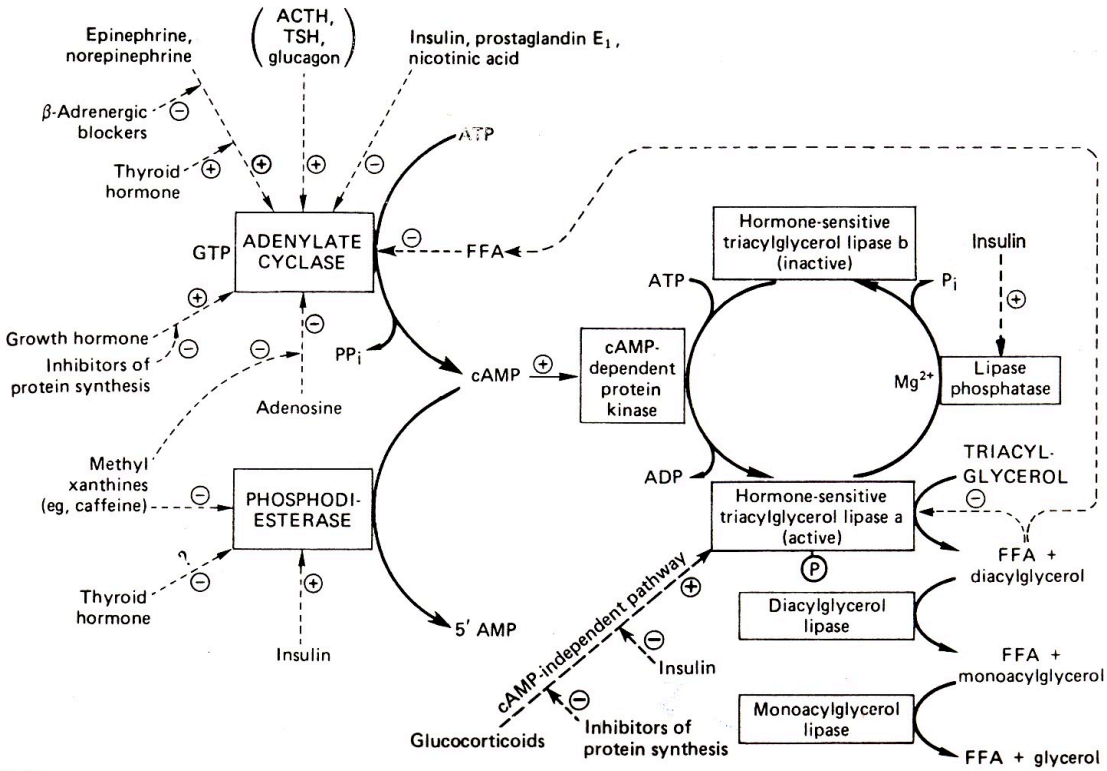
II. Overview of lipid metabolism in liver

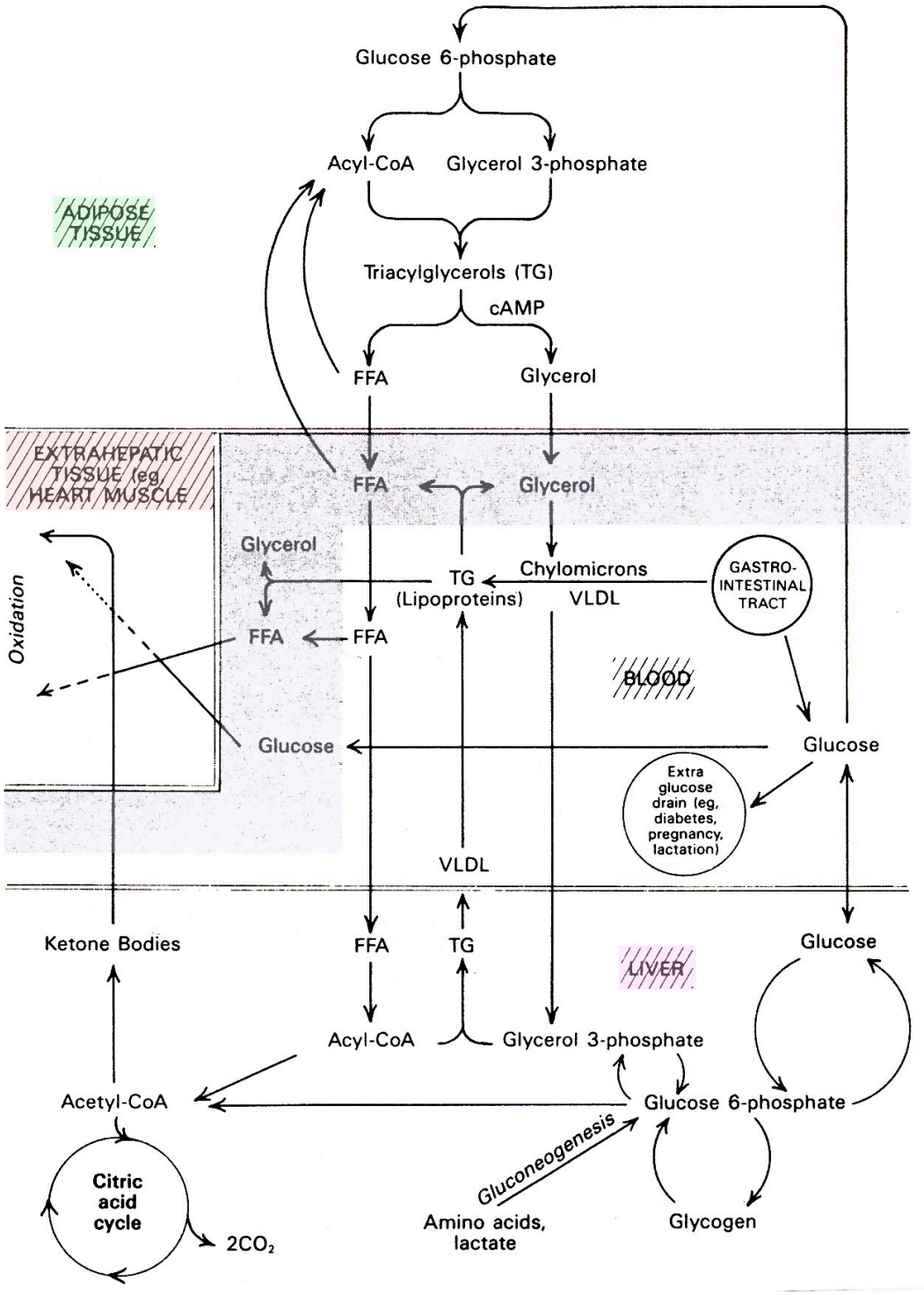
A. Fatty acids converted to triacylglycerols, packaged as VLDL

1. Fatty acids synthesized in liver in most species (except livestock).
2. Fatty acids also obtained from circulatory system (from adipose tissue).
3. VLDL transports fatty acids (as triacylglycerols) back to other tissues.

B. Excess of fatty acids leads to ketone body formation.

1. Conversion of fatty acids to acetyl-CoA exceeds ability of liver to oxidize the acetyl-CoA.
2. Excess acetyl-CoA is used to synthesize ketone bodies.
3. Glycerol (from adipose tissue) is converted to glucose in liver.
4. Fatty acids, ketone bodies and glucose are used for energy by muscle.





III. Effects of starvation and exercise on substrate utilization by muscle

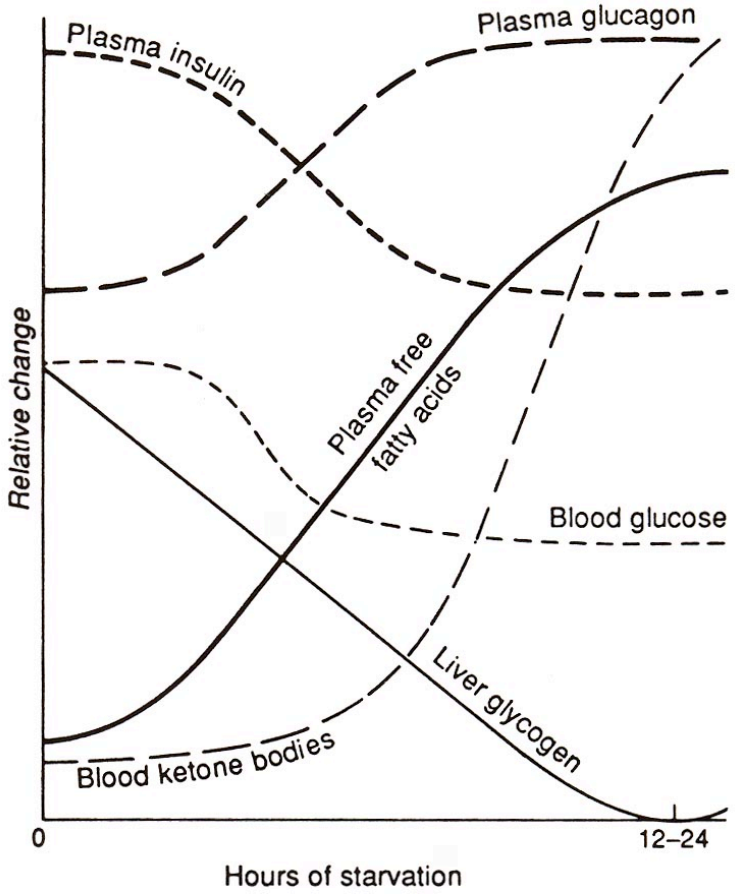
A. Blood glucose decreases.

1. Liver glycogen is depleted.

2. In response to decrease in blood glucose, insulin decreases and glucagon release from pancreas is increased.

B. Nonesterified fatty acids increase in blood.

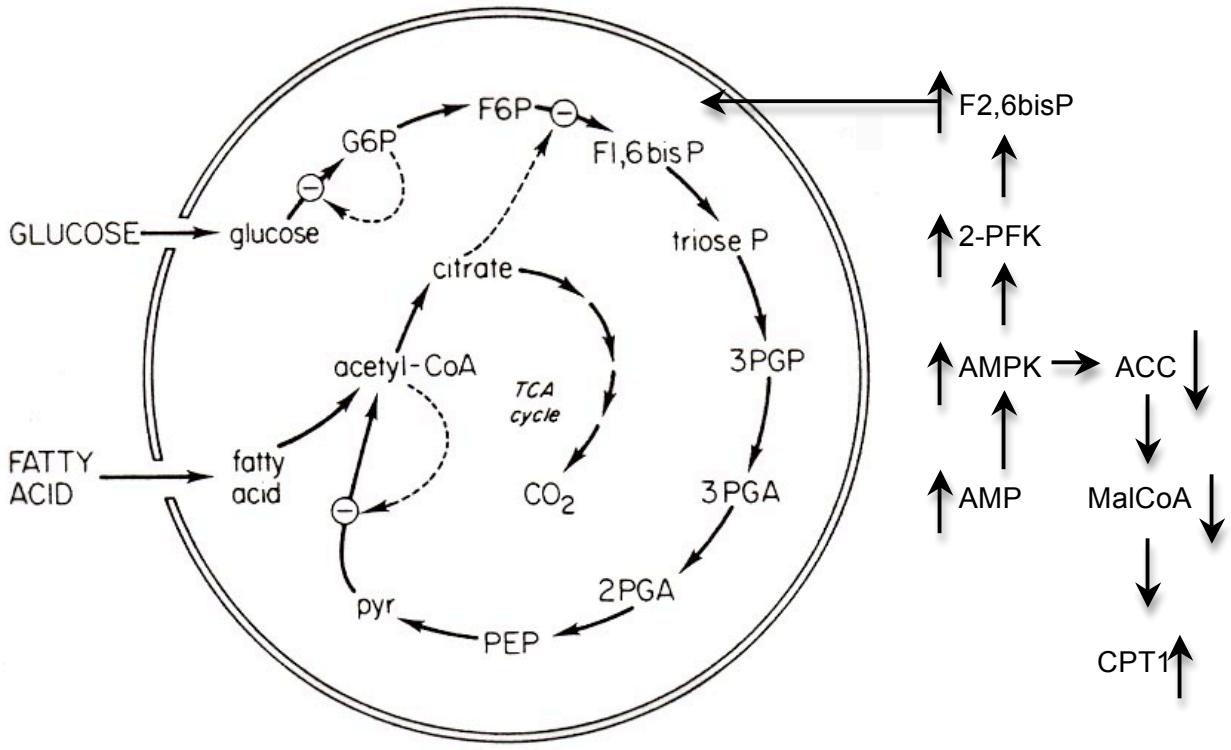
1. Epinephrine is released:
   a. Stimulates hormone sensitive lipase, fatty acid and glycerol release.
   b. Inhibits triglyceride synthesis.
2. Insulin is not available for:
   a. Inhibition of hormone sensitive lipase.
   b. Increased uptake of glucose (→ G-3-P).



IV. Glucose:fatty acid cycle

A. Ketone bodies and muscle metabolism.

1. Ketone bodies are water soluble, and are activated in mitochondria where they are metabolized (very fast).
2. The metabolism of ketone bodies and fatty acids elevates mitochondrial acetyl-CoA:
   a. Elevates mitochondrial citrate.
   b. Citrate exits mitochondria, elevates cytosolic citrate.
3. Citrate and fatty acyl-CoAs inhibit 6-PFK.
   a. Inhibition at 6-PFK causes increase of F-6-P and G-6-P.
   b. Elevation of G-6-P inhibits hexokinase, spares glucose for other tissues.



B. AMP-dependent protein kinase

1. AMP-dependent protein kinase normally stimulates glycolysis.

   a. Increases in AMP concentrations activate the protein kinase.

   b. Active AMPK induces the expression of 6-phosphofructose-2-kinase, which causes the production of fructose-2,6-bisphosphate, which strongly stimulates 6-PFK activity.

2. **AMPK and fatty acid oxidation**

   a. AMPK phosphorylates acetyl-CoA carboxylase, thereby decreasing ACC activity.

   b. Inhibition of ACC depresses malonyl-CoA concentrations, removing inhibition of CPT1.

   c. This promotes fatty acid oxidation.

Effect of 1 h swimming on metabolite concentrations in plasma and soleus muscles for 48 h-starved rats
Values are means ±S.E.M. for six to 20 observations per group. Rats swam for 1 h with a weight (4% of body wt.) tied to their tails in water maintained at 33-35° C. They were anaesthetized immediately after exercise. Plasma metabolites are expressed in μmol/ml and solus metabolites in nmol/g, except for ATP and phosphocreatine, which are in μmol/g. *Value significantly different from that of the resting group, at *P* , 0.05.

	Rest	**Post-exercise**
Plasma, μmol/mL		
Glucose	5.2 ± 0.4	4.4 ± 0.4*
Lactate	1.0 ± 0.2	2.6 ± 0.4*
Non-esterified fatty acids	0.37 ± 0.05	1.89 ± 0.12*
β-Hydroxybutyrate	0.74 ± 0.10	1.57 ± 0.10*
Soleus intermediates, nmol/g		
Glycogen	18 ± 2	17 ± 3
Citrate	231 ± 21	440 ± 20*
Glucose 6-phosphate	90 ± 20	287 ± 50*
Fluctose 6-phosphate	25 ± 5	64 ± 11*
Fructose 1,6-bisphosphate	25 ± 4	15 ± 4
High energy phosphates, μmol/g		
ATP, μmol/g	3.1 ± 0.1	3.5 ± 0.1
ADP, μmol/g	1.0 ± 0.05	0.2 ± 0.02
AMP, μmol/g	0.1 ± 0.01	0.5 ± 0.01
Phosphocreatine, μmol/g	8.8 ± 0.9	10.3 ± 1.0

C. Lactate metabolism and inhibition of PFK.

1. Lactate enters mitochondria via the monocarboxylic shuttle.
2. Lactate is converted to pyruvate via mitochondrial LDH and enters the TCA cycle.
3. The accumulation of NADH inhibits ICDH, and increases citrate levels.