Announcements

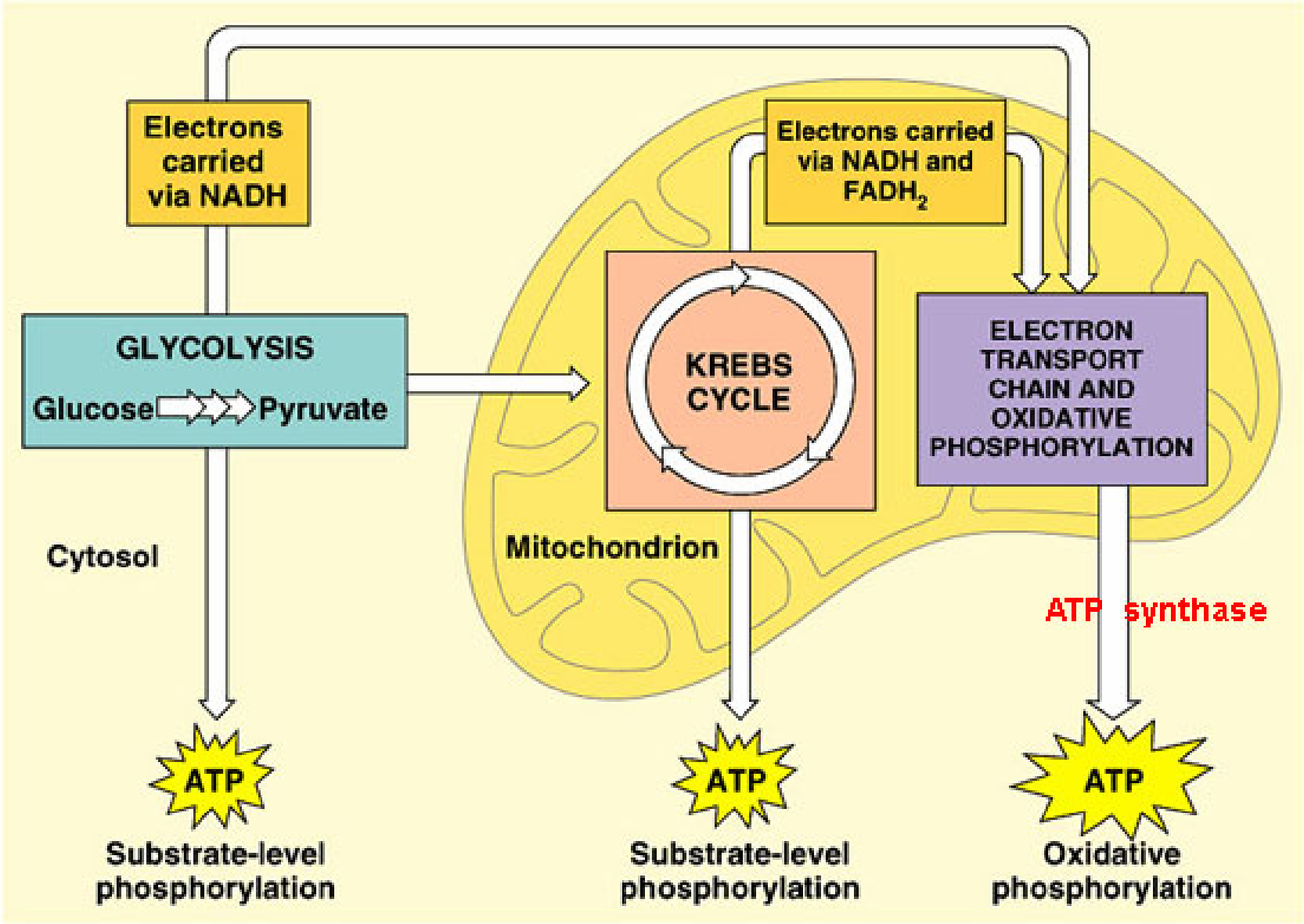
- Quiz next week
  - Chapters 16-19, 23, 12
  - Lectures thru Friday
- Office hour change
  - Tues 11-12pm
  - Wed 10-11am
- Office hours today cancelled

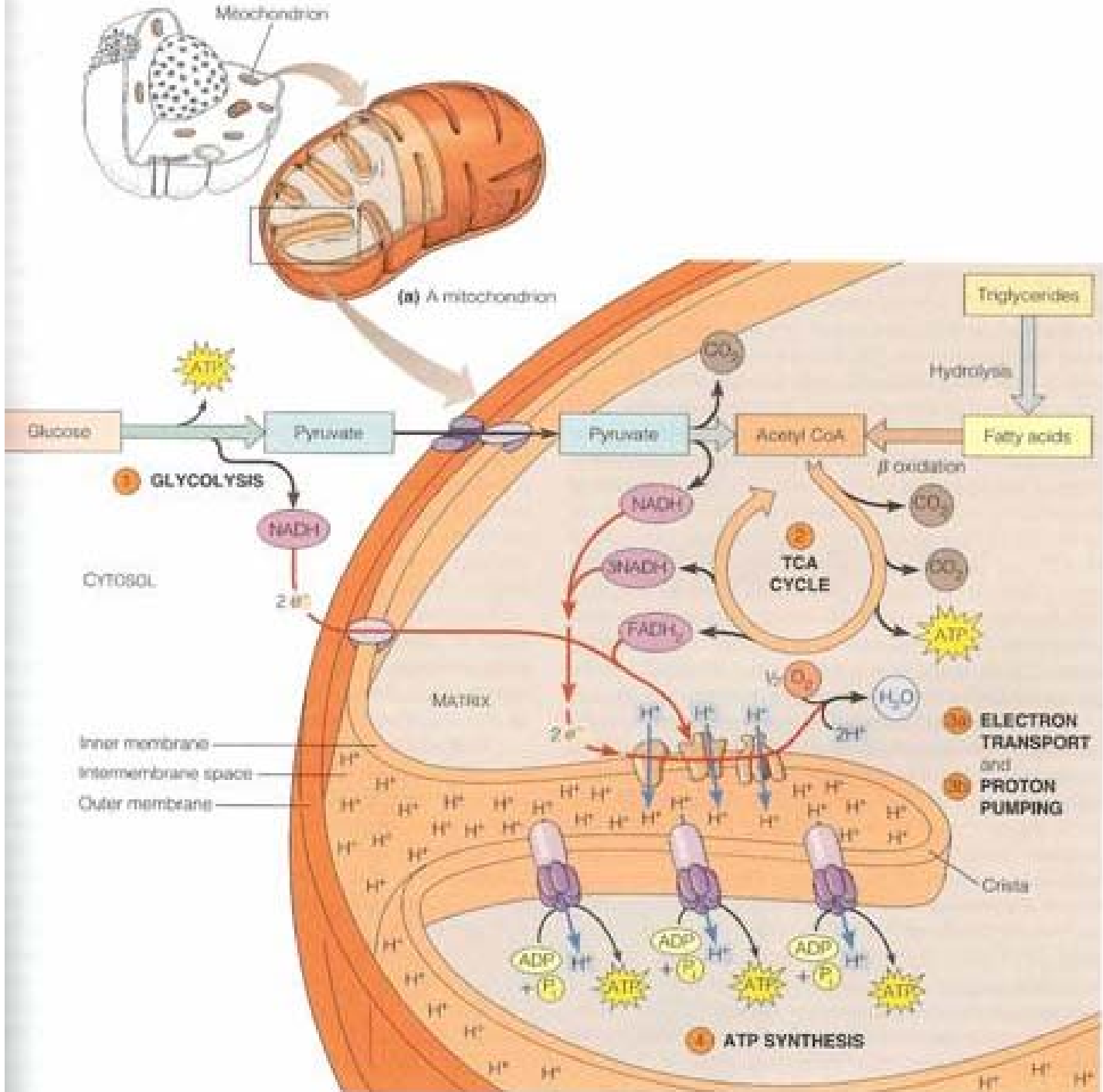
Study tips

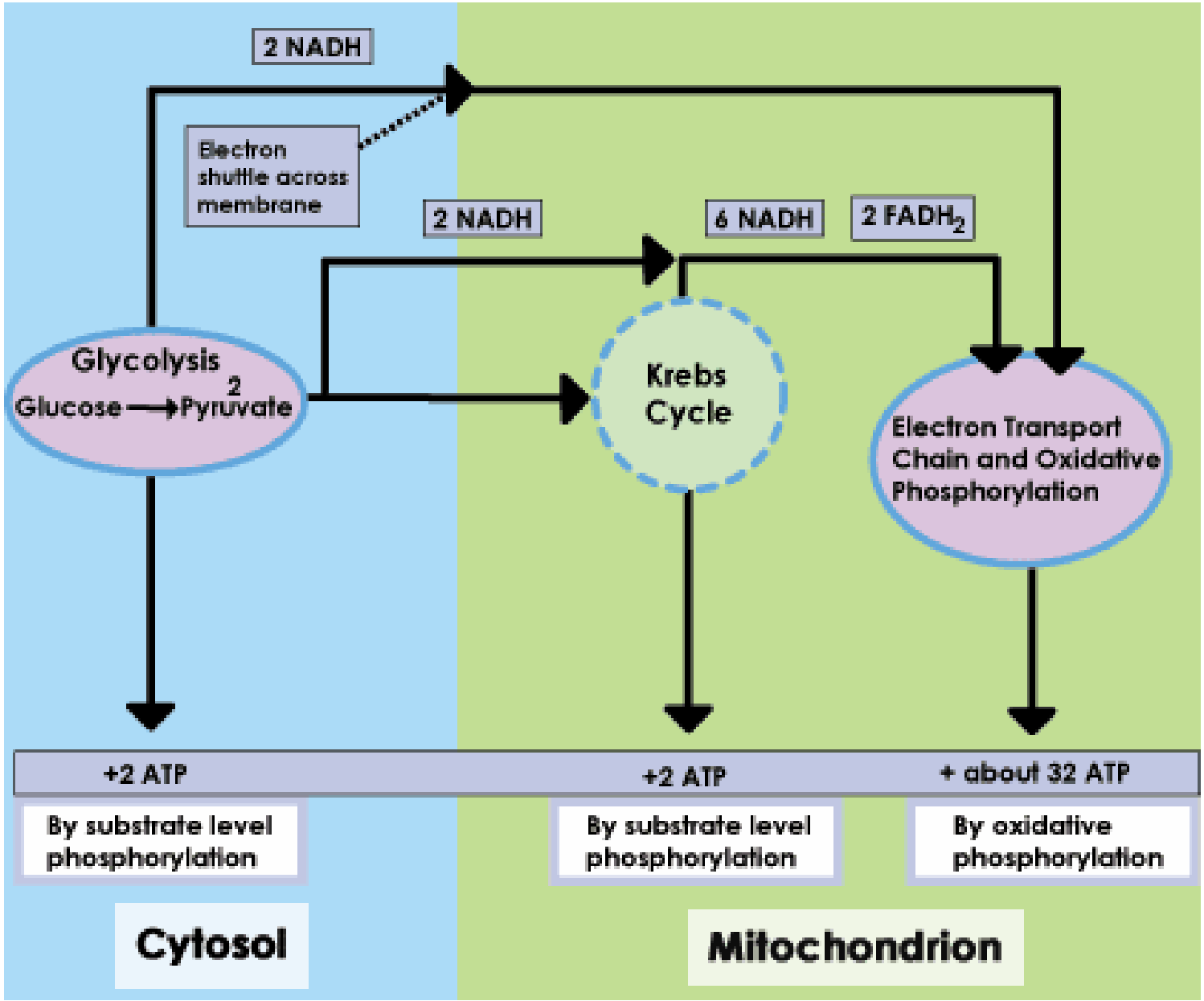
You should try to understand why each step has to occur, look at what is happening and how the names of the intermediates and enzymes reflect the structure and function.

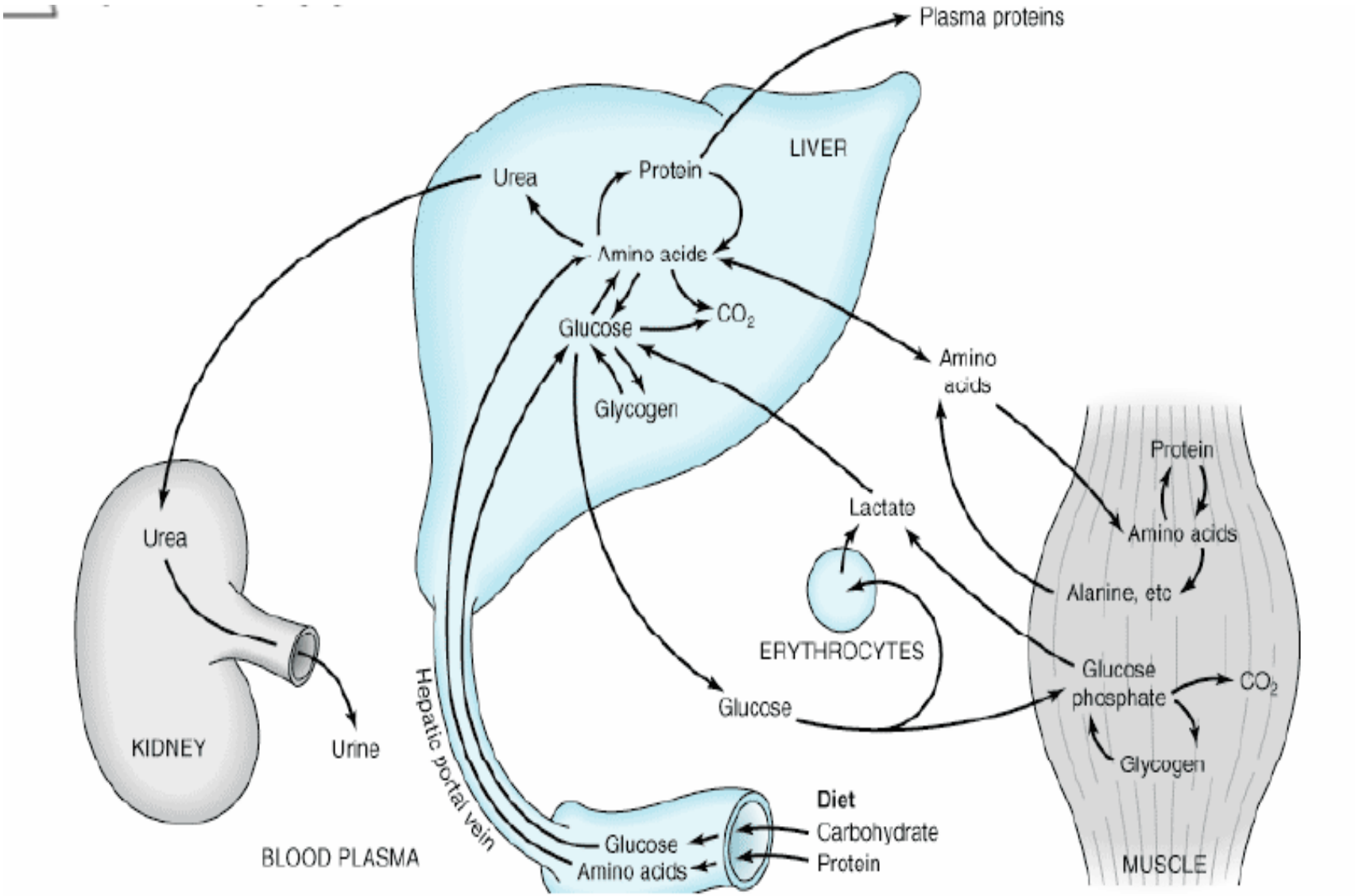
But in case you get stuck, here is an example of a mnemonic for glycolysis:

Goodness (Glucose)
Gracious, (Glucose-6-P)
Father (Fructose-6-P)
Franklin (Fructose-1,6-diP)
Did (Dihydroxyacetone-P)
Go (Glyceraldehyde-P)
By (1,3-Biphosphoglycerate)
Picking (3-phosphoglycerate)
Pumpkins (2-phosphoglycerate)
(to)
PrEPare (Phosphoenolpyruvate [PEP])
Pies (Pyruvate)

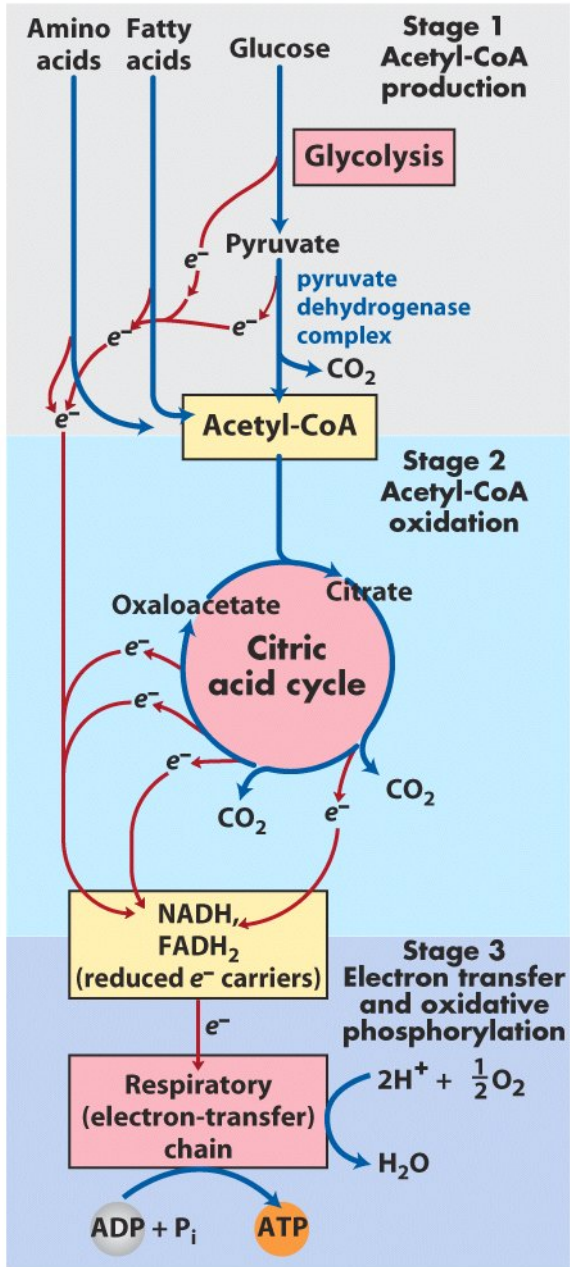


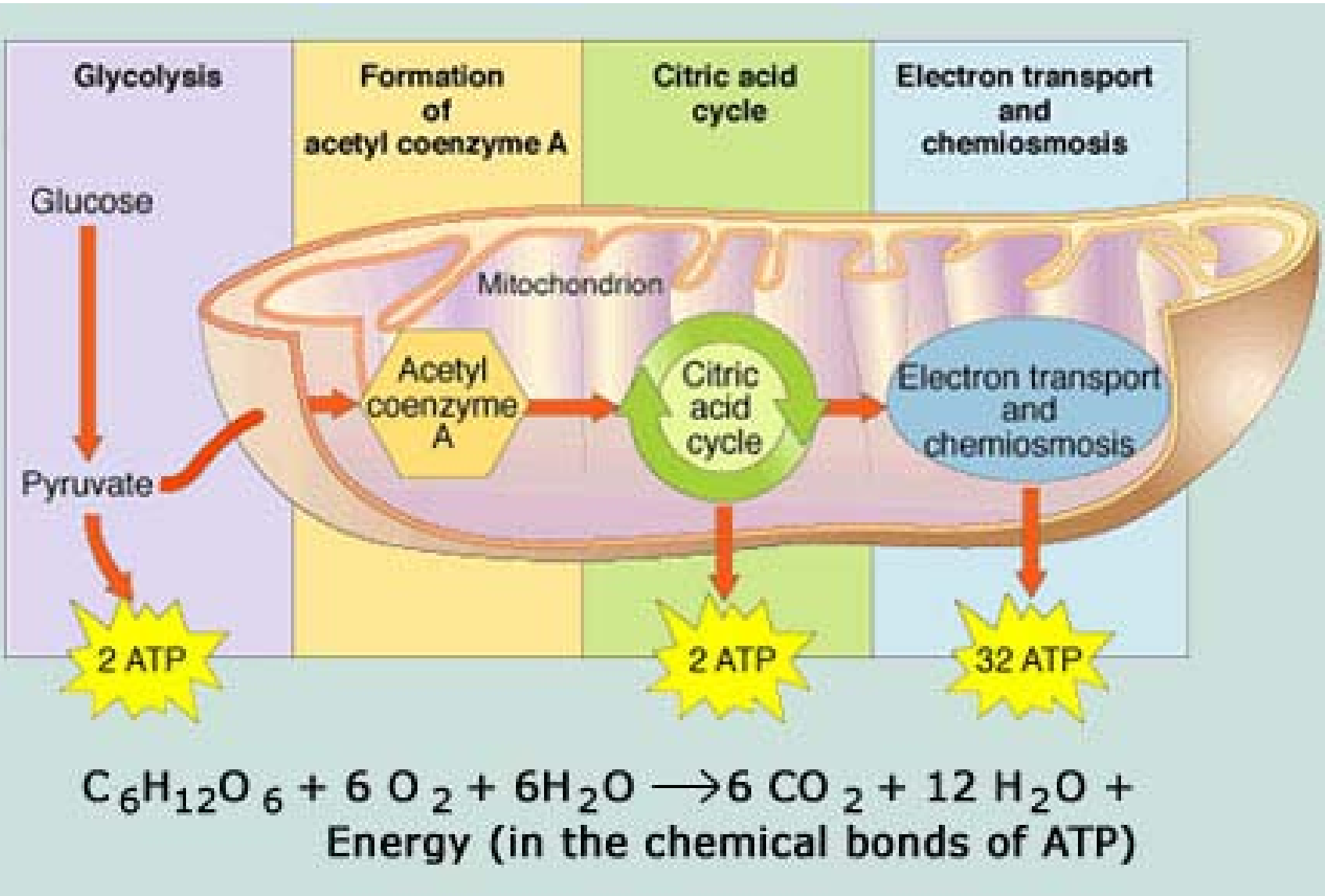

Mitochondrion
(a) A mitochondrion
Triglycerides
Hydrolysis
ATP
Glucose
Pyruvate
Pyruvate
Acetyl CoA
Fatty acids
β oxidation
1 GLYCOLYSIS
NADH
CYTOSOL
2 e⁻
NADH
FADH₂
2 TCA CYCLE
ATP
Matrix
2 e⁻
2H⁺
3a ELECTRON TRANSPORT and
3b PROTON PUMPING
Inner membrane
Intermembrane space
Outer membrane
Crista
ADP + Pi
ATP
4 ATP SYNTHESIS


2 NADH
Electron shuttle across membrane
2 NADH
6 NADH
2 FADH2
Glycolysis
Glucose → 2 Pyruvate
Krebs Cycle
Electron Transport Chain and Oxidative Phosphorylation
+2 ATP
+2 ATP
+ about 32 ATP
By substrate level phosphorylation
By substrate level phosphorylation
By oxidative phosphorylation
Cytosol
Mitochondrion

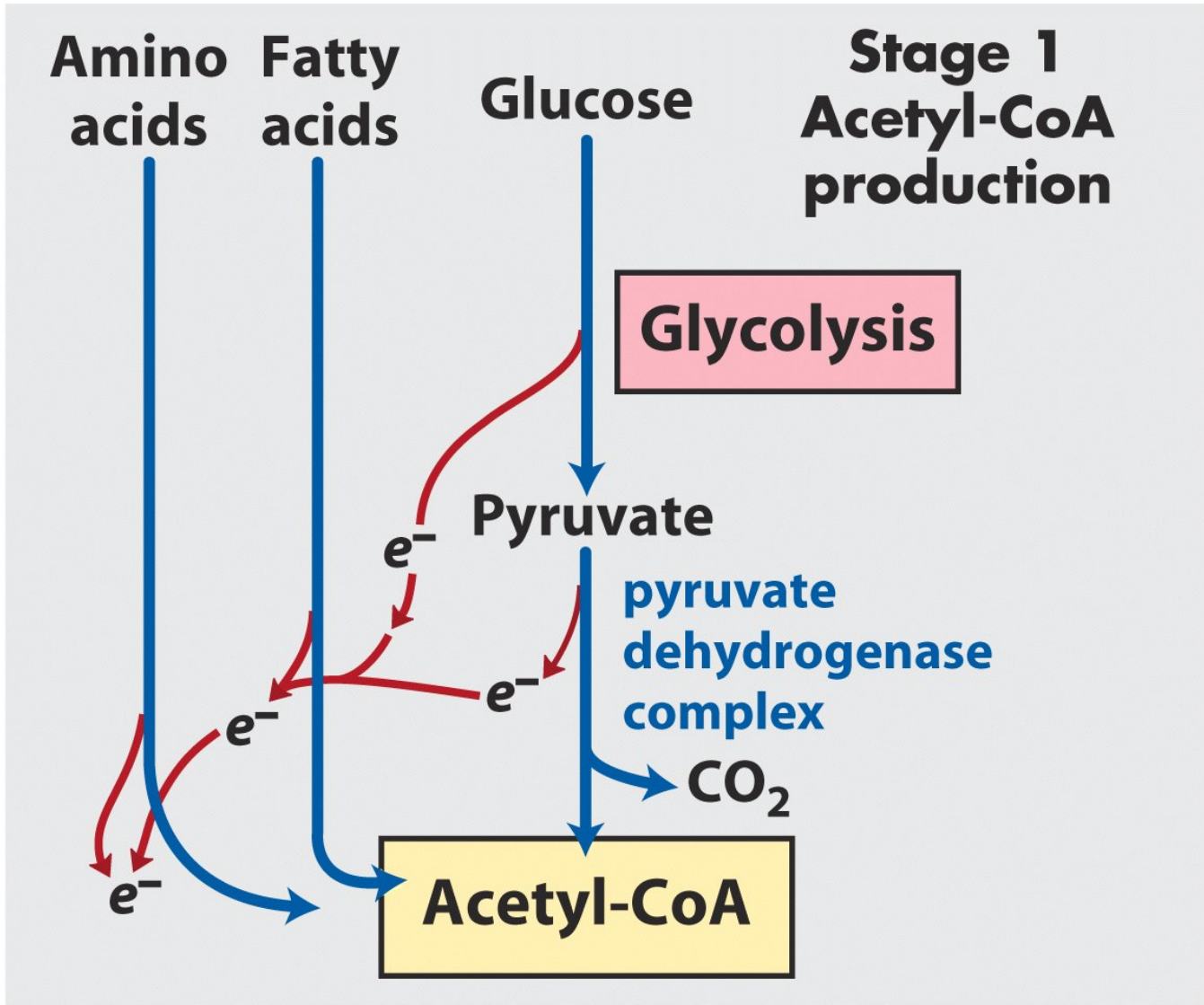

Plasma proteins
LIVER
Urea
Protein
Amino acids
Glucose
CO_2
Glycogen
Amino acids
Protein
Amino acids
Alanine, etc
Lactate
ERYTHROCYTES
Glucose
Glucose phosphate
CO_2
Glycogen
MUSCLE
Urea
KIDNEY
Urine
Hepatic portal vein
Diet
Carbohydrate
Protein
Glucose
Amino acids
BLOOD PLASMA

The Citric Acid Cycle





$$C_6H_{12}O_6 + 6\,O_2 + 6H_2O \longrightarrow 6\,CO_2 + 12\,H_2O + \text{Energy (in the chemical bonds of ATP)}$$


Amino acids
Fatty acids
Glucose
Stage 1
Acetyl-CoA
production
Glycolysis
Pyruvate
e–
e–
e–
e–
pyruvate
dehydrogenase
complex
CO2
Acetyl-CoA

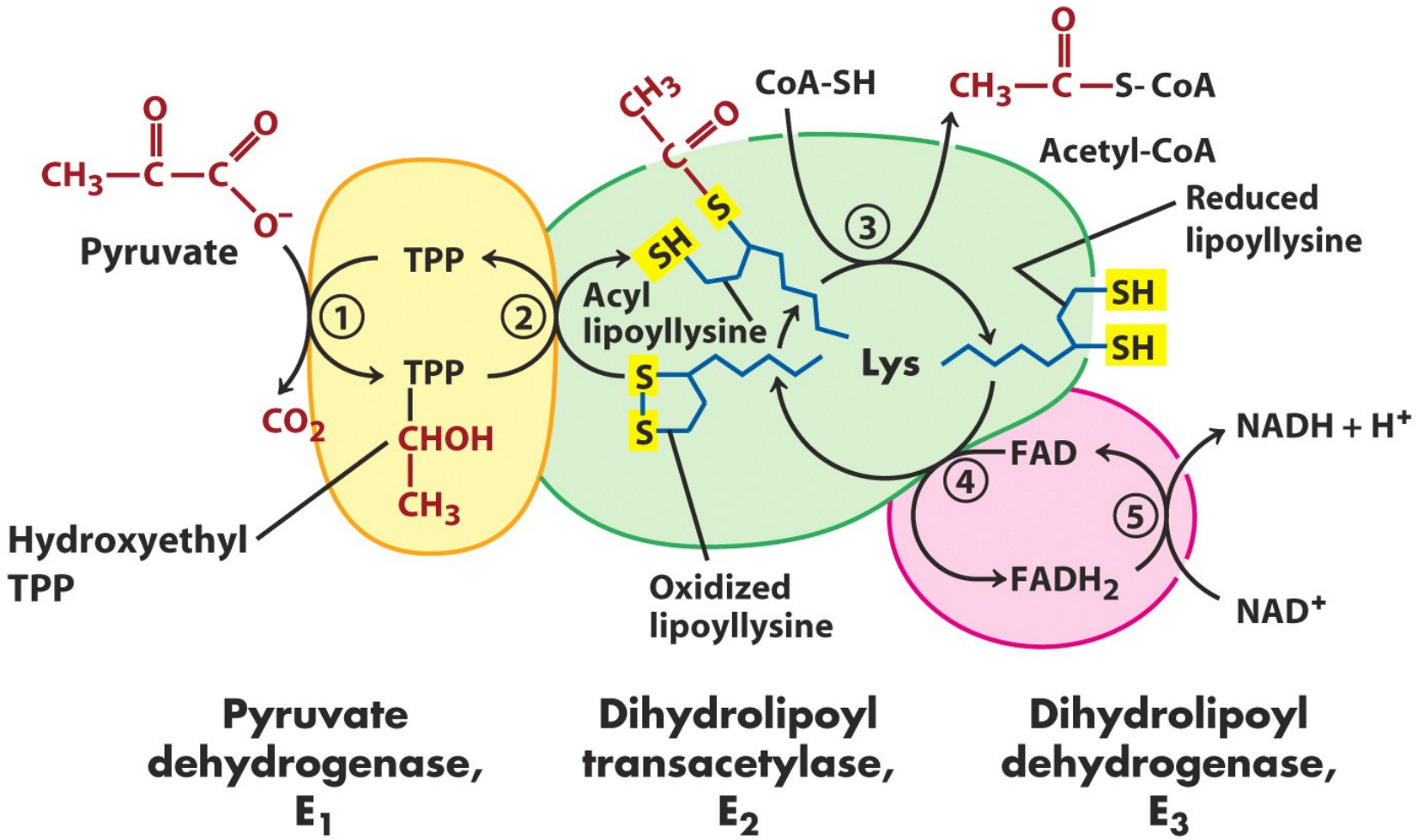
Production of acetyl-CoA (activated acetate)

Match the cofactors below with their roles in the pyruvate dehydrogenase complex reaction.

Cofactors:
A. Coenzyme A (CoA-SH)
B. NAD+
C. Thiamine pyrophosphate (TPP)
D. FAD
E. Lipoic acid in oxidized form

Roles:
_____ Attacks and attaches to the central carbon in pyruvate.
_____ Oxidizes FADH2.
_____ Accepts the acetyl group from reduced lipoic acid.
_____ Oxidizes the reduced form of lipoic acid.
_____ Initial electron acceptor in oxidation of pyruvate.

Pyruvate Dehydrogenase Complex Reaction



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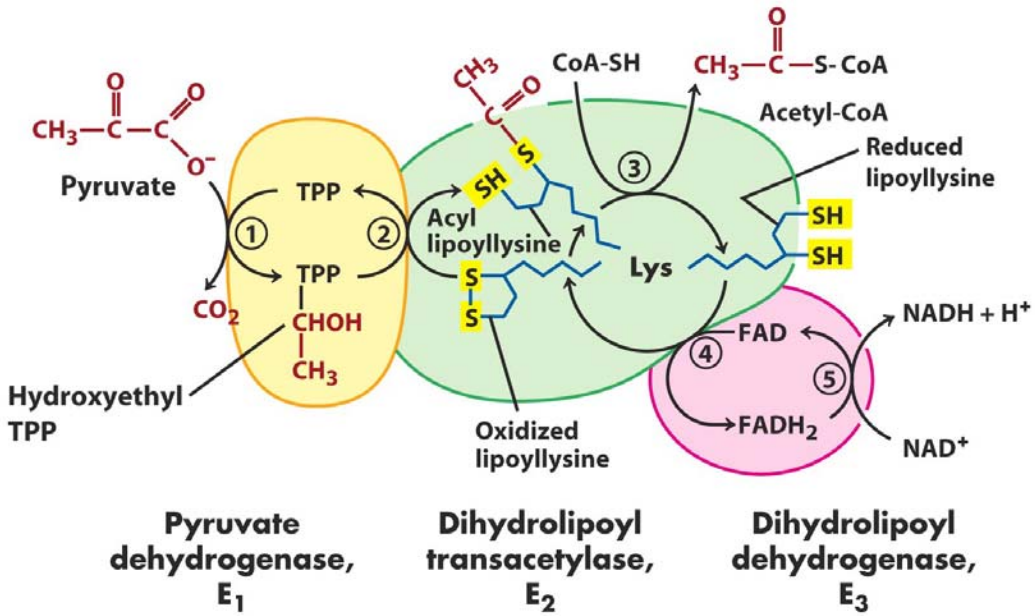
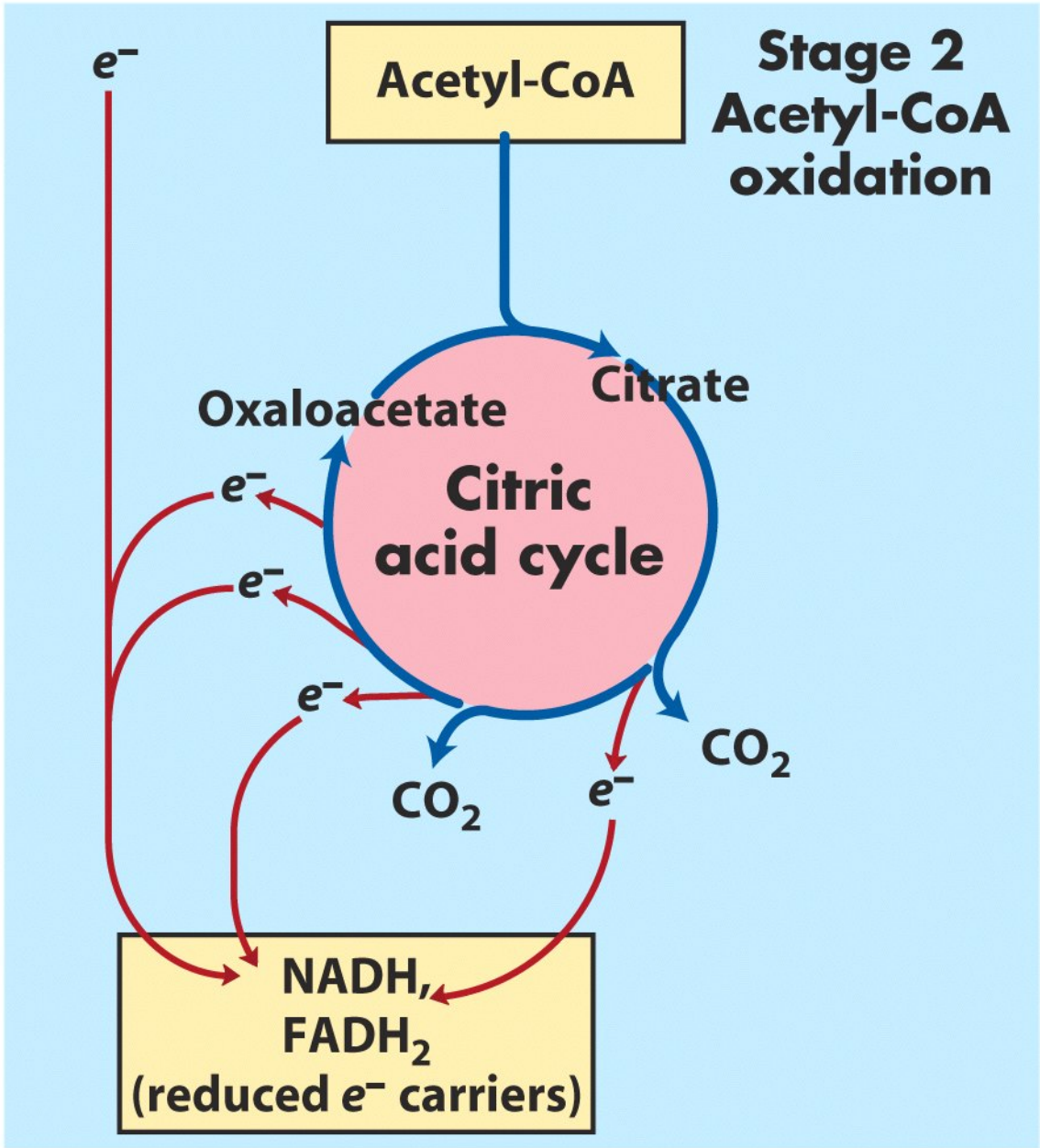
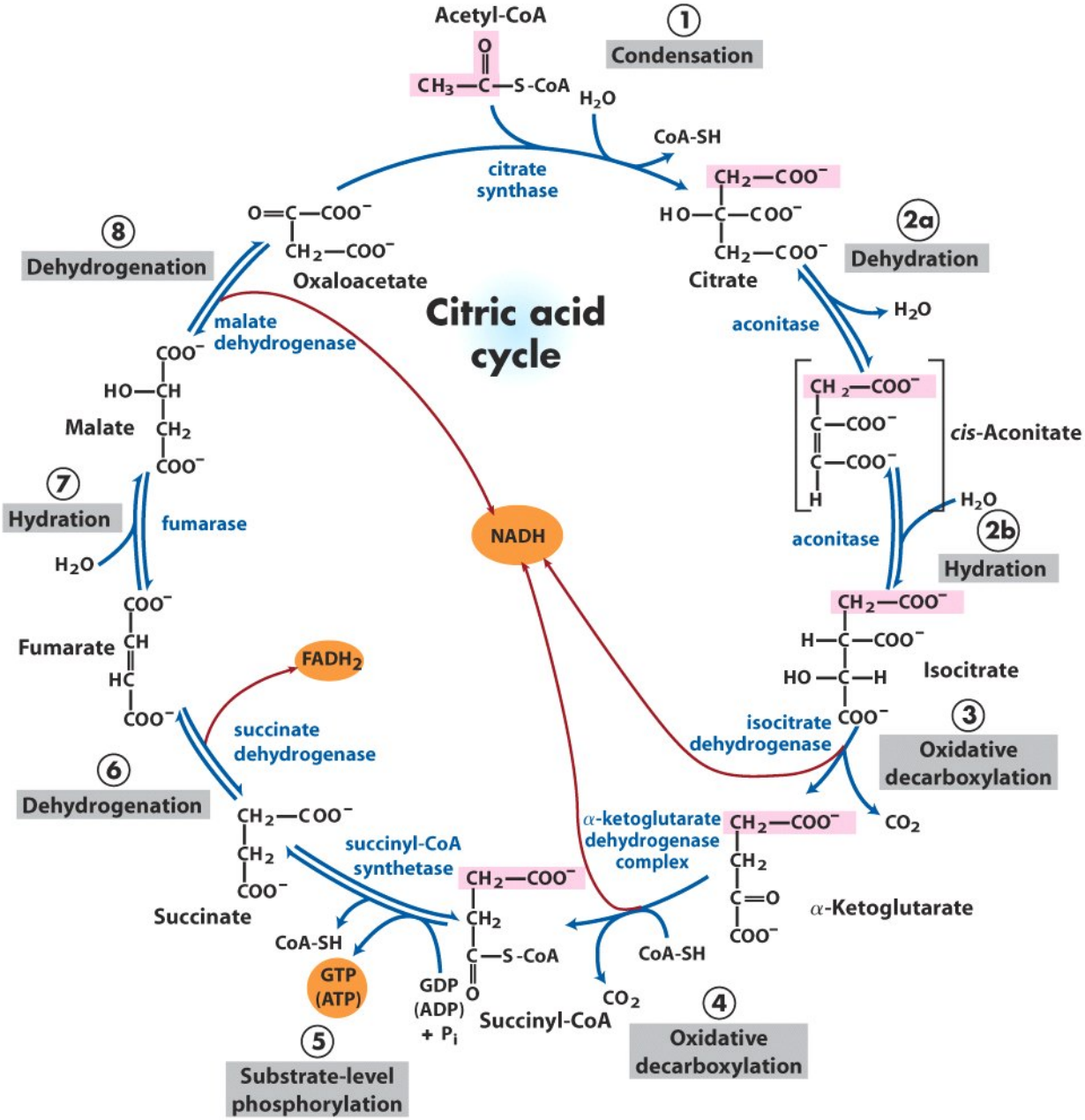


Roles:

___C___ Attacks and attaches to the central carbon in pyruvate.
___B___ Oxidizes FADH2.
___A___ Accepts the acetyl group from reduced lipoic acid.
___D___ Oxidizes the reduced form of lipoic acid.
___E___ Initial electron acceptor in oxidation of pyruvate.

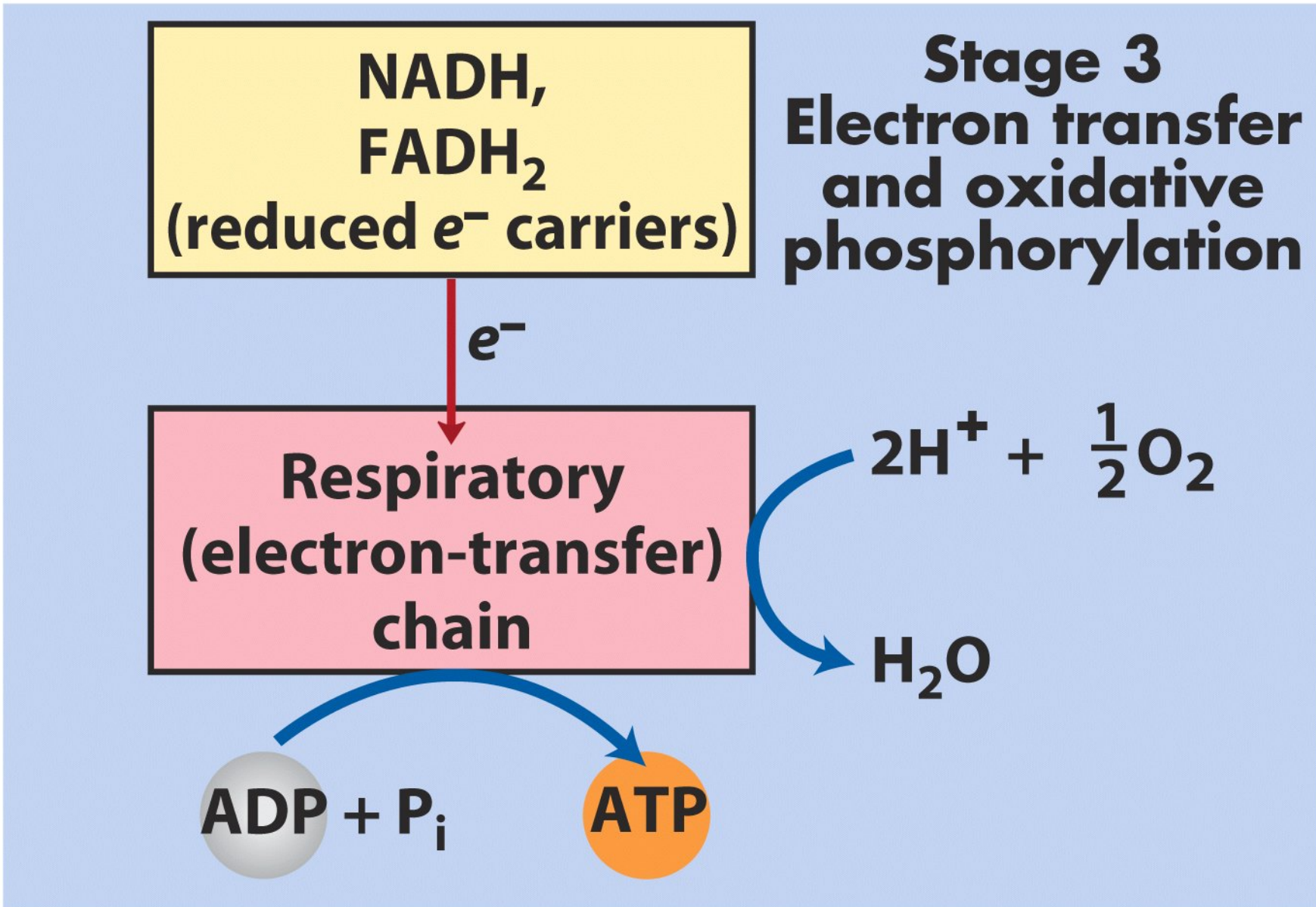

Stage 2
Acetyl-CoA
oxidation
Acetyl-CoA
e⁻
Citrate
Oxaloacetate
Citric
acid cycle
e⁻
e⁻
e⁻
CO2
CO2
e⁻
NADH,
FADH2
(reduced e⁻ carriers)

The citric acid cycle is frequently described as the major pathway of aerobic catabolism, which means that it is an oxygen-dependent degradative process. However, none of the reactions of the cycle directly involves oxygen as a reactant. Why is the pathway oxygen-dependent?

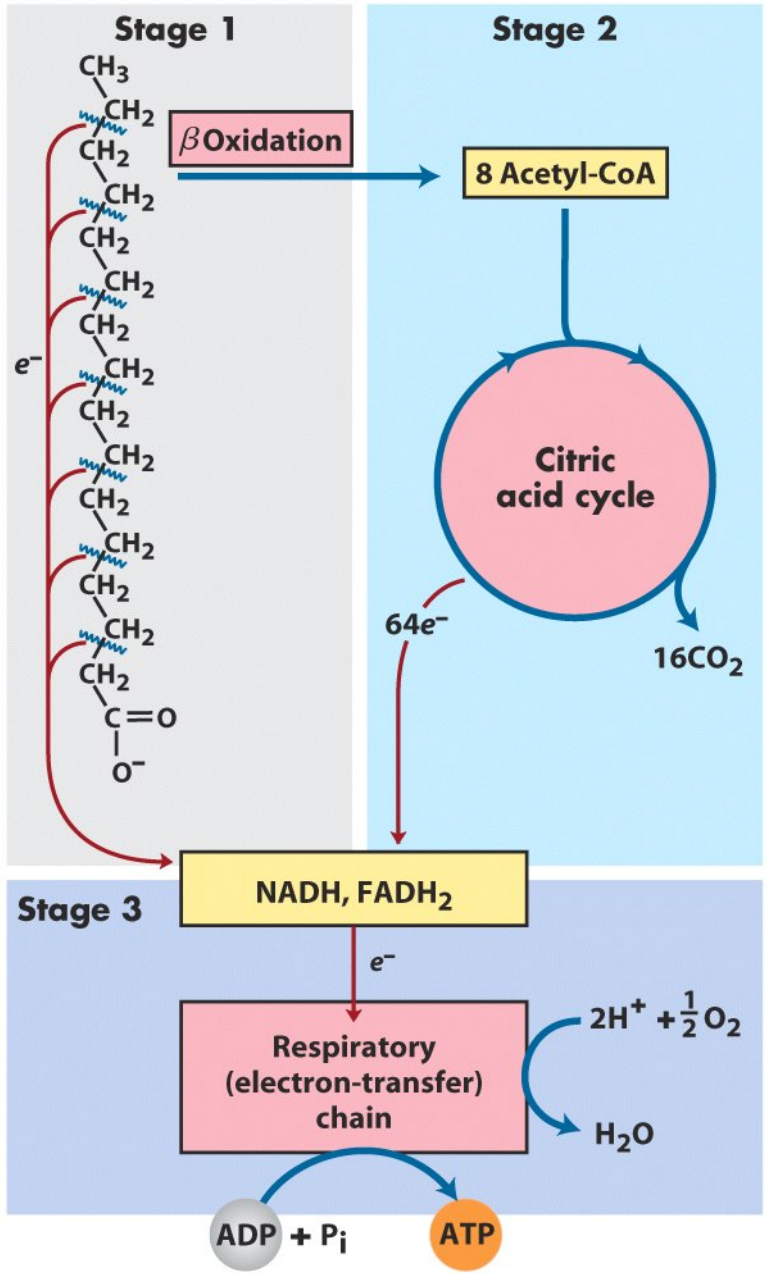

Citric acid cycle
Acetyl-CoA
1
Condensation
H_2O
CoA-SH
citrate synthase
Oxaloacetate
Citrate
2a
Dehydration
aconitase
H_2O
cis-Aconitate
aconitase
H_2O
2b
Hydration
Isocitrate
isocitrate dehydrogenase
3
Oxidative decarboxylation
CO_2
NADH
α-ketoglutarate dehydrogenase complex
α-Ketoglutarate
CoA-SH
CO_2
4
Oxidative decarboxylation
Succinyl-CoA
GDP (ADP) + P_i
GTP (ATP)
5
Substrate-level phosphorylation
succinyl-CoA synthetase
Succinate
CoA-SH
$FADH_2$
succinate dehydrogenase
6
Dehydrogenation
Fumarate
H_2O
7
Hydration
fumarase
Malate
8
Dehydrogenation
malate dehydrogenase

The citric acid cycle is frequently described as the major pathway of aerobic catabolism, which means that it is an oxygen-dependent degradative process. However, none of the reactions of the cycle directly involves oxygen as a reactant. Why is the pathway oxygen-dependent?

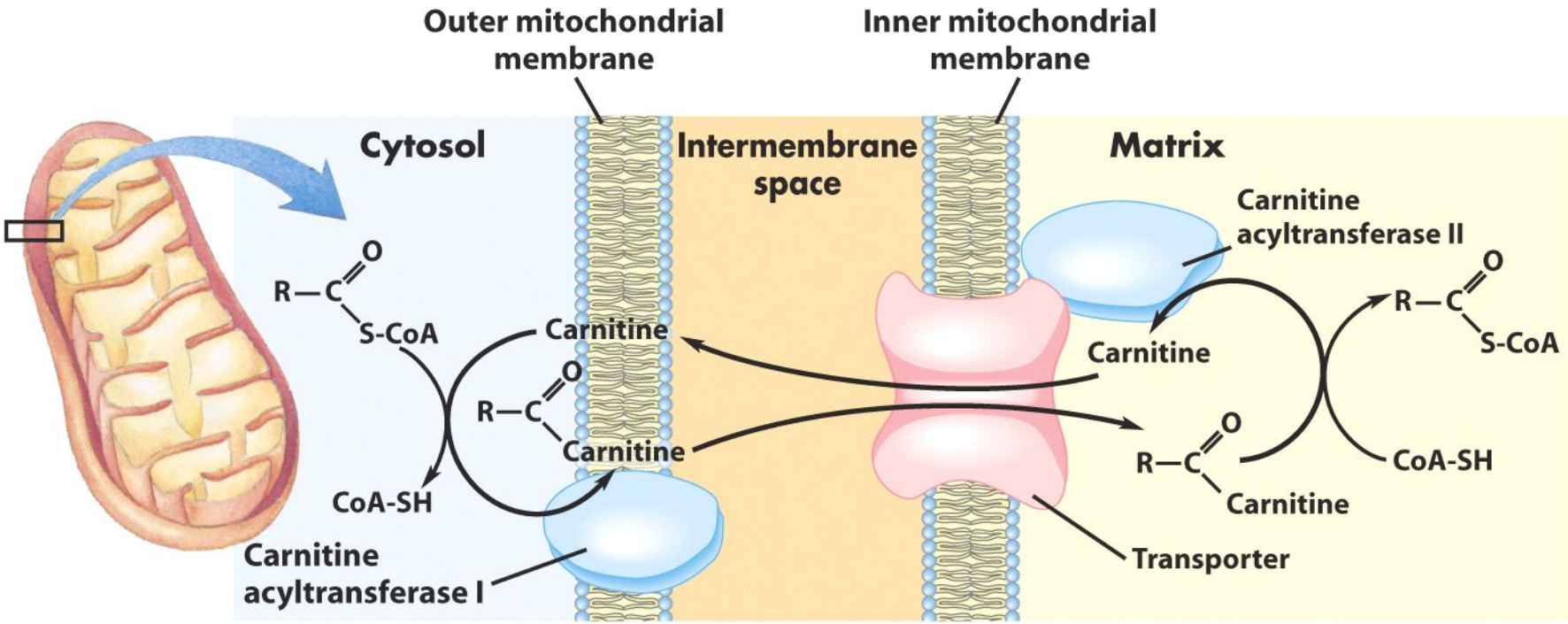
Ans: The citric acid cycle produces NADH, which normally is recycled by passage of electrons from NADH to O2 via the respiratory chain. With no O2 to accept electrons from NADH, the accumulation of NADH effectively stops the citric acid cycle.


NADH,
FADH2
(reduced e– carriers)
Stage 3
Electron transfer
and oxidative
phosphorylation
e–
Respiratory
(electron-transfer)
chain
2H+ + ½O2
H2O
ADP + Pi
ATP

β–oxidation


Stage 1
Stage 2
Stage 3
βOxidation
8 Acetyl-CoA
Citric acid cycle
64e⁻
16CO2
NADH, FADH2
e⁻
Respiratory (electron-transfer) chain
2H⁺ + ½O2
H2O
ADP + Pi
ATP

The oxidation of acetyl-CoA added to isolated, intact mitochondria is stimulated strongly by carnitine. Why?


Outer mitochondrial membrane
Inner mitochondrial membrane
Cytosol
Intermembrane space
Matrix
Carnitine acyltransferase II
R—C(=O)—S-CoA
Carnitine
R—C(=O)—Carnitine
CoA-SH
Carnitine acyltransferase I
Carnitine
R—C(=O)—S-CoA
R—C(=O)—Carnitine
CoA-SH
Transporter

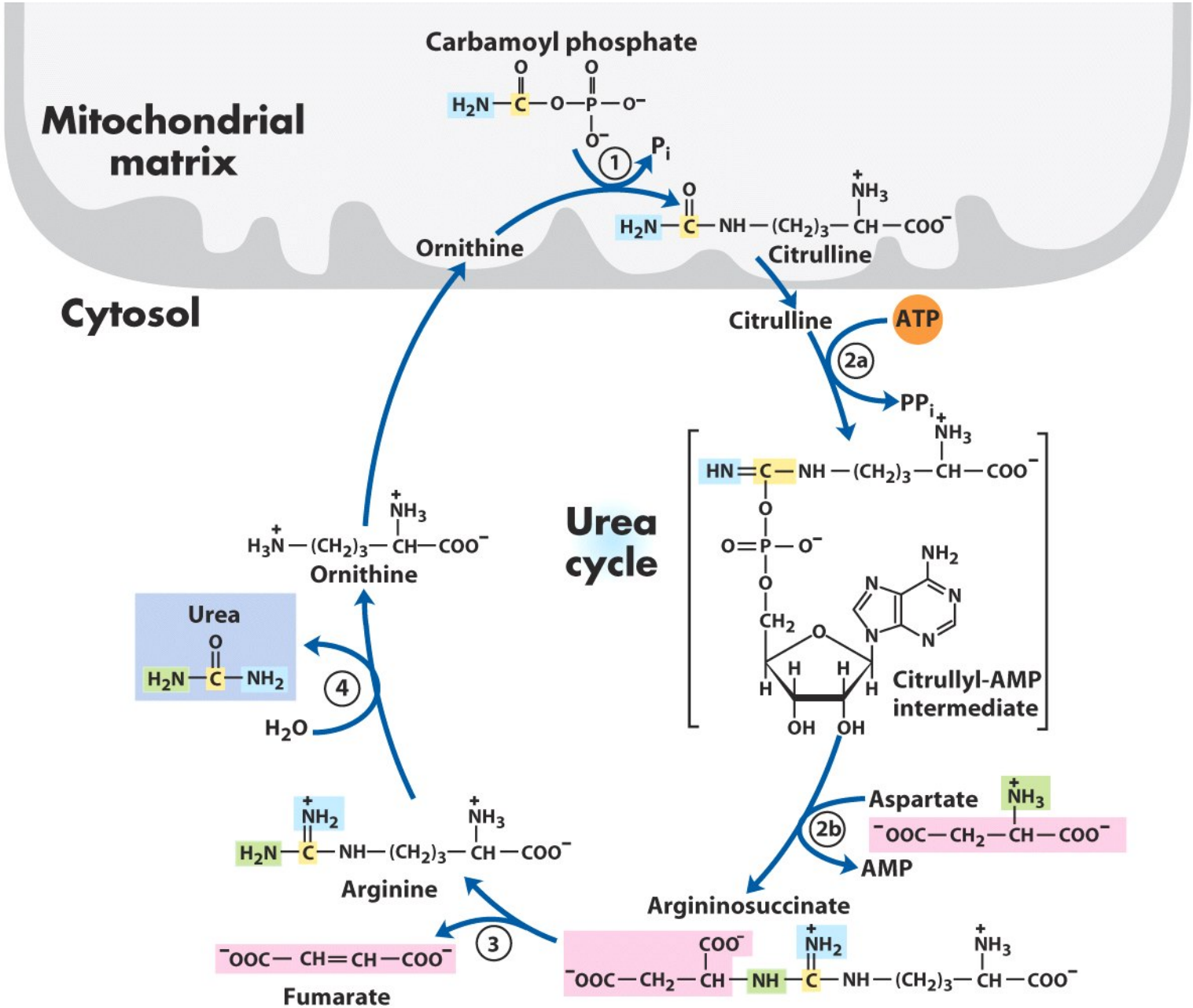
The oxidation of acetyl-CoA added to isolated, intact mitochondria is stimulated strongly by carnitine. Why?

Ans: Carnitine is essential in the transport of fatty acyl groups into the mitochondrial matrix, where fatty acid oxidation occurs.

Nitrogen excretion and the urea cycle

Which substance is *not* involved in the production of urea from NH4+ via the urea cycle?

A. Aspartate
B. ATP
C. Carbamoyl phosphate
D. Malate
E. Ornithine


Mitochondrial matrix
Cytosol
Carbamoyl phosphate
Ornithine
Citrulline
Citrulline
ATP
2a
PPi
Urea cycle
Citrullyl-AMP intermediate
Aspartate
2b
AMP
Argininosuccinate
3
Fumarate
Arginine
4
H2O
Urea
Ornithine

Nitrogen excretion and the urea cycle

Which substance is *not* involved in the production of urea from NH4+ via the urea cycle?

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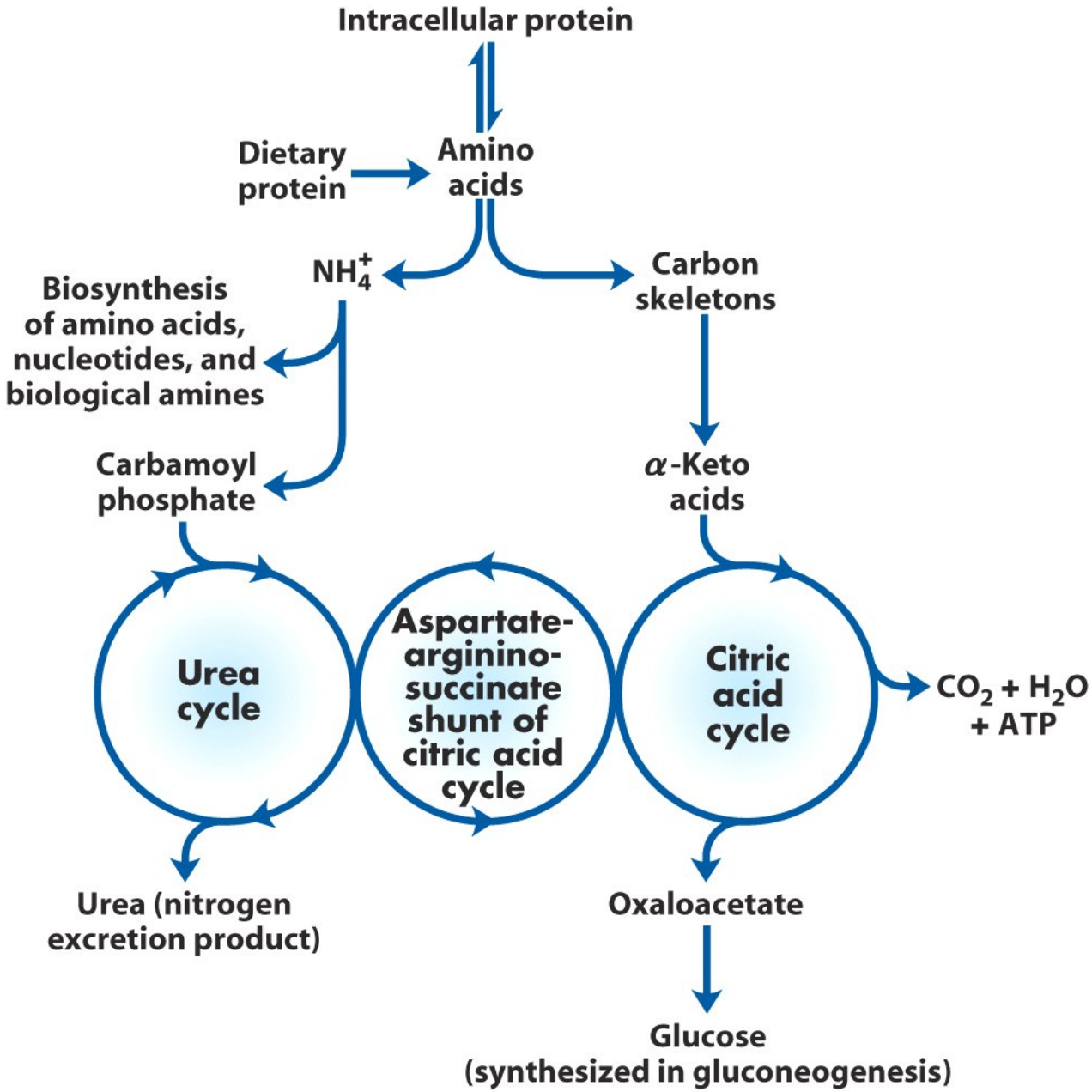
E. Ornithine

If a person's urine contains unusually high concentrations of urea, which one of the following diets has he or she probably been eating recently?

A. High carbohydrate, very low protein
B. Very high carbohydrate, no protein, no fat
C. Very very high fat, high carbohydrate, no protein
D. Very high fat, very low protein
E. Very low carbohydrate, very high protein


Intracellular protein
Dietary protein
Amino acids
NH_4^+
Carbon skeletons
Biosynthesis of amino acids, nucleotides, and biological amines
Carbamoyl phosphate
α-Keto acids
Urea cycle
Aspartate-arginino-succinate shunt of citric acid cycle
Citric acid cycle
$CO_2 + H_2O$ + ATP
Urea (nitrogen excretion product)
Oxaloacetate
Glucose (synthesized in gluconeogenesis)

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C. Very very high fat, high carbohydrate, no protein
D. Very high fat, very low protein
E. Very low carbohydrate, very high protein

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