University of Fallujah
College of Medicine

Pyruvate Metabolism

Lecture : 3

Stage : 2nd Stage

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Learn Objectives

-What is Pyruvate?

-Metabolic pathway of pyruvate metabolism

-TCA cycle ?

Formation of pyruvic acid (P.A.) in the body:

1- From oxidation of glucose (**glycolysis**).

2- From **lactic acid** by oxidation.

3- Deamination of **alanine**.

4- **Glucogenic amino acids-**pyruvate forming.

5- Decarboxylation of oxaloacetic acid (**OAA**)

Fate of pyruvic acid (P.A.):

1- Form acetyl CoA by oxidative decarboxylation (in presence of O2)).

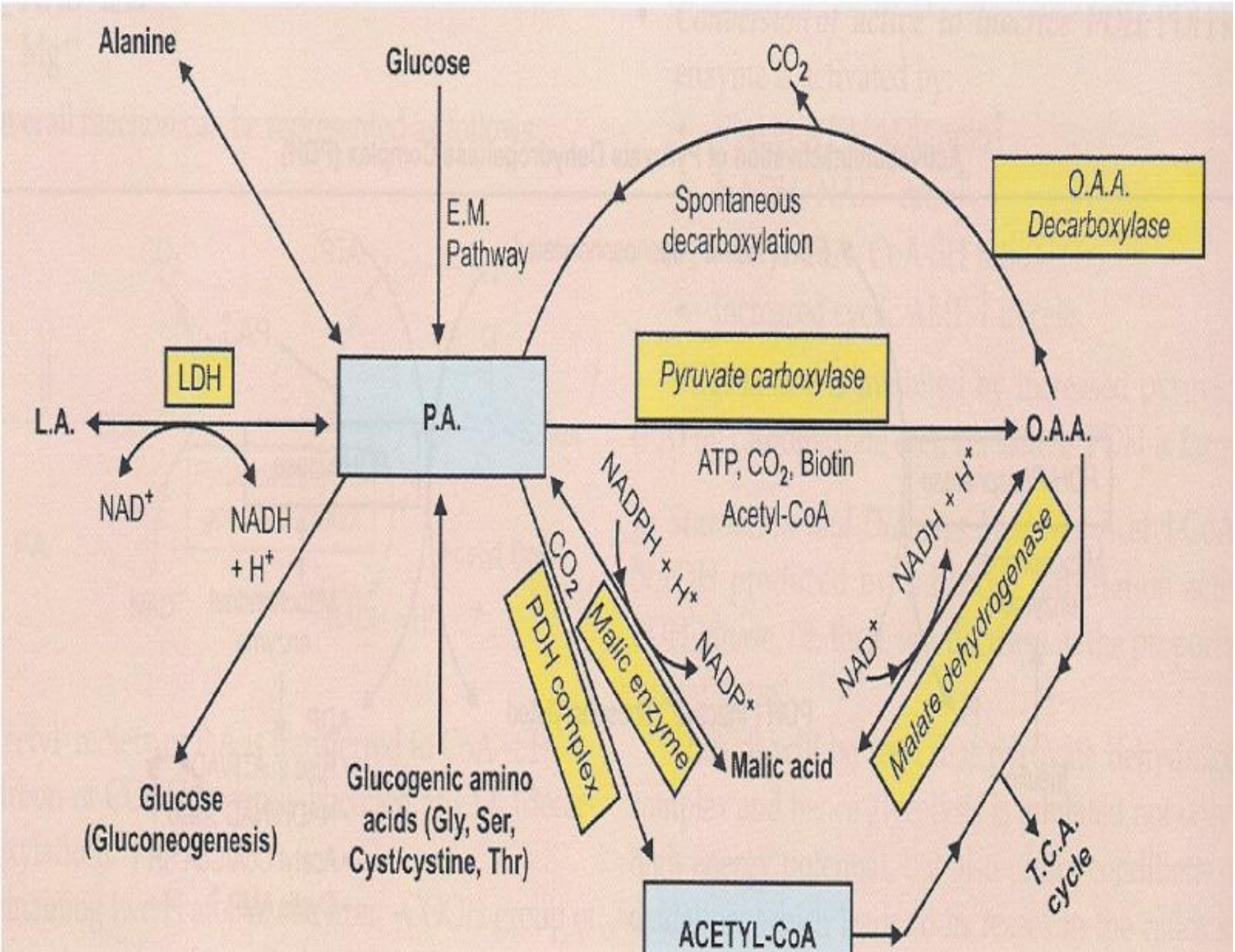
2-Forms lactic acid by reduction (in absence of O2)

3-Forms alanine by amination.

4-Forms glucose (gluconeogenesis).

5-Forms malic acid → to O.A.A (oxaloacetic acid).

6-Forms oxaloacetic acid (O.A.A) by CO2-fixation reaction (carboxylation).


Alanine
Glucose
CO_2
E.M. Pathway
Spontaneous decarboxylation
O.A.A. Decarboxylase
LDH
L.A.
P.A.
Pyruvate carboxylase
O.A.A.
NAD^+
$NADH + H^+$
ATP, CO_2, Biotin
Acetyl-CoA
$NADPH + H^+$
CO_2
PDH complex
Malic enzyme
$NADP^+$
Malic acid
$NADH + H^+$
NAD^+
Malate dehydrogenase
Glucose (Gluconeogenesis)
Glucogenic amino acids (Gly, Ser, Cyst/cystine, Thr)
ACETYL-CoA
T.C.A. cycle

*Before pyruvate can enter the TCA cycle, it must be transported into the mitochondria via a special pyruvate transporter that aids its passage across the inner mitochondrial membrane. Within the mitochondria, pyruvate is oxidatively decarboxylated to acetyl-CoA; this reaction is catalyzed by sequentially multienzyme complex (pyruvate dehydrogenase complex).

The citric acid cycle (TCA) cycle

1-TCA cycle (tricarboxylic acid cycle), also known as the **citric acid pathways in the major energy production** , is **cycle or the Krebs' cyclethe body.**

*The cycle occurs in the mitochondria.

2- It is a cyclic process.

3-The cycle involves a sequence of compounds inter-related by **oxidation-reduction** and other reactions which finally produces [CO2 and H2O].

or catabolism of breakdown of **n pathway final commo**It is the -

4**carbohydrates, fats and proteins**.

5-Acetyl CoA derived mainly from oxidation of either glucose or β-oxidation of FA and partly from certain amino acids combines with oxaloacetic acid (OAA) to **form "citrate" the first reaction of TCA cycle**.

In this reaction acetyl CoA transfers its' acetyl-group' (**2 C)** to OAA.

6-By step wise dehydrogenations and loss of two molecules of CO2, accompanied by internal re-arrangements, the citric acid **is reconverted to OAA**, which again starts the cycle by taking up another acetyl group from acetyl-CoA.

7-**All the enzymes** of the TCA cycle are in the mitochondrial matrix, except succinate dehydrogenase which is in the inner mitochondrial membrane.
8-**Electrons** are transferred by the cycle to NAD+ (Nicotinamide Adenine Dinucleotide) and FAD (Flavin Adenine Dinucleotide).
9-As the electrons subsequently are passed to O2 by the electron transport . **ATP is generated by the process of oxidative phosphorylation**chain,
10-**ATP is also generated from GTP** (Guanosine Triphosphate), produced in one reaction of the cycle by substrate level phosphorylation.

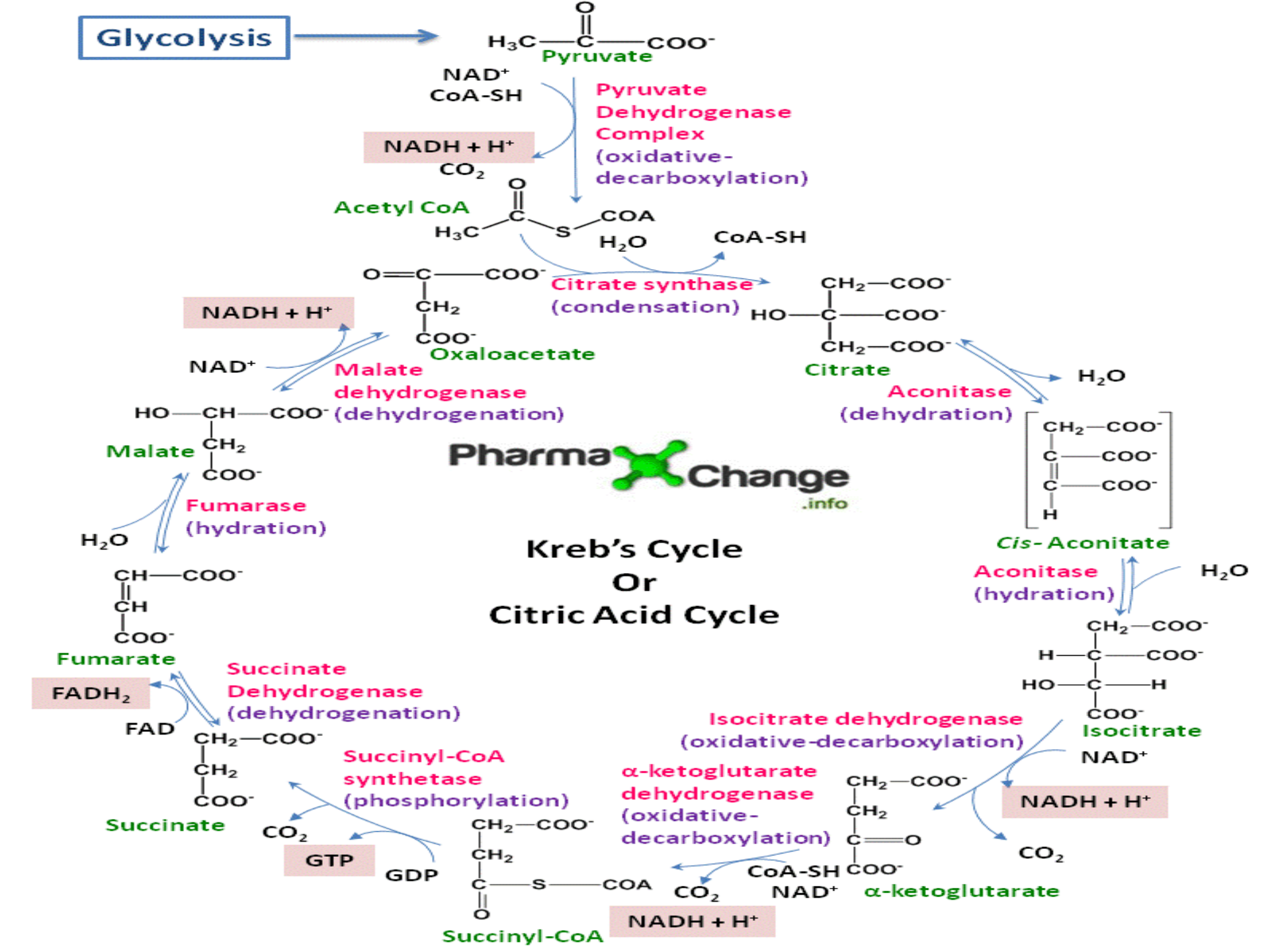
11-**The whole process is aerobic**, requiring O2 as the final oxidant of the reducing equivalents. Absence of O2 (anoxia) or partial deficiency of O2 (hypoxia) causes total or partial inhibition of the cycle.
12-The **H atoms removed** in the successive dehydrogenations are accepted by corresponding coenzymes. Reduced coenzymes transfer the reducing equivalents to electron-transport system, where oxidative phosphorylation product ATP molecules.

There are three key enzymes in TCA cycle:

1-Citrate synthase

2- Isocitrate dehydrogenase (I.C.D)

3- α-ketoglutarate dehydrogenase or named α-oxoglutarate dehydrogenase


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