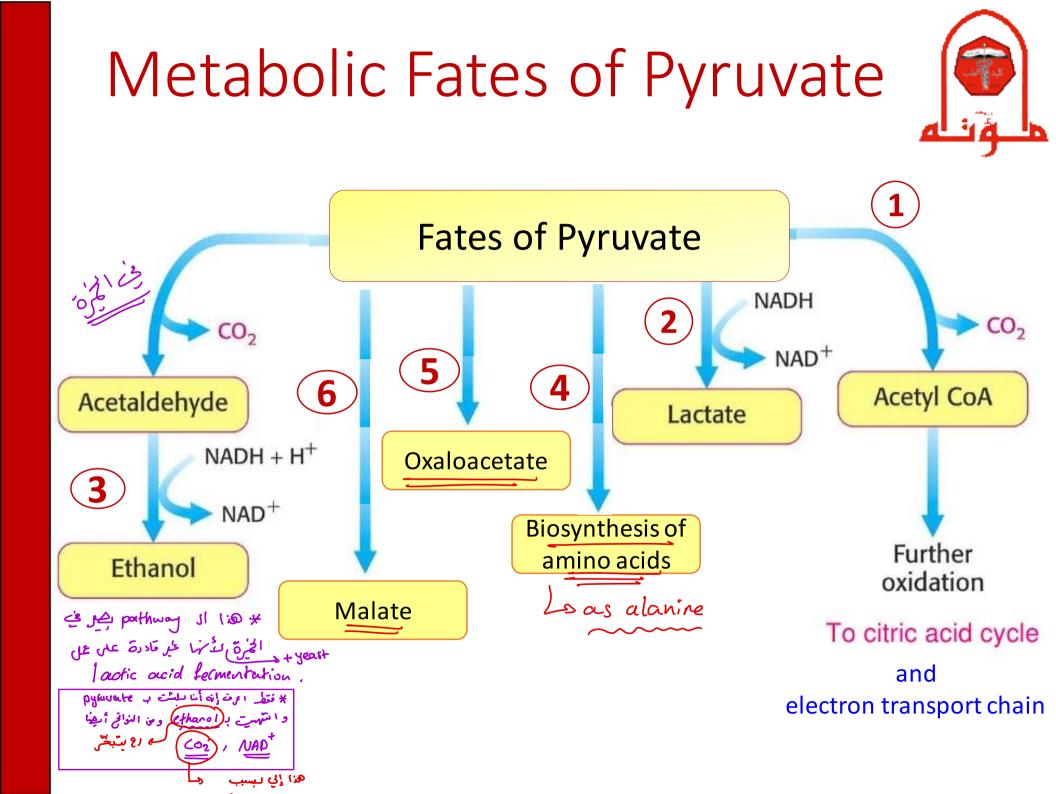


حلف عنوي (NAD وما في وقت كودرع (<u>213</u>) إلي هي تعبّر إحدى طرف إستاجه! الحلي هو "latic acid fermentation" إلي من إحدى نواتجه NAD إهانة إلى ذلا إنّه جدرع ليبرعة ، عسمن هلا ، مدف من حدوث هذا الا مسمهم من تحكين المحصه العدمي و إيّا تحوين م NAD حتى إنه عليه كانه المن تقدر تسمّر بالحديث.

Cori Cycle

 Cori cycle "lactic acid cycle" is the metabolic pathway in which lactic acid produced in muscles during the time of oxygen depletion is converted back to glucose in the liver by GLYCOLYSIS **GLUCONEOGENESIS** gluconeogenesis process Muscle Glucose Glucose Pyruvate Pyruvate niversi Lactate Liver

Lactate





Metabolic Fates of Pyruvate



- In aerobic conditions, pyruvate is converted to acetyl CoA which enters the citric acid cycle for further oxidation to CO₂ followed by oxidative phosphorylation
- In anaerobic conditions like in lactic acid bacteria and some human cells (e.g. RBCs and O₂-starved muscle cells), pyruvate is reduced to lactic acid with the concomitant oxidation of NADH to NAD⁺ (lactic acid fermentation)
- 3. In anaerobic conditions like in some M.O's (e.g. yeast), pyruvate is converted to ethanol
- 4. Amino acid biosynthesis: pyruvate is a precursor of some amino acids like alanine
- 5. & 6. Pyruvate can be used for synthesis of oxaloacetate or malate (both are TCA cycle intermediates)

Fluoride as Inhibitor of Enolase



- Oral bacteria depends on the food debris or dietary sugars found on the tooth surface as a primary source of energy. Acids are produced through fermentation process (harmful)
- Fluoride is a competitive inhibitor of enolase enzyme catalyzing Step 9
- Drinking fluoridated water or using a toothpaste containing fluoride inhibit the oral bacteria enolase activity. Consequently, this disrupts the bacteria glycolytic pathway and prevents formation of dental caries

* تستوس الأسنان

Fluoride as Inhibitor of Enolase



- Sodium fluoride is known to have antiglycolytic effect that inhibits glycolysis by erythrocytes
- NaF tubes (gray top) are widely used for blood collection for glucose measurement
- Fluoride-containing tubes are suitable for blood collection if there is a long delay in blood separation following collection (false negative result) المراد المراد عده عدى دتركمتا فزة من الزمن (false negative result) المراد بعربن فدهمتا رو تعرف بايد مسترى علمه عنده عدى لأنه علية دندهاه يواع المرب



Glycolysis as Anabolic Pathway

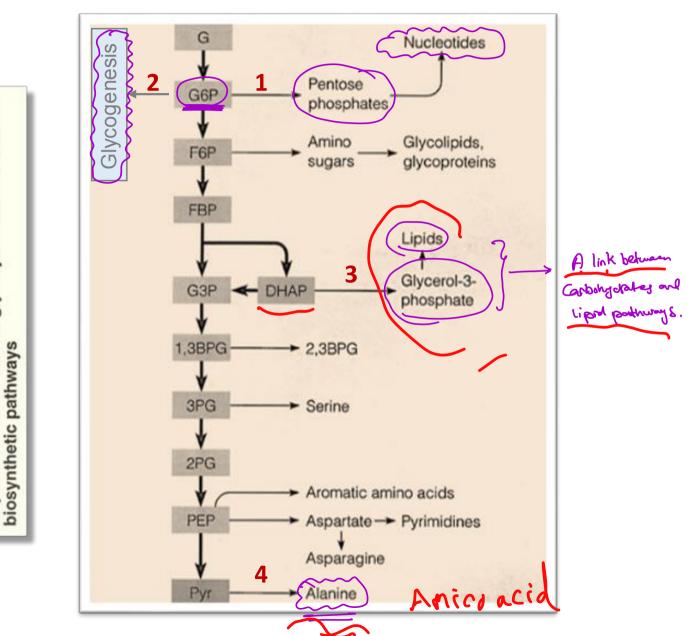


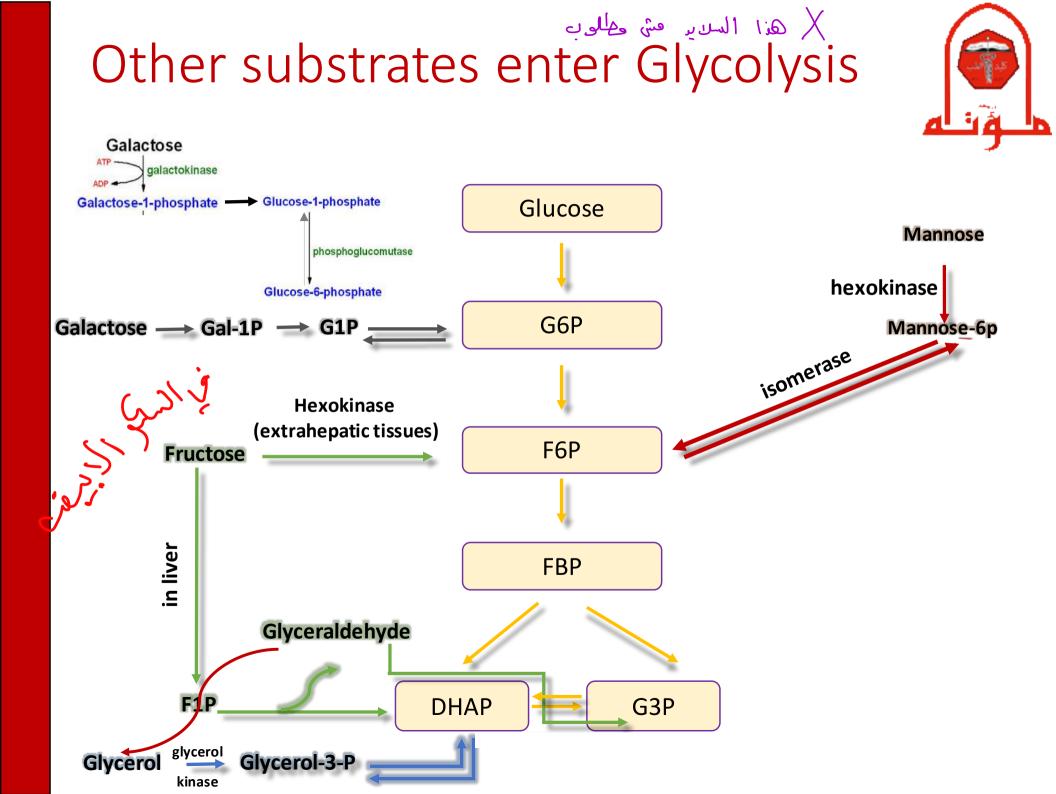
- Glycolysis acts as catabolic as well as anabolic pathway. Therefore, glycolysis is very important central metabolic pathway
- Glycolysis intermediates with biosynthetic roles:
 - Nucleotides biosynthesis: G6P is an initial substrate in pentose phosphate pathway (metabolic pathway which generates pentoses)
- 2. Glycogenesis via G6P (production of glycogen)
- 3. Lipids biosynthesis: DHAP is converted to glycerol-3-P
- 4. Amino acids biosynthesis: pyruvate as precursor of alanine

Glycolysis as Anabolic Pathway

Major alternative fates of glycolytic intermediates in

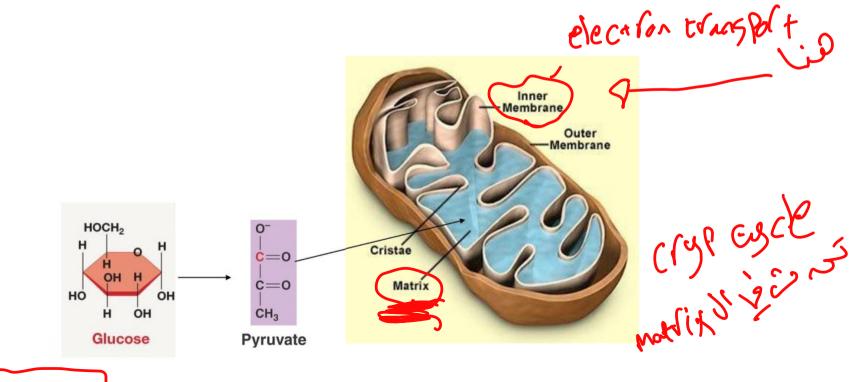


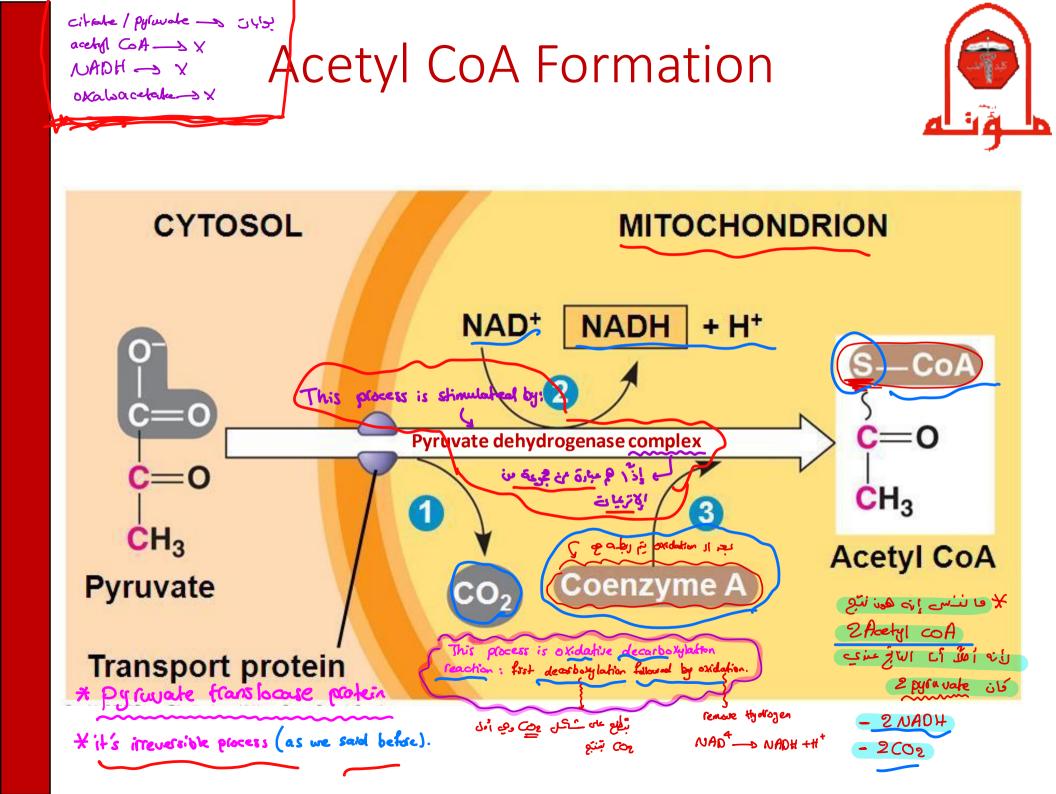




Acetyl CoA Formation

- In aerobic respiration, pyruvate (3C) joins the citric acid cycle after its conversion to acetyl CoA (2C)
- Citric acid cycle occurs in the mitochondrial matrix. Shuttling of pyruvate from the cytosol is facilitated by a transporter protein embedded in the inner mitochondrial membrane called pyruvate translocase



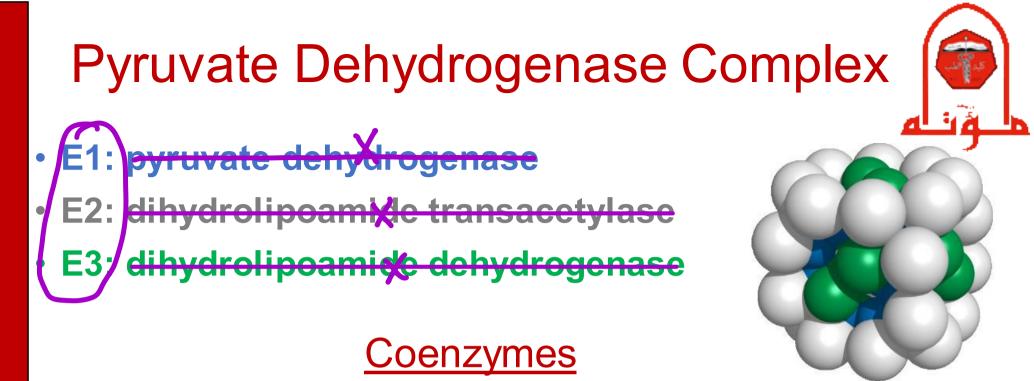


Acetyl CoA Formation

- Pyruvate dehydrogenase complex (PDC) catalyzes the **irreversible** oxidative decarboxylation of pyruvate into Acetyl CoA with the release of CO₂
- Energy-rich molecule "NADH" is also produced.
 Coenzyme A (CoA) acts as acetyl group carrier due to its free sulfhydryl (-SH) end capable of forming thioester bond
- PDC is a multi-enzyme system consists of three catalytic enzymes and five coenzymes (three of them are prosthetic groups as they are tightly bound to their corresponding enzymes)

· structure of enzyme go bis user coenzyme JI (*)

Cuenzyne llo

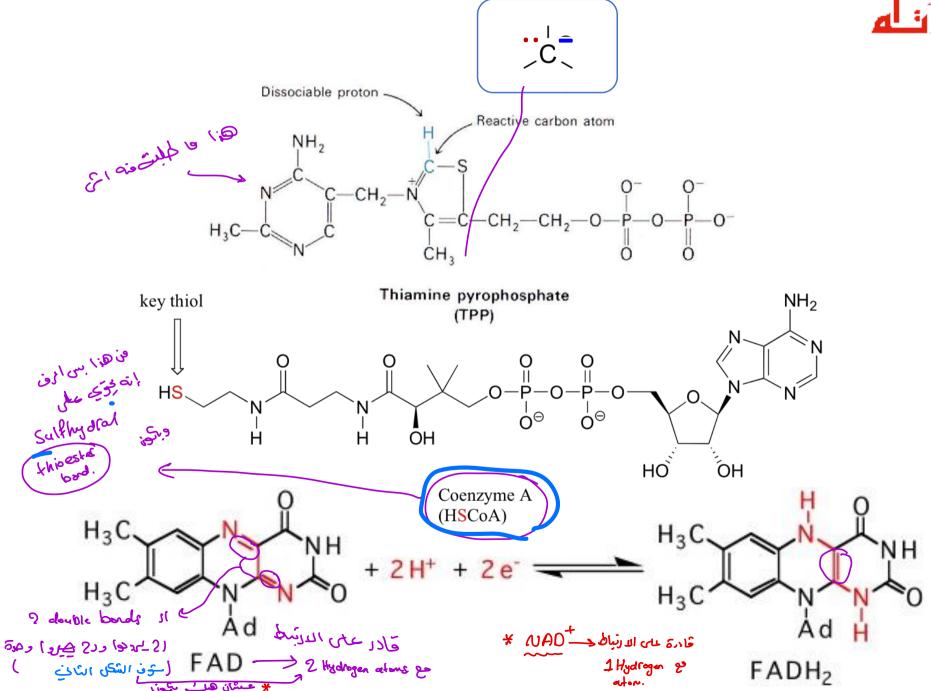


Bl

- Thiamine pyrophosphate (TPP) a prosthetic group of E1
- Lipoic acid (lipoamide) a prosthetic group of E2
- Flavin adenine dinucleotide (FAD) a prosthetic group of E3
- Coenzyme A (CoA or CoA-SH)
- Nicotinamide adenine dinucleotide (NAD⁺)

Coenzymes Structure





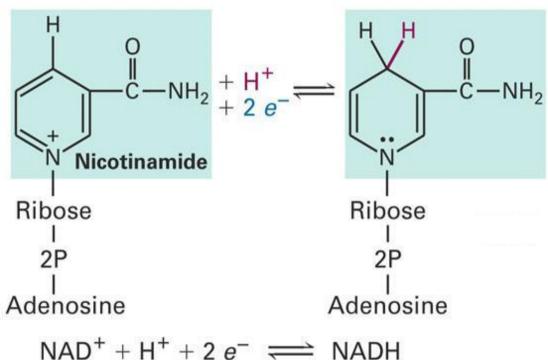


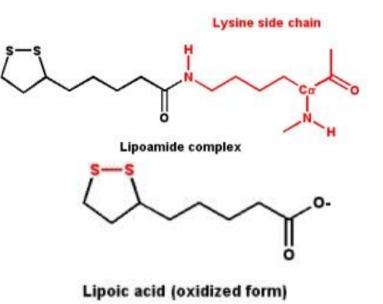
Coenzymes Structure X

Reduced: NADH



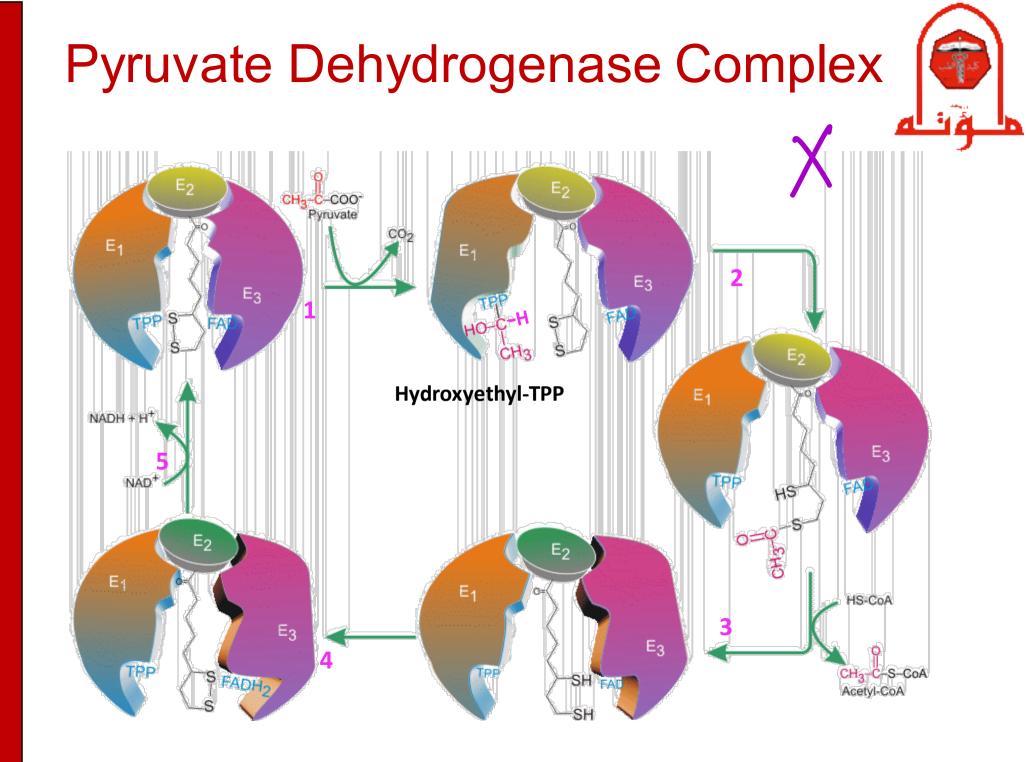
Oxidized: NAD⁺





SH HS

Lipoic acid (reduced form)



Mechanism of PDC

- The mechanism by which this complex catalyzes the reaction is complicated but the main processes involve (5 steps):
- 1.Decarboxylation of pyruvate and the release of CO₂ a reaction catalyzed by E1-TPP. The product of this reaction "Hydroxyethyl moiety" is a substrate for the next reaction
- 2.The transfer of Hydroxyethyl moiety from TPP of E1 to lipoic acid of E2. This step is mediated by an oxidation of Hydroxyethyl to acetyl group coupled with reduction of disulfide bond
- 3.Transfer of acetyl group from lipoamide to CoA forming thioester bond and consequently Acetyl CoA is produced

Mechanism of PDC X



- 4. Regeneration of disulfide bond of lipoamide via FAD (E3 prosthetic group) which is reduced to FADH2
- Regeneration of FAD by NAD⁺ which is reduced to NADH with the electrons transferred during the reaction (originally from Hydroxyethyl oxidation)