Lec. 2 /2 nd term Biochemistry II
3 rd stage

The citric acid cycle

By

Ph. Dr. SAFA W. AZIZ

" Citric acid cycle is the final common pathway for the complete oxidation of acetyl CoA to CO_2 & generating energy."

Also called as common metabolic pathway because it acts as the final common pathway for the oxidation of carbohydrate, fat & proteins.

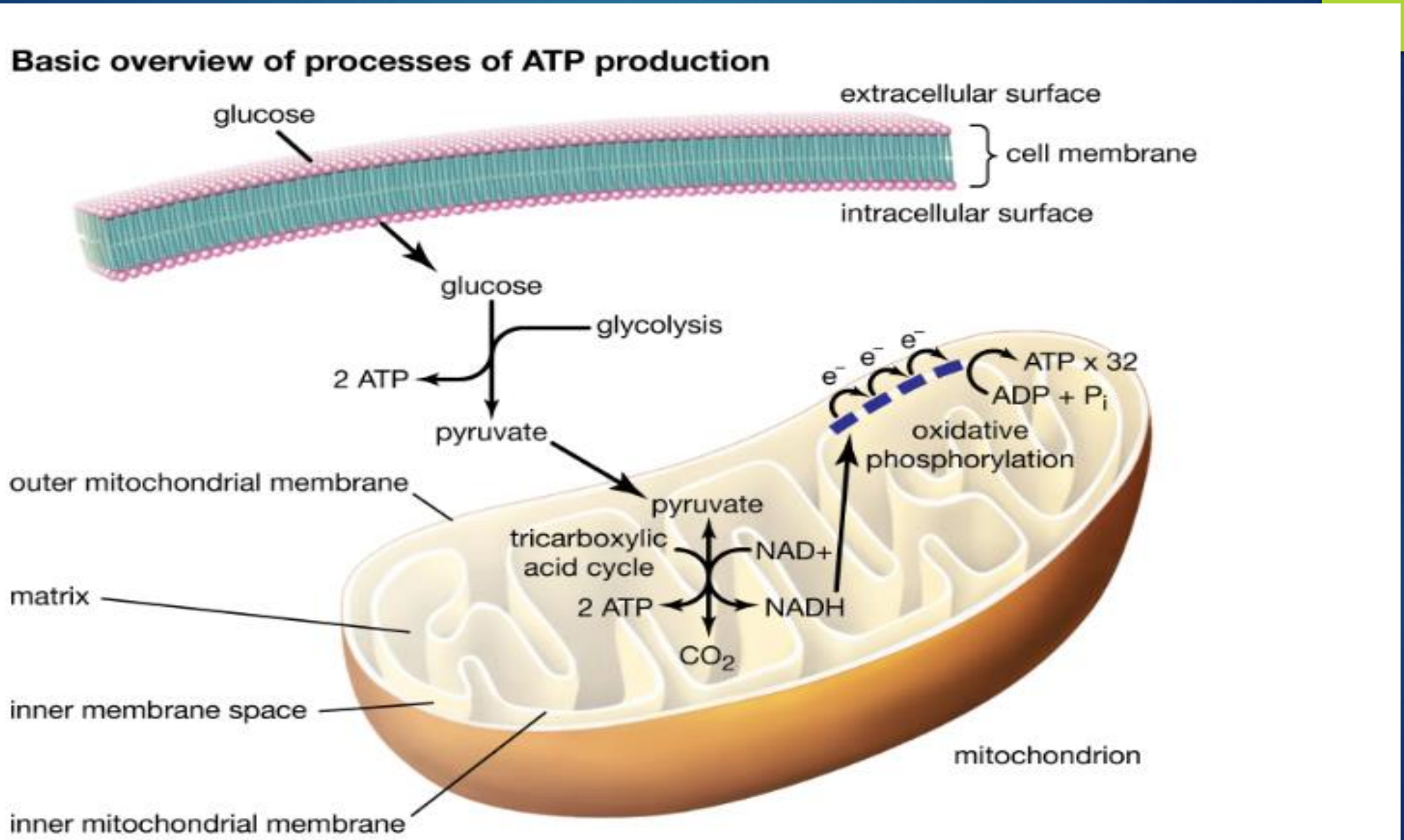
The acetyl CoA, the product of CHO, lipid & protein catabolism is taken into the cycle, together with H_2O & oxidized to CO_2 with release of reducing equivalents.

SITE : **All tissues except mature RBC's.**

Mitochondrial matrix.

Importance of TCA

- ATP production
- common catabolic pathway for all nutrients
- It is a major source of succinyl-CoA which is used for:
  - Synthesis of hemoglobin and other porphyrins.
  - Ketolysis:
  - Detoxication by conjugation
- It provides intermediates for synthesis of non-essential amino acids, e.g.,
  - α-Ketoglutarate can give rise to glutamic acid by transamination.
  - Oxaloacetate can give rise to asparatic acid by transamination.
- It is an amphibolic pathway for gluconeogenesis, transamination, deamination, and lipogenesis particularly in the liver


Basic overview of processes of ATP production
extracellular surface
glucose
cell membrane
intracellular surface
glucose
glycolysis
2 ATP
pyruvate
e⁻
e⁻
e⁻
e⁻
ATP x 32
ADP + Pi
oxidative
phosphorylation
outer mitochondrial membrane
pyruvate
tricarboxylic
acid cycle
NAD+
matrix
2 ATP
NADH
CO2
inner membrane space
mitochondrion
inner mitochondrial membrane

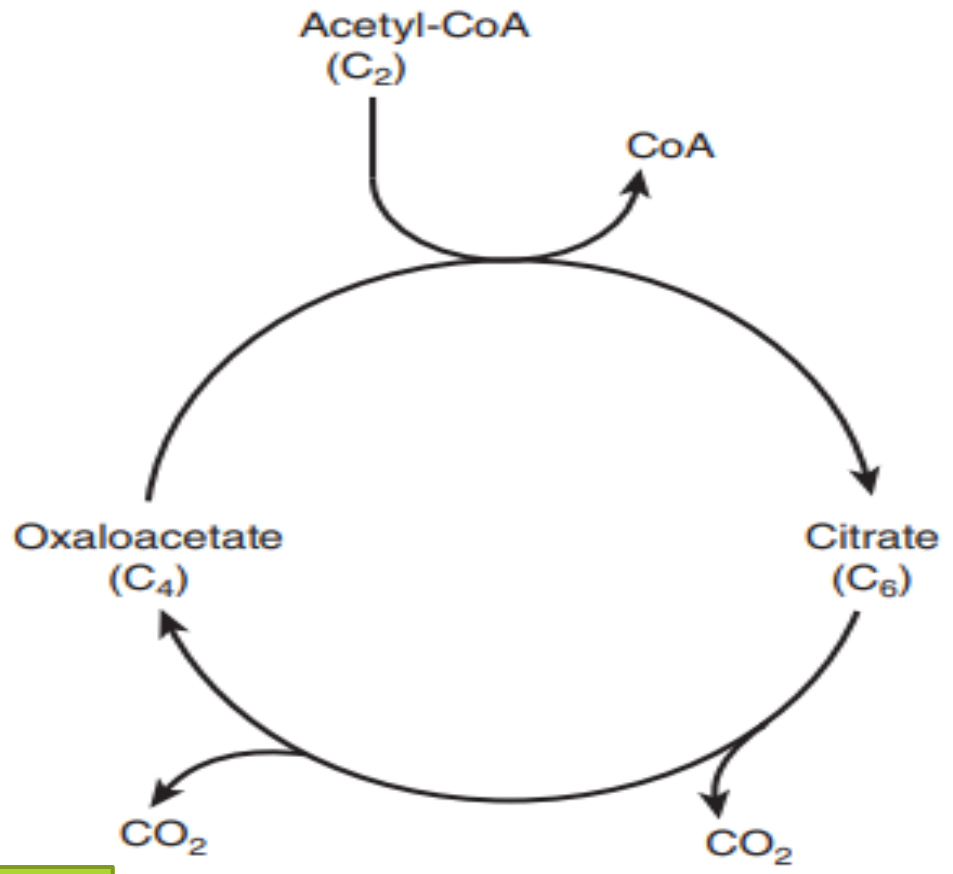


FIGURE 1 The citric acid cycle, illustrating the catalytic role of oxaloacetate.

Carbohydrate

protien

Lipids

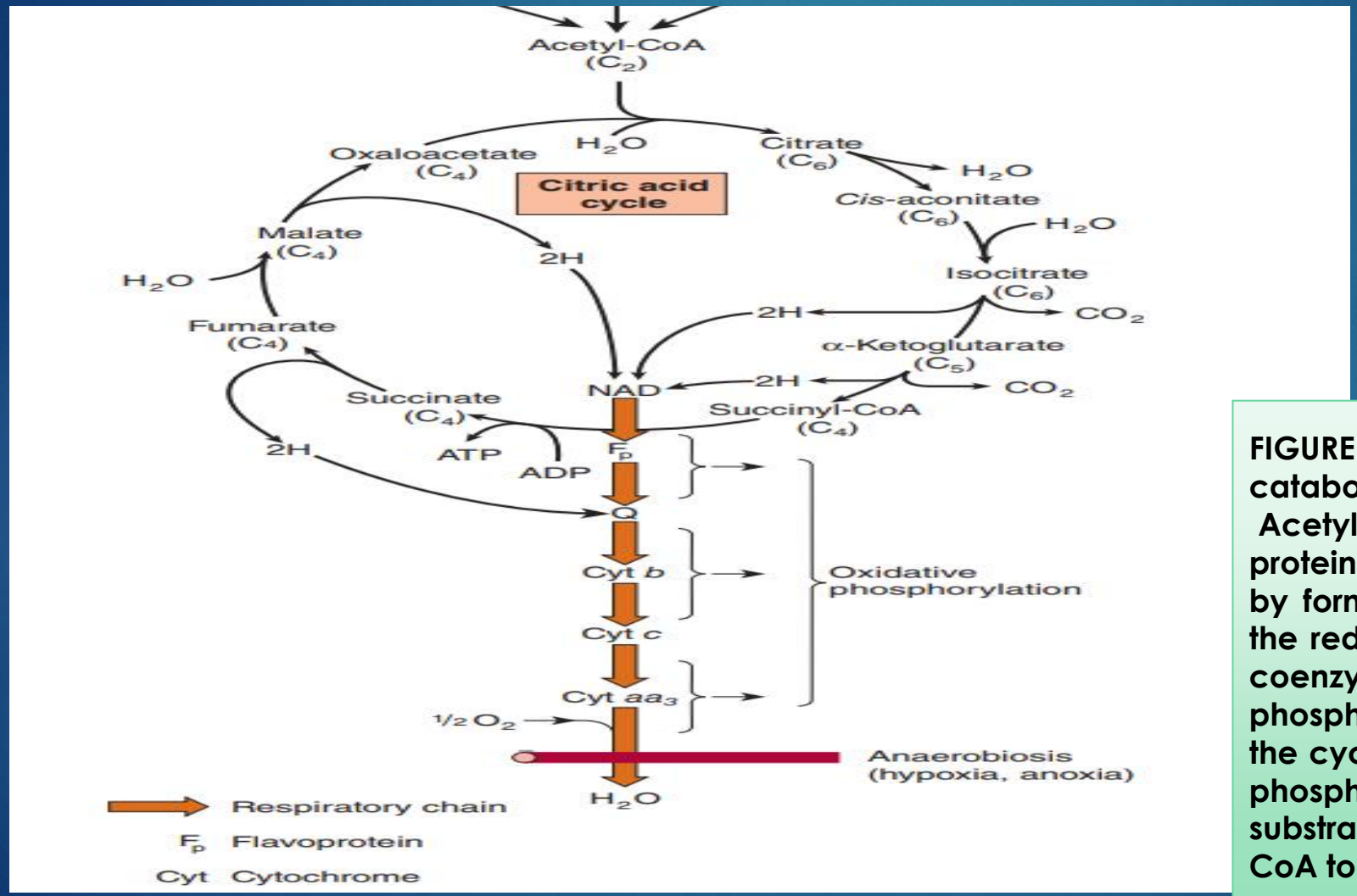
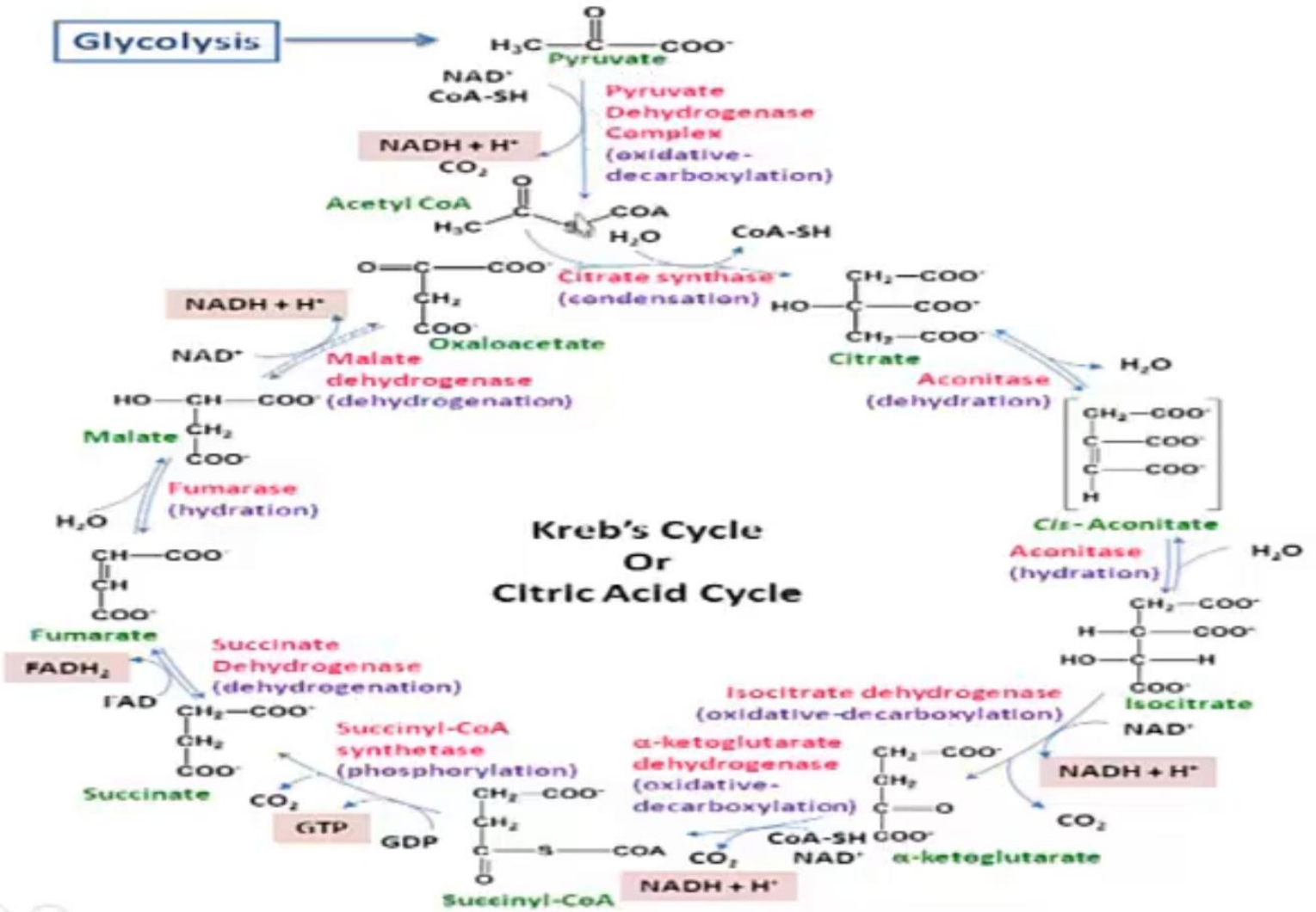


FIGURE 2: **The citric acid cycle: the major catabolic pathway for acetyl-CoA.**

Acetyl-CoA, the product of carbohydrate, protein, and lipid catabolism, enters the cycle by forming citrate and is oxidized to CO2 with the reduction of coenzymes. Reoxidation of the coenzymes in the respiratory chain leads to the phosphorylation of ADP to ATP. For one turn of the cycle, nine ATP are generated via oxidative phosphorylation and one ATP (or GTP) arises at substrate level from the conversion of succinyl-CoA to succinate.


Glycolysis
Pyruvate
NAD+
CoA-SH
NADH + H+
CO2
Pyruvate Dehydrogenase Complex (oxidative-decarboxylation)
Acetyl CoA
COA
H2O
CoA-SH
Citrate synthase (condensation)
Oxaloacetate
NADH + H+
NAD+
Malate dehydrogenase (dehydrogenation)
Malate
Fumarase (hydration)
H2O
Fumarate
FADH2
FAD
Succinate Dehydrogenase (dehydrogenation)
Succinate
Succinyl-CoA synthetase (phosphorylation)
CO2
GTP
GDP
Succinyl-CoA
Kreb's Cycle
Or
Citric Acid Cycle
Citrate
Aconitase (dehydration)
H2O
Cis-Aconitate
Aconitase (hydration)
H2O
Isocitrate
Isocitrate dehydrogenase (oxidative-decarboxylation)
NAD+
NADH + H+
CO2
α-ketoglutarate dehydrogenase (oxidative-decarboxylation)
CO2
CoA-SH
NAD+
NADH + H+
α-keteglutarate

THE CITRIC ACID CYCLE PROVIDES SUBSTRATES FOR THE RESPIRATORY CHAIN

- The cycle starts with reaction between the acetyl moiety of acetyl-CoA and the four-carbon dicarboxylic acid oxaloacetate, forming a six-carbon tricarboxylic acid, citrate. In the subsequent reactions, two molecules of CO_2 are released, and oxaloacetate is regenerated (Figure 1). Only a small quantity of oxaloacetate is needed for the oxidation of a large quantity of acetyl-CoA; it can be considered as playing a catalytic role, since it is regenerated at the end of the cycle. The citric acid cycle provides the main pathway for ATP formation linked to the oxidation of metabolic fuels. During the oxidation of acetyl-CoA, coenzymes are reduced and subsequently reoxidized in the respiratory chain, linked to the formation of ATP (oxidative phosphorylation, Figure 2). This process is aerobic, requiring oxygen as the final oxidant of the reduced coenzymes. The enzymes of the citric acid cycle are located in the mitochondrial matrix, either free or attached to the inner mitochondrial membrane and the crista membrane, where the enzymes and coenzymes of the respiratory chain are also found.

REACTIONS OF THE CITRIC ACID CYCLE

- In the TCA cycle, oxaloacetate is first condensed with an acetyl group from acetyl coenzyme A (CoA), and then is regenerated as the cycle is completed.
- Thus, the entry of one acetyl CoA into one round of the TCA cycle does not lead to the net production or consumption of intermediates.
- Two carbons entering the cycle as acetyl CoA are balanced by two CO2 exiting.
- The initial reaction between acetyl-CoA and oxaloacetate to form citrate is catalyzed by citrate synthase, which forms a carbon-carbon bond between the methyl carbon of acetylCoA and the carbonyl carbon of oxaloacetate (Figure 3). The thioester bond of the resultant citryl-CoA is hydrolyzed, releasing citrate and CoASH—an exothermic reaction.

- Citrate is isomerized to isocitrate by the enzyme aconitase (aconitate hydratase);

- dehydration to cis-aconitate and 2- rehydration to isocitrate.
- Although citrate is a symmetric molecule, aconitase reacts with citrate asymmetrically, so that the two carbon atoms that are lost in subsequent reactions of the cycle are not those that were added from acetyl-CoA. This asymmetric behavior is the result of channeling—transfer of the product of citrate synthase directly onto the active site of aconitase, without entering free solution. This provides integration of citric acid cycle activity and the provision of citrate in the cytosol as a source of acetyl-CoA for fatty acid synthesis. Citrate is only available in free solution to be transported from the mitochondria to the cytosol for fatty acid synthesis when aconitase is inhibited by accumulation of its product, isocitrate.

- The poison fluoracetate is found in some of plants, and their consumption can be fatal to grazing animals. Some **fluorinated compounds** used as **anticancer** agents and industrial chemicals (including pesticides) are metabolized to fluoroacetate. It is toxic because fluoroacetyl-CoA condenses with oxaloacetate to form fluorocitrate, which inhibits aconitase, causing citrate to accumulate Isocitrate undergoes dehydrogenation catalyzed by isocitrate dehydrogenase to form, initially, oxalosuccinate, which remains enzyme bound and undergoes decarboxylation to a-ketoglutarate.

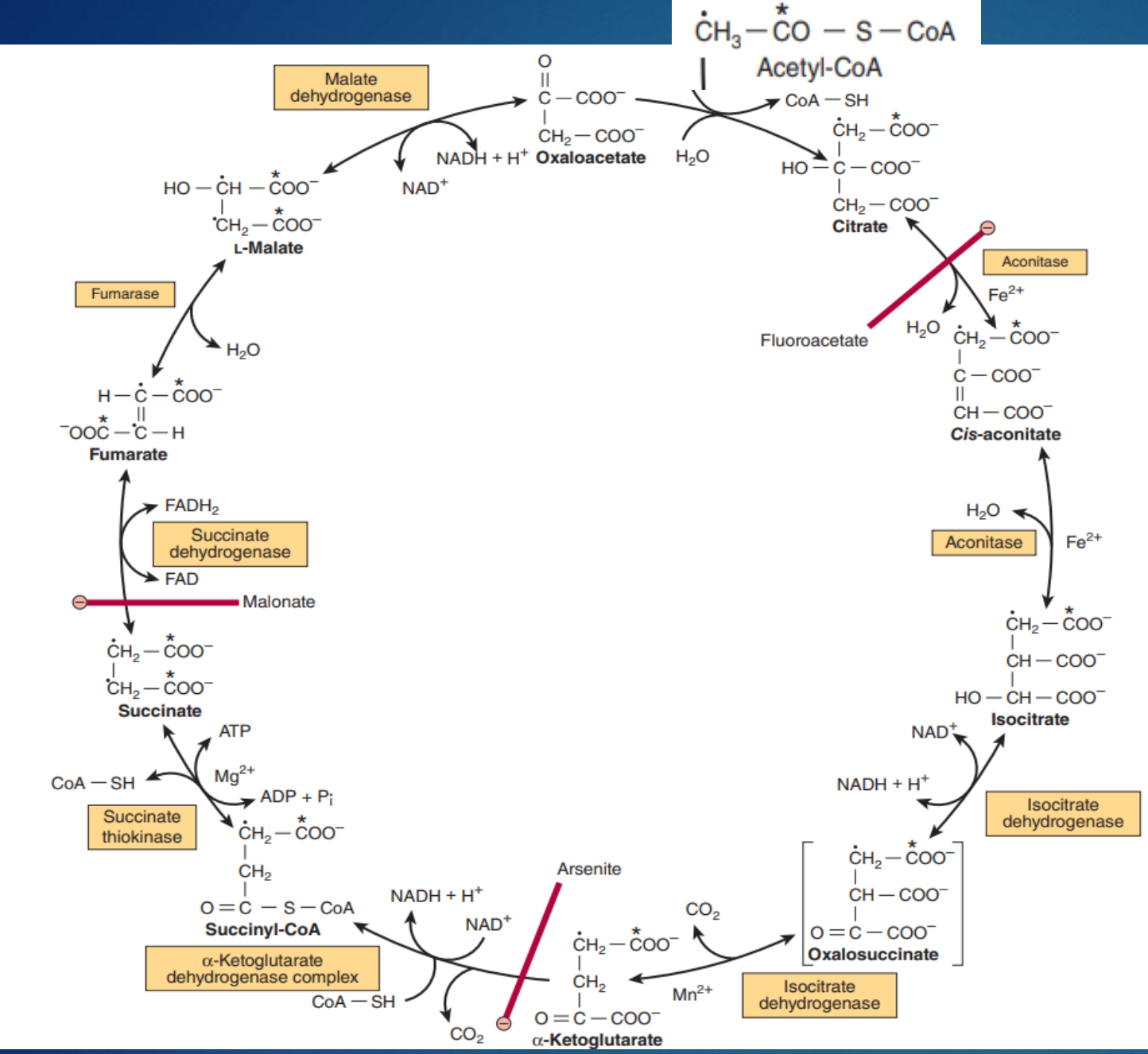
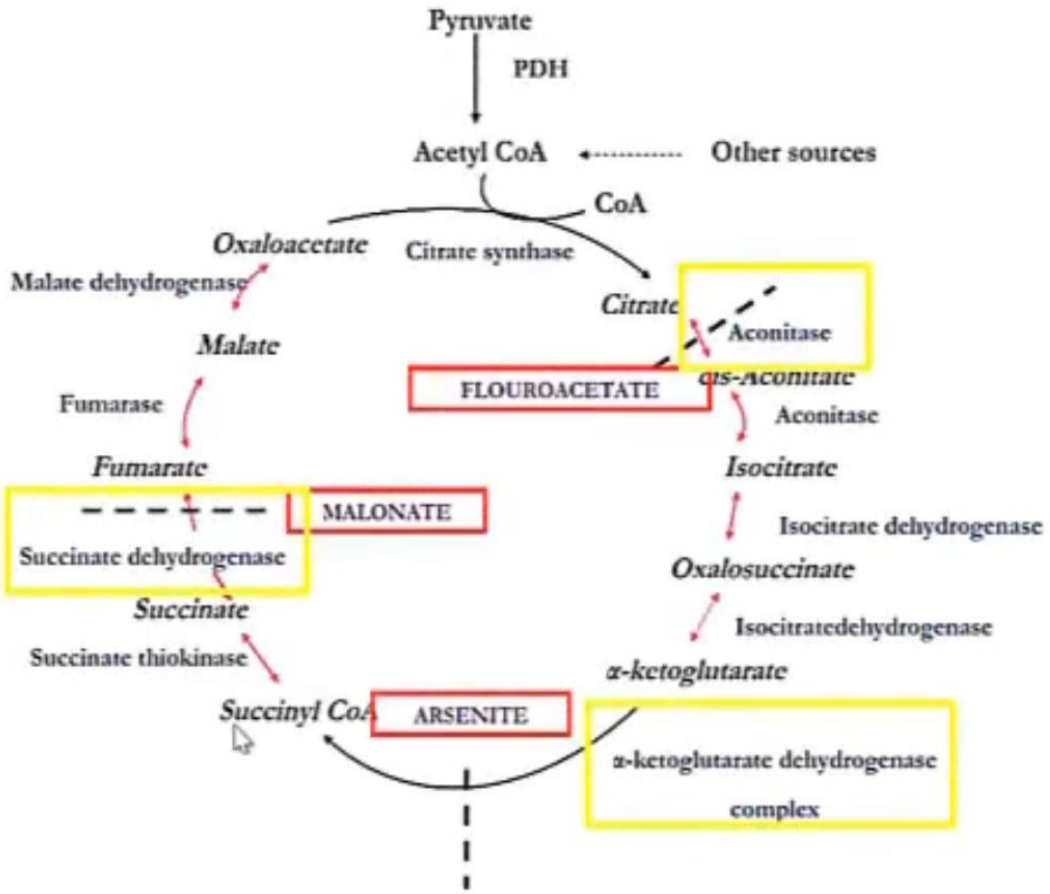


FIGURE 3: The citric acid (Krebs) cycle. Oxidation of NA FADH2 in the respiratory chain leads to the formation of oxidative phosphorylation. In order to follow the pas acetyl-CoA through the cycle, the two carbon atom acetyl moiety are shown labeled on the carboxyl ca and on the methyl carbon (·). Although two carbon at lost as CO2 in one turn of the cycle, these atoms derived from the acetyl-CoA that has immediately ente cycle, but from that portion of the citrate molecule t derived from oxaloacetate. However, on completio single turn of the cycle, the oxaloacetate that is regene now labeled, which leads to labeled CO2 being during the second turn of the cycle. Because succin symmetric compound, "randomization" of label occu step so that all four carbon atoms of oxaloacetate ap be labeled after one turn of the cycle. gluconeogenesis, some of the label in oxaloac incorporated into glucose and glycogen (Figure 20–1). of inhibition (−) by fluoroacetate, malonate, and arse indicated.

Inhibitors of Krebs' cycle



- The decarboxylation requires Mg2+ or Mn2+ ions. There are three isoenzymes of isocitrate dehydrogenase. One, which uses NAD+ , is found only in mitochondria. The other two use NADP+ and are found in mitochondria and the cytosol. Respiratory-chain-linked oxidation of isocitrate occurs through the NAD+ - dependent enzyme. a-Ketoglutarate undergoes oxidative decarboxylation in a reaction catalyzed by a multienzyme complex similar to that involved in the oxidative decarboxylation of pyruvate.
- The a-ketoglutarate dehydrogenase complex requires the same cofactors as the pyruvate dehydrogenase complex—thiamin diphosphate, lipoate, NAD+ , FAD, and CoA— and results in the formation of succinyl-CoA. The equilibrium of this reaction is so much in favor of succinyl-CoA formation that it must be considered to be physiologically unidirectional. As in the case of pyruvate oxidation, arsenite inhibits the reaction, causing the substrate, a-ketoglutarate, to accumulate.

- High concentrations of ammonia inhibit α-ketoglutarate dehydrogenase. Succinyl-CoA is converted to succinate by the enzyme succinate thiokinase (succinyl-CoA synthetase). This is the only example of substrate level phosphorylation in the citric acid cycle. Tissues in which gluconeogenesis occurs (the liver and kidney) contain two isoenzymes of succinate thiokinase, one specific for GDP and the other for ADP. The GTP formed is used for the decarboxylation of oxaloacetate to phosphoenolpyruvate in gluconeogenesis, and provides a regulatory link between citric acid cycle activity and the withdrawal of oxaloacetate for gluconeogenesis. Nongluconeogenic tissues have only the isoenzyme that phosphorylates ADP.
- When ketone bodies are being metabolized in extrahepatic tissues, there is an alternative reaction catalyzed by succinylCoA–acetoacetate-CoA transferase (thiophorase), involving transfer of CoA from succinyl-CoA to acetoacetate, forming acetoacetyl-CoA and succinate.
- The onward metabolism of succinate, leading to the regeneration of oxaloacetate, is the same sequence of chemical reactions as occurs in the β-oxidation of fatty acids:
- dehydrogenation to form a carbon-carbon double bond, addition of water to form a hydroxyl group, and a further dehydrogenation to yield the oxo-group of oxaloacetate. The first dehydrogenation reaction, forming fumarate, is catalyzed by succinate dehydrogenase, which is bound to the inner surface of the inner mitochondrial membrane. The enzyme contains FAD and iron-sulfur (Fe-S) protein, and directly reduces ubiquinone in the electron transport chain.
- Fumarase (fumarate hydratase) catalyzes the addition of water across the double bond of fumarate, yielding malate. Malate is oxidized to oxaloacetate by malate dehydrogenase, linked to the reduction of NAD+ . Although the equilibrium of this reaction strongly favors malate, the net flux is to oxaloacetate because of the continual removal of oxaloacetate (to form citrate, as a substrate for gluconeogenesis, or to undergo transamination to aspartate) and also the continual reoxidation of NADH.

TEN ATP ARE FORMED PER TURN OF THE CITRIC ACID CYCLE

- As a result of oxidations catalyzed by the dehydrogenases of the citric acid cycle, three molecules of NADH and one of FADH2 are produced for each molecule of acetyl-CoA catabolized in one turn of the cycle. These reducing equivalents are transferred to the respiratory chain, where reoxidation of each NADH results in formation of ~2.5 ATP, and of FADH2 , ~1.5 ATP. In addition, 1 ATP (or GTP) is formed by substrate-level phosphorylation catalyzed by succinate thiokinase.

VITAMINS PLAY KEY ROLES IN THE CITRIC ACID CYCLE

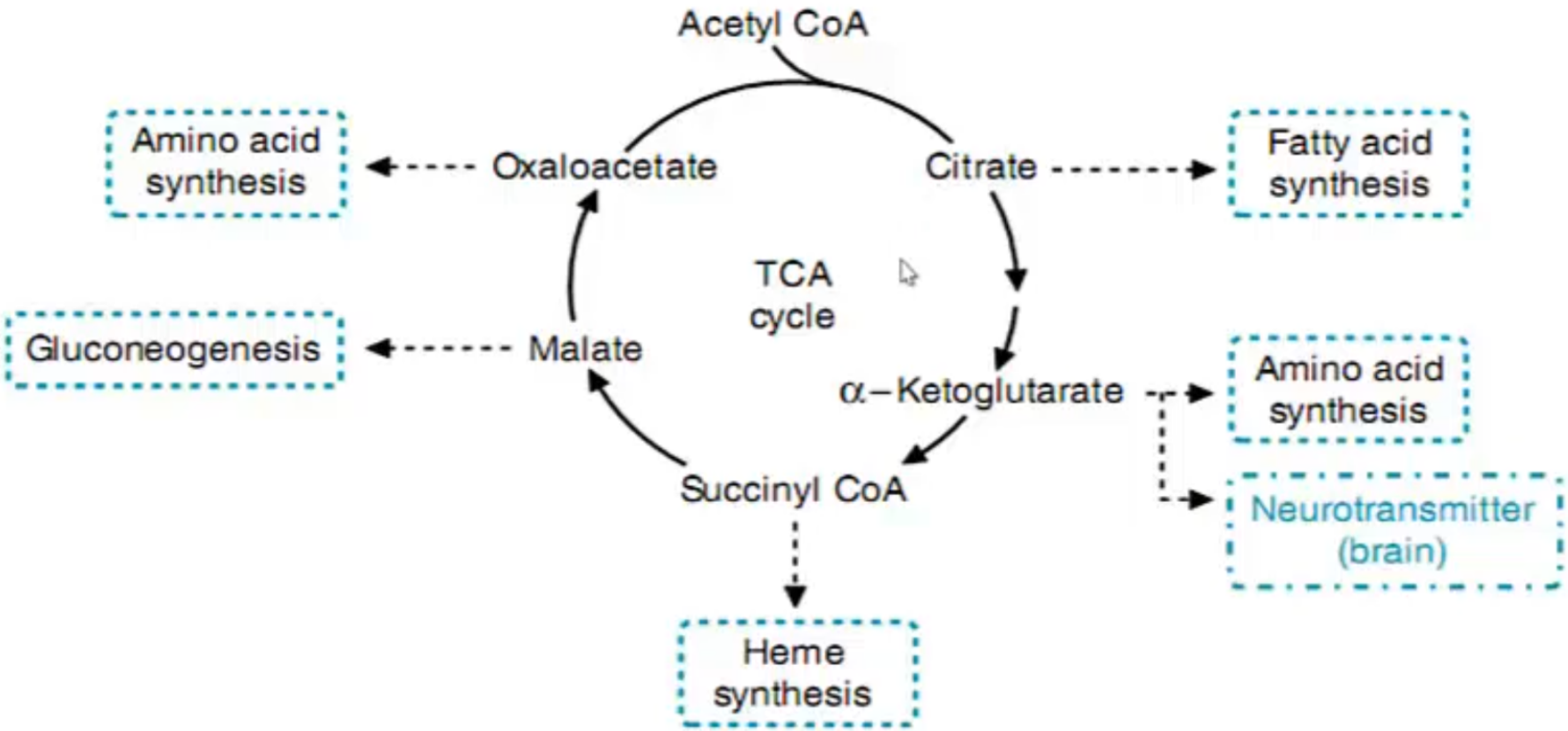
- **Four of the B vitamins** are essential in the citric acid cycle and hence energy-yielding metabolism: riboflavin, in the form of flavin adenine dinucleotide (FAD), a cofactor for succinate dehydrogenase; niacin, in the form of nicotinamide adenine dinucleotide (NAD+), the electron acceptor for isocitrate dehydrogenase, a-ketoglutarate dehydrogenase, and malate dehydrogenase; thiamin (vitamin B1), as thiamin diphosphate, the coenzyme for decarboxylation in the a-ketoglutarate dehydrogenase reaction; and pantothenic acid, as part of coenzyme A, the cofactor esterified to "active" carboxylic acid residues: acetyl-CoA and succinyl-CoA.

THE CITRIC ACID CYCLE PLAYS A PIVOTAL ROLE IN METABOLISM

- The citric acid cycle is not only a pathway for oxidation of two carbon units, but is also a major pathway for interconversion of metabolites arising from transamination and deamination of amino acids, and providing the substrates for amino acid synthesis by transamination, as well as for gluconeogenesis and fatty acid synthesis. Because it functions in both oxidative and synthetic processes, it is amphibolic.

The Citric Acid Cycle Takes Part in Gluconeogenesis, Transamination, & Deamination

- All the intermediates of the cycle are potentially glucogenic, since they can give rise to oxaloacetate, and hence net production of glucose (in the liver and kidney, the organs that carry out gluconeogenesis. The key enzyme that catalyzes net transfer out of the cycle into gluconeogenesis is phosphoenolpyruvate carboxykinase, which catalyzes the decarboxylation of oxaloacetate to phosphoenolpyruvate, with GTP acting as the phosphate donor. The GTP required for this reaction is provided by the GDPdependent isoenzyme of succinate thiokinase. This ensures that oxaloacetate will not be withdrawn from the cycle for gluconeogenesis if this would lead to depletion of citric acid cycle intermediates, and hence reduced generation of ATP. Net transfer into the cycle occurs as a result of several reactions. Among the most important of such anaplerotic reactions is the formation of oxaloacetate by the carboxylation of pyruvate, catalyzed by pyruvate carboxylase (Figure 16–4). This reaction is important in maintaining an adequate concentration of oxaloacetate for the condensation reaction with acetylCoA. If acetyl-CoA accumulates, it acts as both activator of pyruvate carboxylase and an inhibitor of pyruvate dehydrogenase, thereby ensuring a supply of oxaloacetate. Lactate, an important substrate for gluconeogenesis, enters the cycle via oxidation to pyruvate and then carboxylation to oxaloacetate. Glutamate and glutamine are important anaplerotic substrates because they yield a-ketoglutarate as a result of the reactions catalyzed by glutaminase and glutamate dehydrogenase. Transamination of aspartate leads directly to the formation of oxaloacetate, and a variety of compounds that are metabolized to yield propionyl CoA, which can be carboxylated and isomerized to succinyl CoA are also important anaplerotic substrates.


Acetyl CoA
Amino acid synthesis
Oxaloacetate
Citrate
Fatty acid synthesis
TCA cycle
Gluconeogenesis
Malate
α–Ketoglutarate
Amino acid synthesis
Succinyl CoA
Neurotransmitter (brain)
Heme synthesis

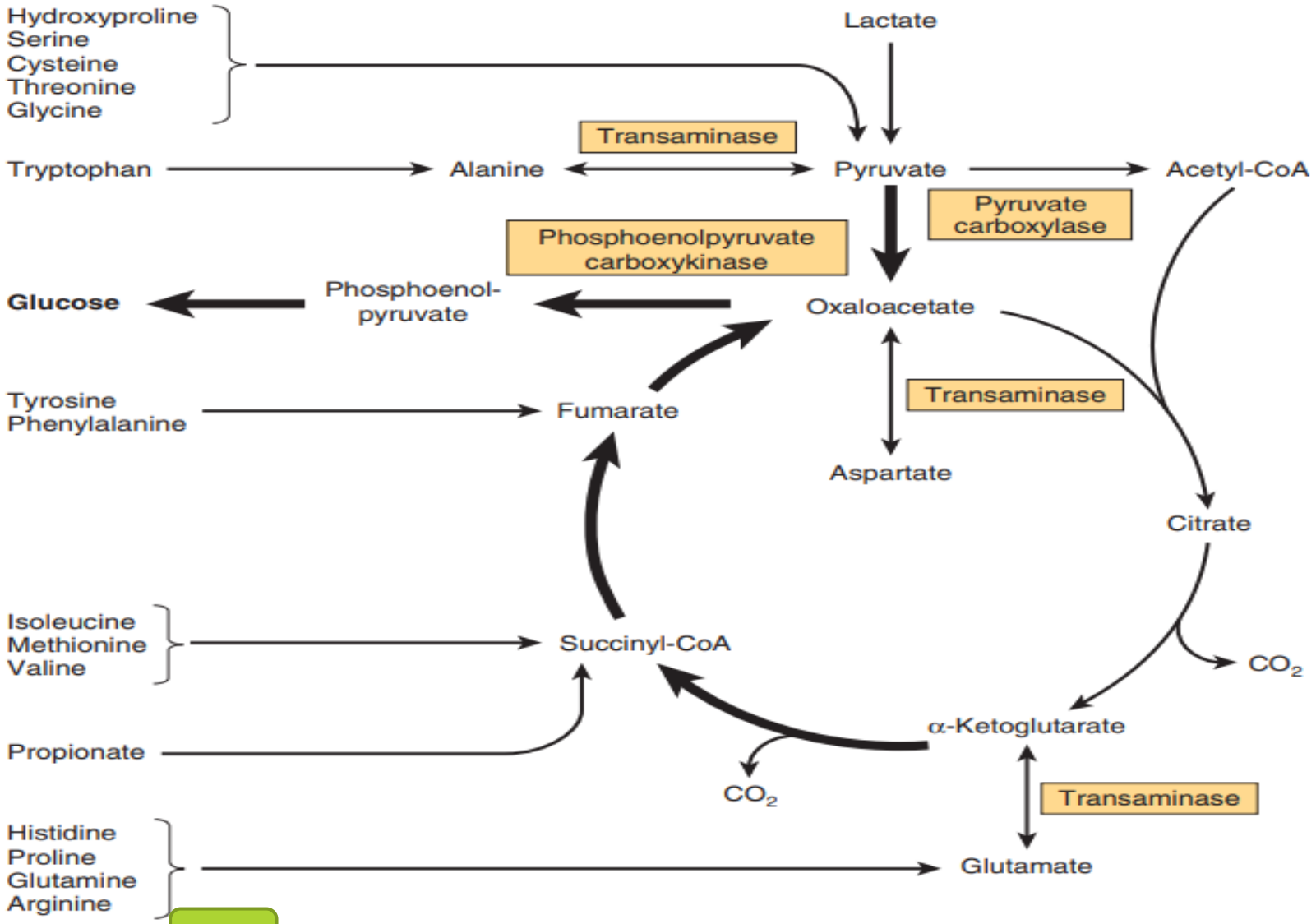


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FIGURE **Involvement of the citric acid cycle in transamination and gluconeogenesis.** The bold arrows indicate the main pathway of gluconeogenesis.

TCA cycle regulation:

- Citrate synthase: inhibited by ATP, long chain fatty acyl-CoA (allosteric) and succinyl-CoA (competitive).
- Isocitrate dehydrogenase: allosterically activated by **ADP** and **NAD** and inhibited by **ATP** and **$NADH.H^+$.**
- α-Ketoglutarate dehydrogenase: phosphorylation/dephosphorylation (like pyruvate dehydrogenase). Also inhibited by accumulation of **ATP**, **succinyl-CoA** and **$NADH.H^+$**.
- Succinate dehydrogenase: inhibited by oxaloacetate
- Respiratory chain controls Krebs' cycle by controlling ATP/ADP ratio.

- Aminotransferase (transaminase) reactions form pyruvate from alanine, oxaloacetate from aspartate, and a-ketoglutarate from glutamate. Because these reactions are reversible, the cycle also serves as a source of carbon skeletons for the synthesis of these amino acids. Other amino acids contribute to gluconeogenesis because their carbon skeletons give rise to citric acid cycle intermediates. Alanine, cysteine, glycine, hydroxyproline, serine, threonine, and tryptophan yield pyruvate; arginine, histidine, glutamine, and proline yield a-ketoglutarate; isoleucine, methionine, and valine yield succinyl-CoA; tyrosine and phenylalanine yield fumarate (see Figure 4). The citric acid cycle itself does not provide a pathway for the complete oxidation of the carbon skeletons of amino acids that give rise to intermediates such as a-ketoglutarate, succinyl CoA, fumarate and oxaloacetate, because this results in an increase in the amount of oxaloacetate. For complete oxidation to occur, oxaloacetate must undergo phosphorylation and carboxylation to phosphoenolpyruvate (at the expense of GTP) then dephosphorylation to pyruvate (catalyzed by pyruvate kinase) and oxidative decarboxylation to acetyl Co (catalyzed by pyruvate dehydrogenase). In ruminants, whose main metabolic fuel is short-chain fatty acids formed by bacterial fermentation, the conversion of propionate, the major glucogenic product of rumen fermentation, to succinyl-CoA via the methylmalonyl-CoA pathway is especially important

The Citric Acid Cycle Takes Part in Fatty Acid Synthesis

- Acetyl-CoA, formed from pyruvate by the action of pyruvate dehydrogenase, is the major substrate for long-chain fatty acid synthesis in nonruminants (Figure 5). (In ruminants, acetylCoA is derived directly from acetate.) Pyruvate dehydrogenase is a mitochondrial enzyme, and fatty acid synthesis is a cytosolic pathway; the mitochondrial membrane is impermeable to acetyl-CoA. For acetyl-CoA to be available in the cytosol, citrate is transported from the mitochondrion to the cytosol, then cleavedin a reaction catalyzed by citrate lyase (Figure 5). Citrate is only available for transport out of the mitochondrion when aconitase is inhibted by its product and therefore saturated with its substrate, so that citrate cannot be channeled directly from citrate synthase onto aconitase. This ensures that citrate is used for fatty acid synthesis only when there is an adequate amount to ensure continued activity of the cycle. The oxaloacetate released by citrate lyase cannot reenter the mitochondrion, but is reduced to malate, at the expense of NADH, and the malate undergoes oxidative decarboxylation to pyruvate, reducing NADP+ to NADPH. This reaction, catalyzed by the malic enzyme, is the source of half the NADPH required for fatty acid synthesis (the remainder is provided by the pentose phosphate pathway). Pyruvate enters the mitochondrion and is carboxylated to oxaloacetate by pyruvate carboxylase, an ATP-dependent reaction in which the coenzyme is the vitamin biotin.

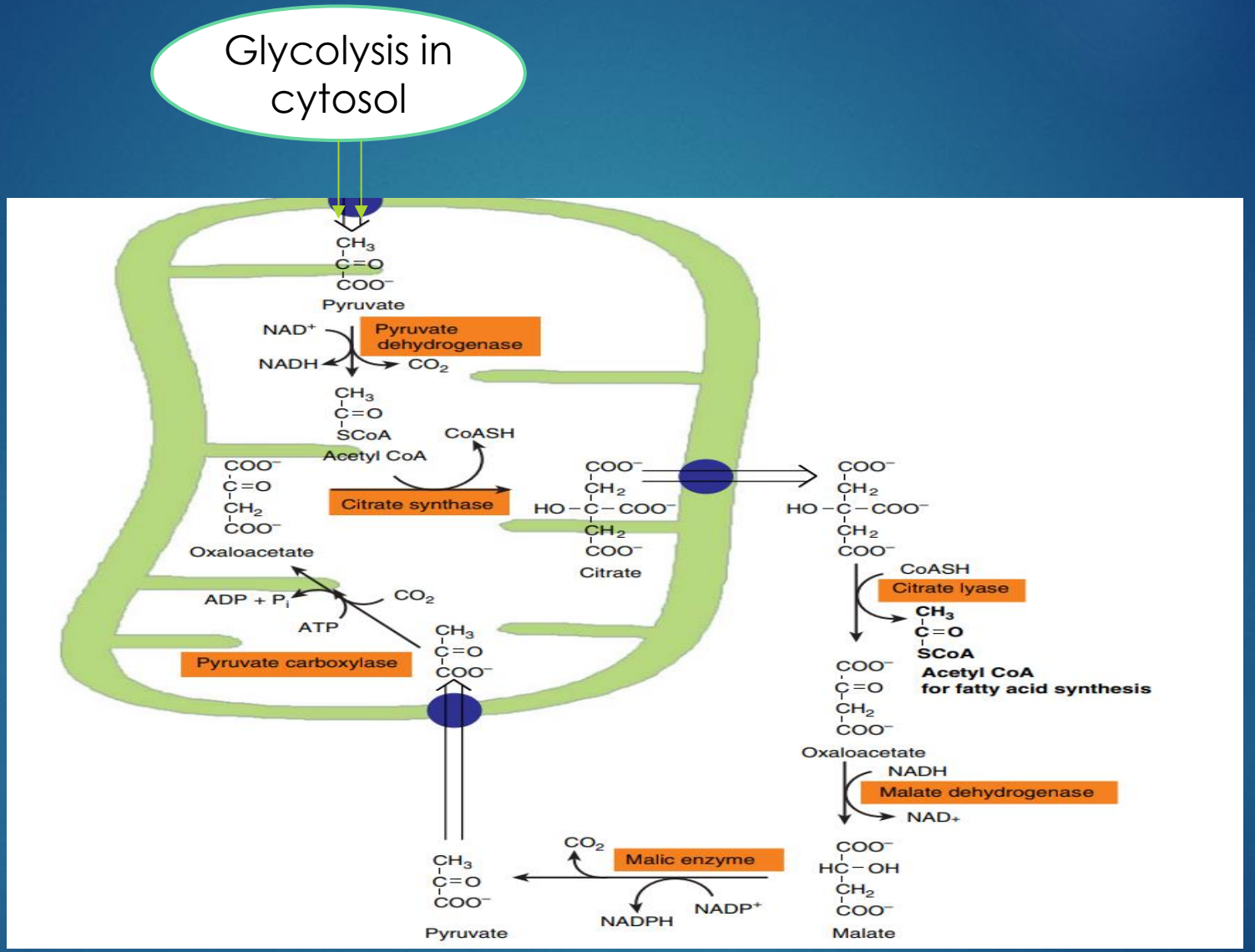

FIGURE 5: Participation of the citric acid cycle in provision of cytosolic acetyl CoA for fatty acid synthesis from glucose.

Anaplerotic reactions

- Anaplerotic reactions are metabolic pathways that replenish oxaloacetate in the citric acid cycle after consumption. The purpose of these reactions is to maintain adequate levels of ATP so that cellular respiration can carry on uninterrupted.

- **What is an Anaplerotic Reaction?**
- The anaplerotic reaction is **the anabolic reaction that helps to generate the intermediate compounds of the biochemical; pathways.** The intermediate reaction step of such a reaction is known as anaplerotic routes. Anaplerotic reactions are an important part of the metabolism; that is, they are an important part of the biochemical pathways like citric acid pathways, lipid biosynthesis. In this article, we mainly focus on the anaplerotic reaction, anaplerotic routes for anaplerotic pathways. It focuses on the physiological role of anaplerosis.

- In the citric acid cycle, amino acid metabolism and synthesis of triglyceride in adipose tissue, which is also known as lipid biosynthesis.

- **What is Anaplerosis?**
- Anaplerosis can be defined as the reaction that can replenish the intermediates of the pathway. In simpler terms, anaplerotic reaction maintains the dynamic balance of an anaplerotic route in such a way that the concentration of the crucial but depleted intermediate has remained as a constant.

- Anaplerotic routes are the reaction steps that are followed to generate the intermediates of the biochemical pathways.

The Physiological Role of Anaplerosis in the Citric Acid Cycle

- Anaplerotic reactions are a very important part of the citric acid cycle, also known as the TCA cycle. The citric acid cycle is an amphibolic pathway. Amphibolic pathways are those pathways that can perform both anabolic reactions as well as catabolic reactions. The anaplerotic reaction is also known as the anaplerotic pathways of the citric acid cycle. They are responsible for the anabolic part of the cycle. The primary role of the citric acid cycle is the oxidation of acetyl-CoA to carbon dioxide.

- It is important to understand that TCA cycle intermediates are sufficient to sustain the oxidative carbon flux during high energy consumption like individuals performing exercise or during lower energy consumption like fasting. It is important to note that there is not a large change in the pool size of TCA intermediates. In several physiological states, there is a large influx of intermediates like 4- and 5-carbon intermediates into the TCA cycle. It is notable that even with the change in the intermediate concentrations, the citric acid cycle can not act as a carbon sink, so it maintains a dynamic balance between incoming and outgoing intermediates by anaplerosis and cataplerosis.

Anaplerotic Reactions of the Citric Acid Cycle

There are four major anaplerotic reactions in the TCA cycle.

- Pyruvate to oxaloacetate
- Phosphoenolpyruvate to oxaloacetate
- Phosphophenol pyruvate to oxaloacetate using PEP carboxykinase.
- Pyruvate to malate

Regulation of the Citric Acid Cycle

- Depends Primarily on a Supply of Oxidized Cofactors In most tissues, where the primary role of the citric acid cycle is in energy-yielding metabolism, respiratory control via the respiratory chain and oxidative phosphorylation regulates citric acid cycle activity. Thus, activity is immediately dependent on the supply of NAD+ , which in turn, because of the tight coupling between oxidation and phosphorylation, is dependent on the availability of ADP and hence, ultimately on the rate of utilization of ATP in chemical and physical work.

- In addition, individual enzymes of the cycle are regulated. The main sites for regulation are the nonequilibrium reactions catalyzed by pyruvate dehydrogenase, citrate synthase, isocitrate dehydrogenase, and a-ketoglutarate dehydrogenase.
- The dehydrogenases are activated by Ca2+ , which increases in concentration during contraction of muscle and during secretion by other tissues, when there is increased energy demand.
- In a tissue such as brain, which is largely dependent on carbohydrate to supply acetyl-CoA, control of the citric acid cycle may occur at pyruvate dehydrogenase.
- Several enzymes are responsive to the energy status as shown by the [ATP]/[ADP] and [NADH]/[NAD+] ratios.
- Thus, there is allosteric inhibition of citrate synthase by ATP and long-chain fatty acyl-CoA. Allosteric activation of mitochondrial NAD-dependent isocitrate dehydrogenase by ADP is counteracted by ATP and NADH.
- The a-ketoglutarate dehydrogenase complex is regulated in the same way as is pyruvate dehydrogenase.
- Succinate dehydrogenase is inhibited by oxaloacetate, and the availability of oxaloacetate, as controlled by malate dehydrogenase, depends on the [NADH]/ [NAD+] ratio. S
- ince the Km of citrate synthase for oxaloacetate is of the same order of magnitude as the intramitochondrial concentration, it is likely that the concentration of oxaloacetate controls the rate of citrate formation

- Hyperammonemia, as occurs in advanced liver disease and a number of (rare) genetic diseases of amino acid metabolism, leads to loss of consciousness, coma and convulsions, and may be fatal. This is largely because of the withdrawal of a-ketoglutarate to form glutamate (catalyzed by glutamate dehydrogenase) and then glutamine (catalyzed by glutamine synthetase), leading to lowered concentrations of all citric acid cycle intermediates, and hence reduced generation of ATP. The equilibrium of glutamate dehydrogenase is finely poised, and the direction of reaction depends on the ratio of NAD+ : NADH and the concentration of ammonium ions. In addition, ammonia inhibits a-ketoglutarate dehydrogenase, and possibly also pyruvate dehydrogenase.

SUMMARY .

- The citric acid cycle is the final pathway for the oxidation of carbohydrate, lipid, and protein. Their common endmetabolite, acetyl-CoA, reacts with oxaloacetate to form citrate. By a series of dehydrogenations and decarboxylations, citrate is degraded, reducing coenzymes, releasing two CO_2 , and regenerating oxaloacetate.
- The reduced coenzymes are oxidized by the respiratory chain linked to formation of ATP. Thus, the cycle is the major pathway for the formation of ATP and is located in the matrix of mitochondria adjacent to the enzymes of the respiratory chain and oxidative phosphorylation.
- The citric acid cycle is amphibolic, since in addition to oxidation it is important in the provision of carbon skeletons for gluconeogenesis, acetyl CoA for fatty acid synthesis, and interconversion of amino acids.

EXPLANATIONS-HOMEWORK

IMPORTANT POSSIBLE QUESTIONS

10 Marks

1. Define Glycolysis. Elaborate the pathway with structures.
2. Define the TCA cycle. Elaborate the pathway with structures.
3. Define HMP shunt. Elaborate the pathway with structures.

10 Marks

4. Write in detail about glycogen storage disease.
5. Give the pathway of Glycogenesis
6. Give the pathway of Glycogenolysis
7. Gluconeogenesis
8. Write in detail about ETC and its diagram.
9. Define oxidative Phosphorylation and its mechanism.

2 Marks

10. Give the total number of ATPs produced from both glycolysis and TCA cycle
11. Inhibitors of ETC
12. Inhibitors of Oxidative phosphorylation
13. Pasteur effect
14. Crabtree effect
15. What is the uses of NADPH
16. What is anaplerotic reactions with examples
17. Write about inhibitors of the TCA cycle
18. von Gierek's disease
19. Wernicke-Korsakoff syndrome