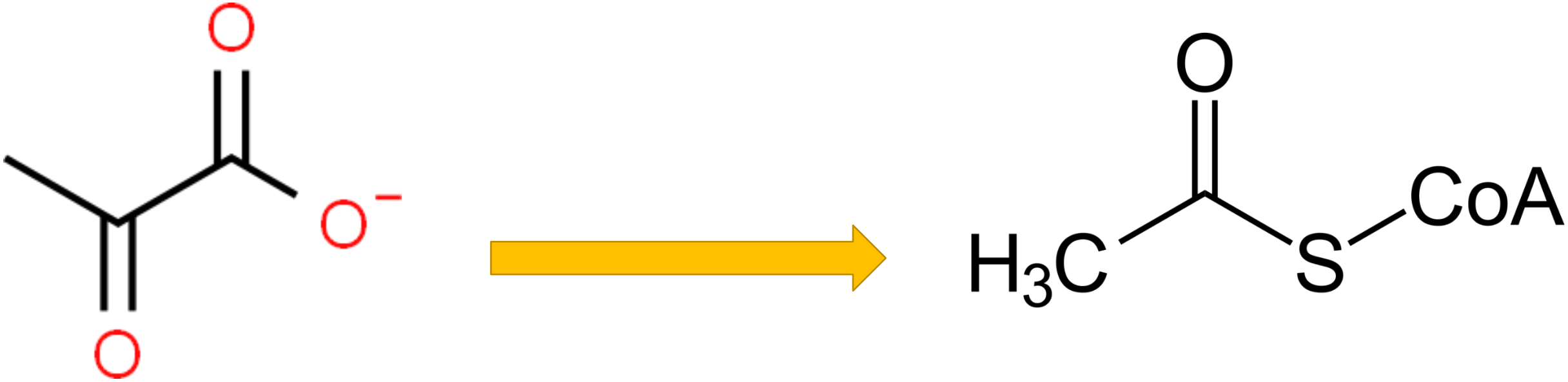


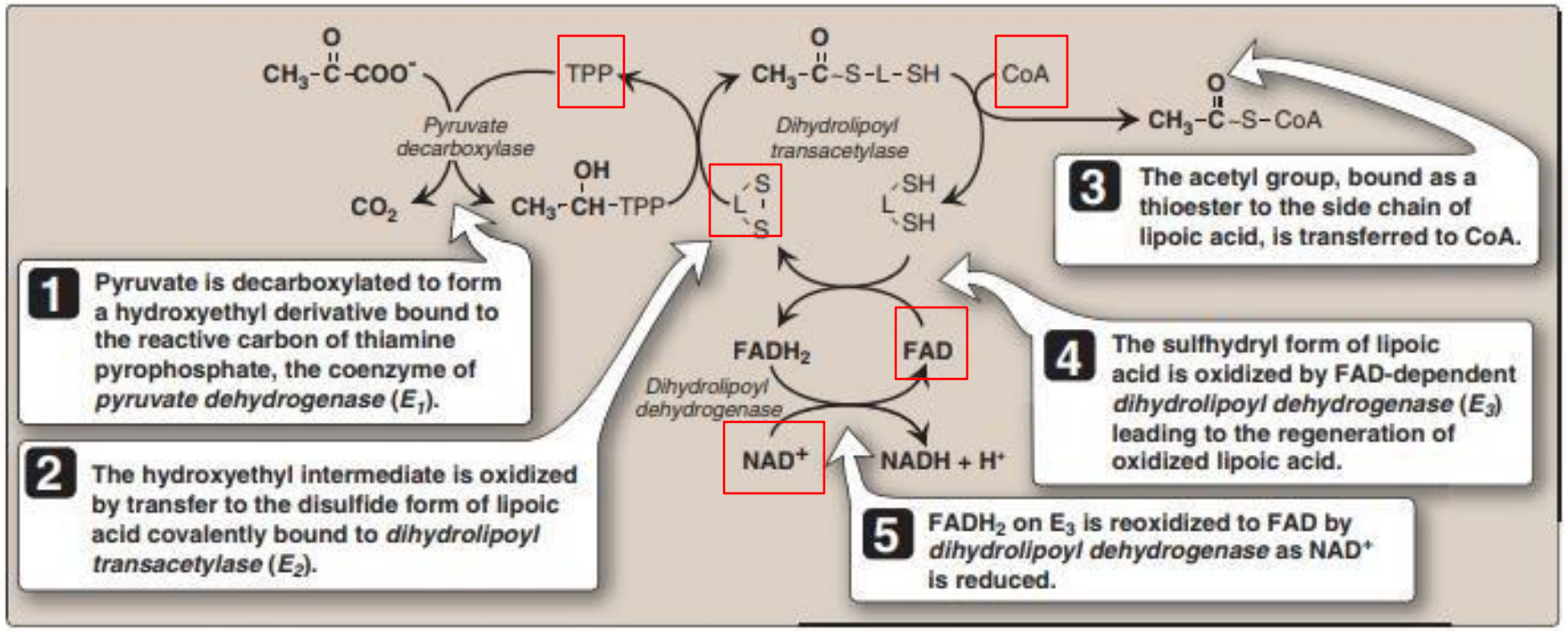
After Glycolysis: From Pyruvate to Acetyl-CoA

Dr. Diala Abu-Hassan, DDS, PhD

From Pyruvate to Acetyl-CoA

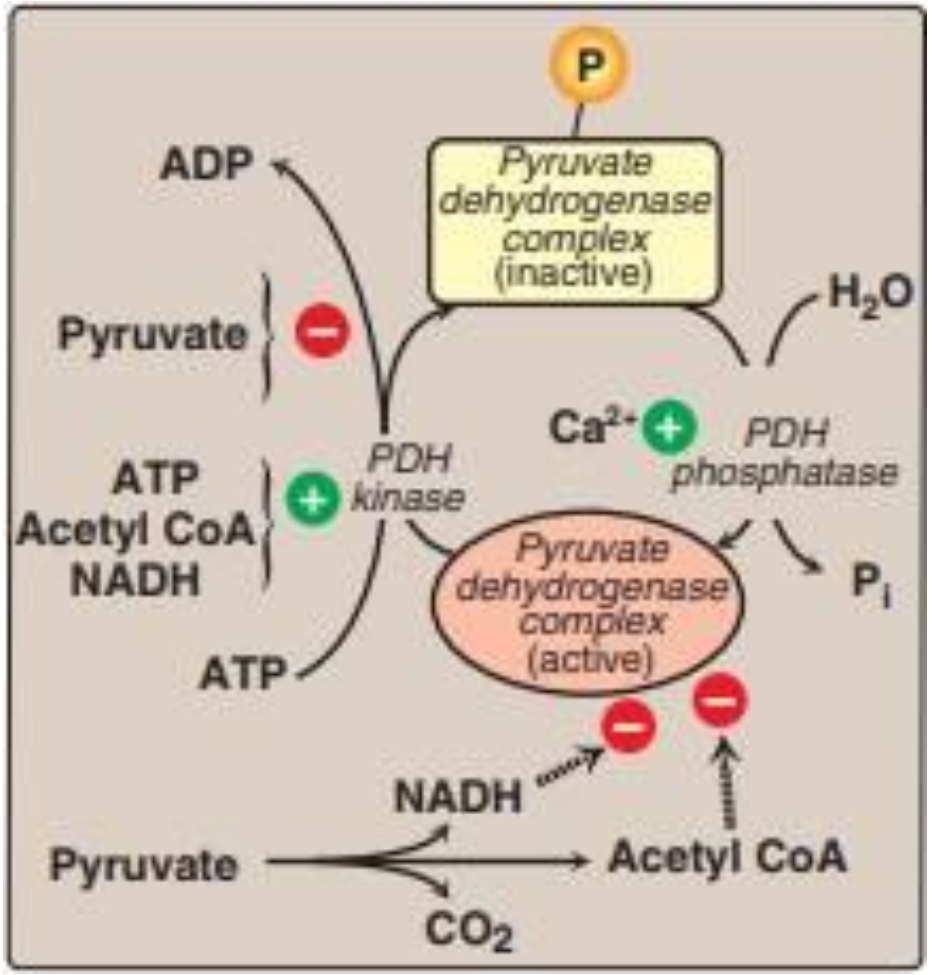
Oxidative decarboxylation of pyruvate

- ✓ Pyruvate is produced in the cytosol and needs to be transported to the mitochondria by a specific pyruvate transporter
- ✓ Once in the matrix, pyruvate is converted to acetyl CoA by the pyruvate dehydrogenase (PDH) complex, which is a multienzyme complex made of 3 enzymes, E1 (decarboxylase), dihydrolipoyl transacetylase (E2), and dihydrolipoyl dehydrogenase (E3).



Regulation of PDH Complex

- ✓ The complex also contains two tightly bound regulatory enzymes, PDH kinase and PDH phosphatase



Clinical Application: PDH deficiency

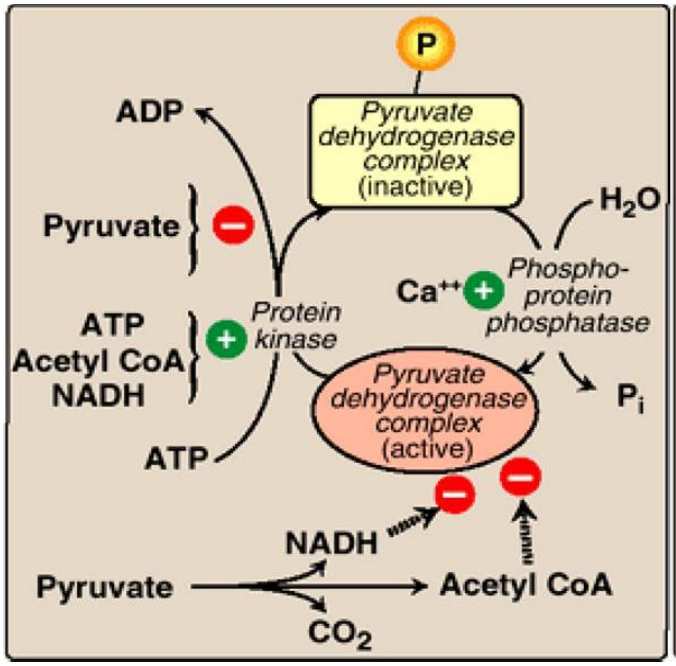
- **Component enzymes**
- **Coenzymes**
- **Regulation of the pyruvate dehydrogenase complex**
  - Pyruvate dehydrogenase deficiency: A deficiency in E_1 component is the most common biochemical cause of congenital lactic acidosis (X-linked, no treatment)

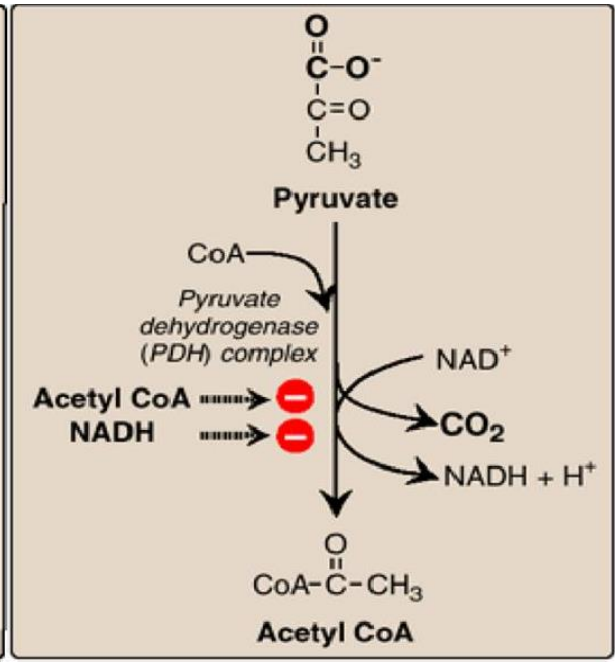
✓ Affected tissues: brain, relies on the TCA cycle for most of its energy, and is sensitive to acidosis.

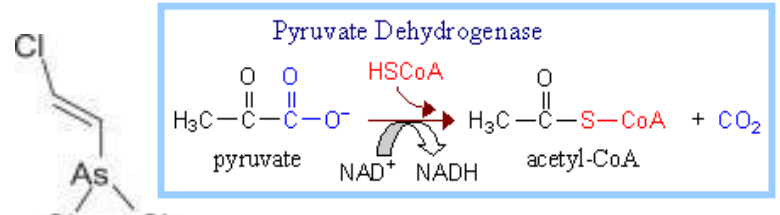
✓ Symptoms are variable and include neurodegeneration, muscle spasticity and, in the neonatal onset form, early death.

✓ Dietary restriction of carbohydrate and supplementation with TPP may reduce symptoms in select patients.

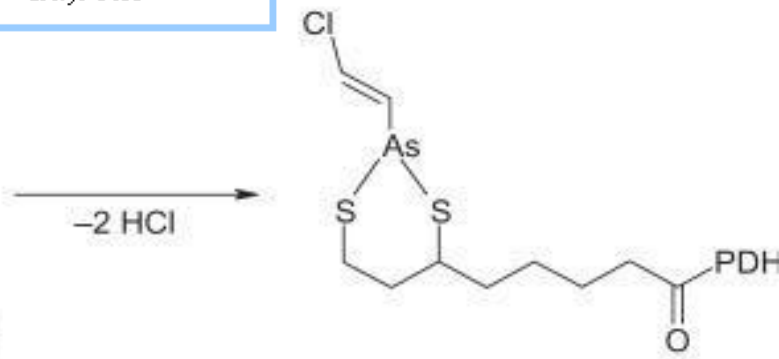
- **Mechanism of arsenic poisoning**







Active lipoate pyruvate dehydrogenase complex



Inhibited lipoate pyruvate dehydrogenase complex