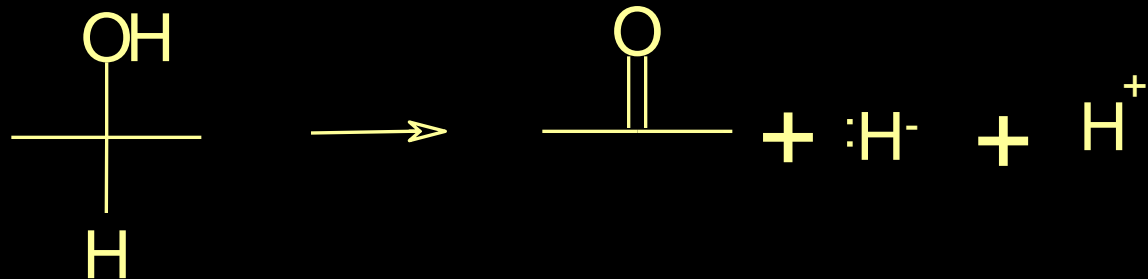
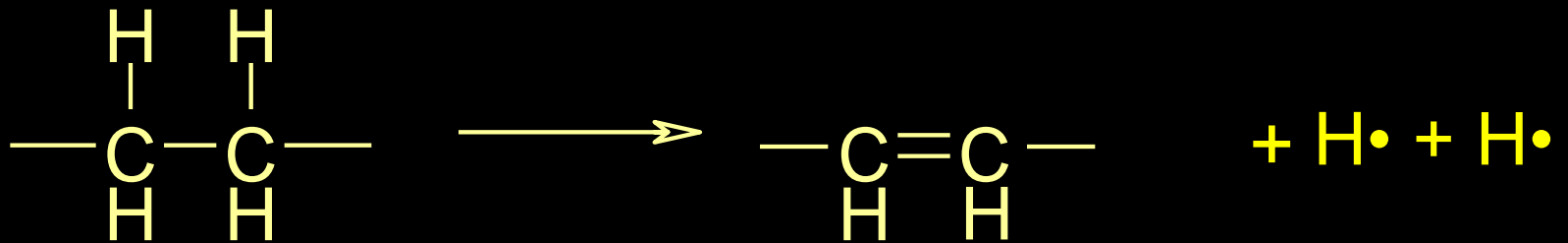
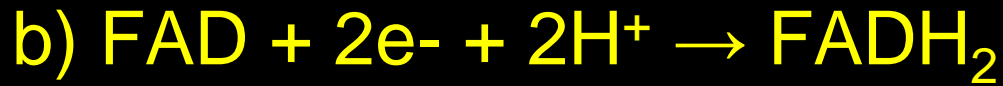


# Biological Oxidations of Organic Compounds

# 1. Dehydrogenation by NAD<sup>+</sup> or FAD (or FMN).



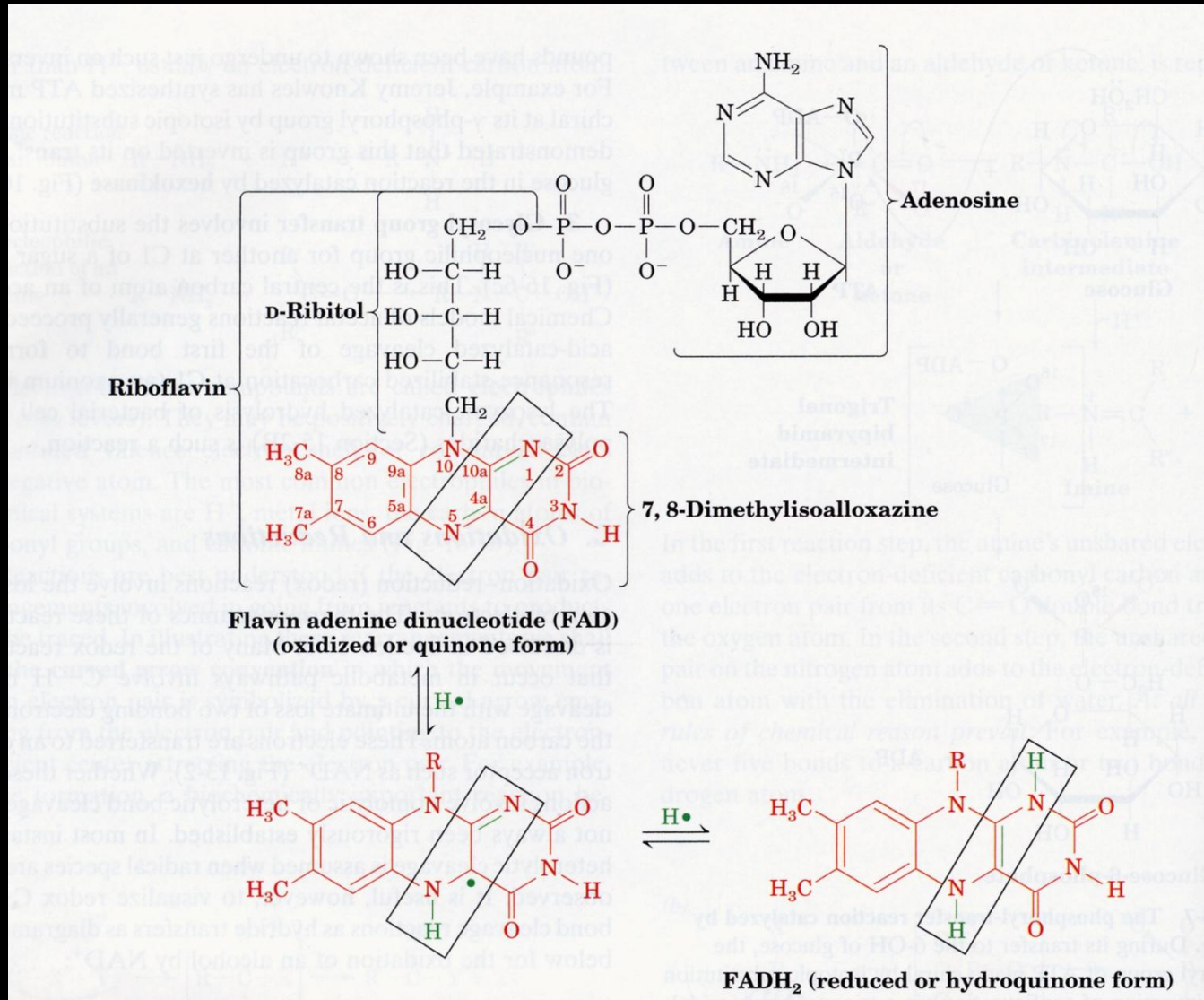
- NAD<sup>+</sup>/NADH is a soluble e<sup>-</sup> carrier
- able to diffuse to its target



FAD/FADH<sub>2</sub> is usually TIGHTLY BOUND as a prosthetic group of an enzyme

All dehydrogenation reactions are catalyzed by  
DEHYDROGENASES

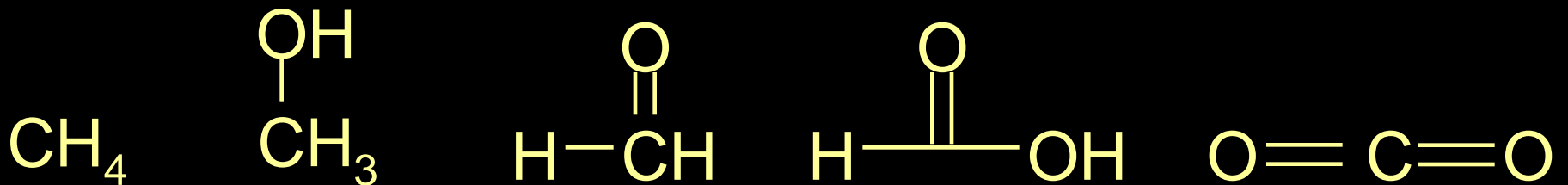
# FAD/FADH<sub>2</sub>



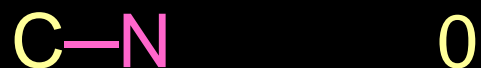
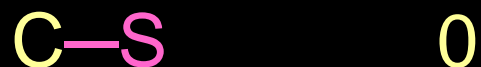
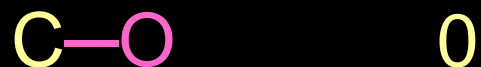
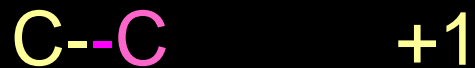
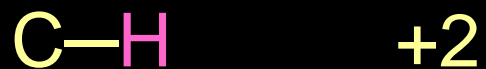
## 2. Combination with O

- Removal of e<sup>-</sup>'s by O which “pulls” e<sup>-</sup>'s away from the C or H nucleus. C or H becomes oxidized ; O becomes reduced.

- These reactions are catalyzed by oxidases



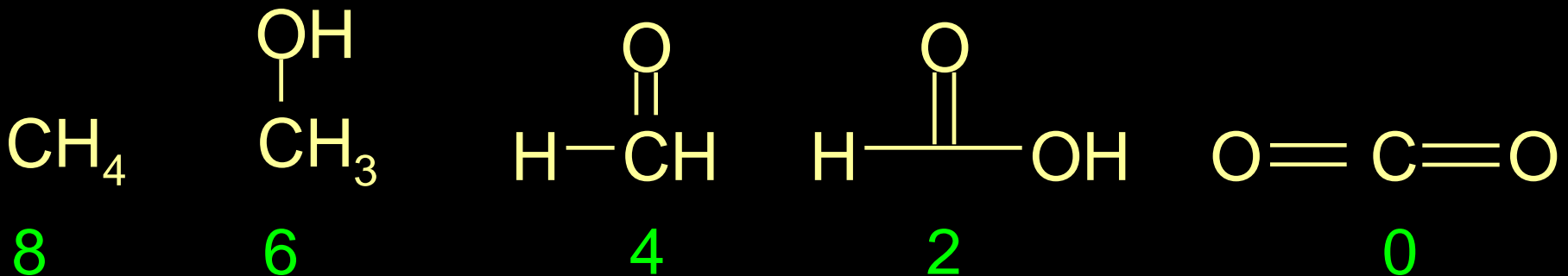
# Oxidation states of carbon



## 2. Combination with O

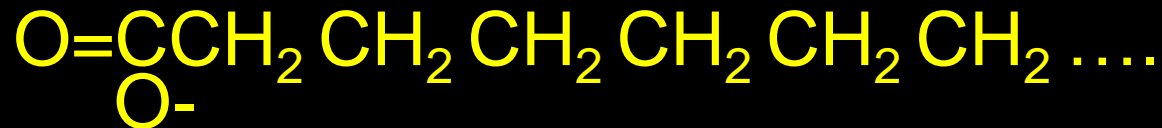
- Removal of e<sup>-</sup>'s by O which “pulls” e<sup>-</sup>'s away from the C or H nucleus. C or H becomes oxidized ; O becomes reduced.

- These reactions are catalyzed by oxidases



Carbohydrates have fewer calories than fats because carbon is already partially oxidized....

- Long Chain FA's (9.3 kcal/g)

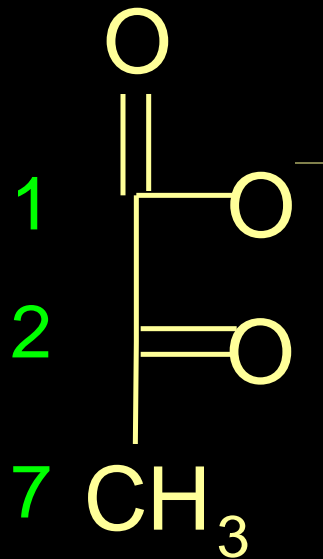


- Carbohydrates (4 kcal/g)





Individual C's can have different  
oxidation states:

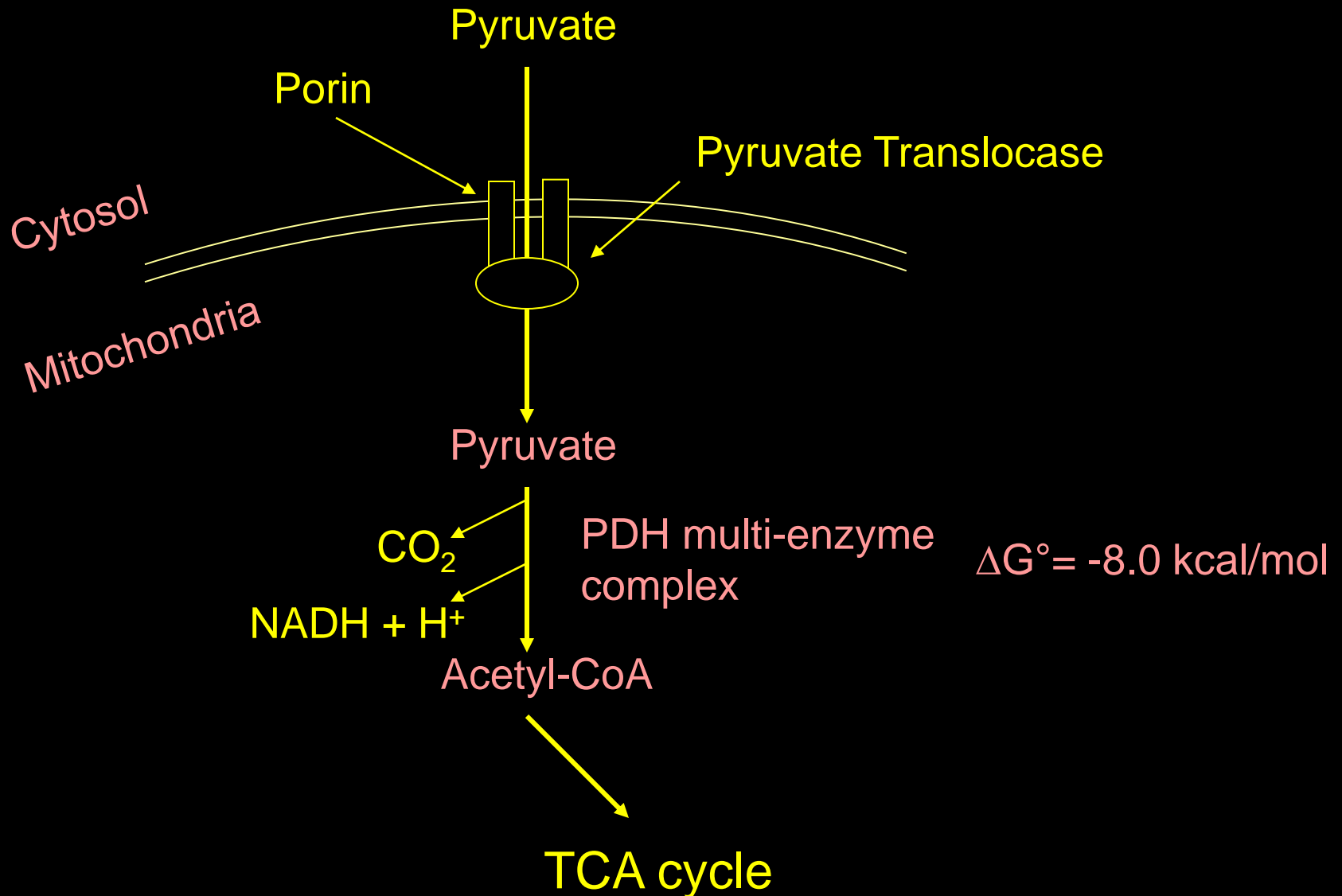


Pyruvate

# Oxidative Metabolism

Production of chemical energy  
via oxidation of pyruvate

# Oxidation of pyruvate occurs in mitochondria



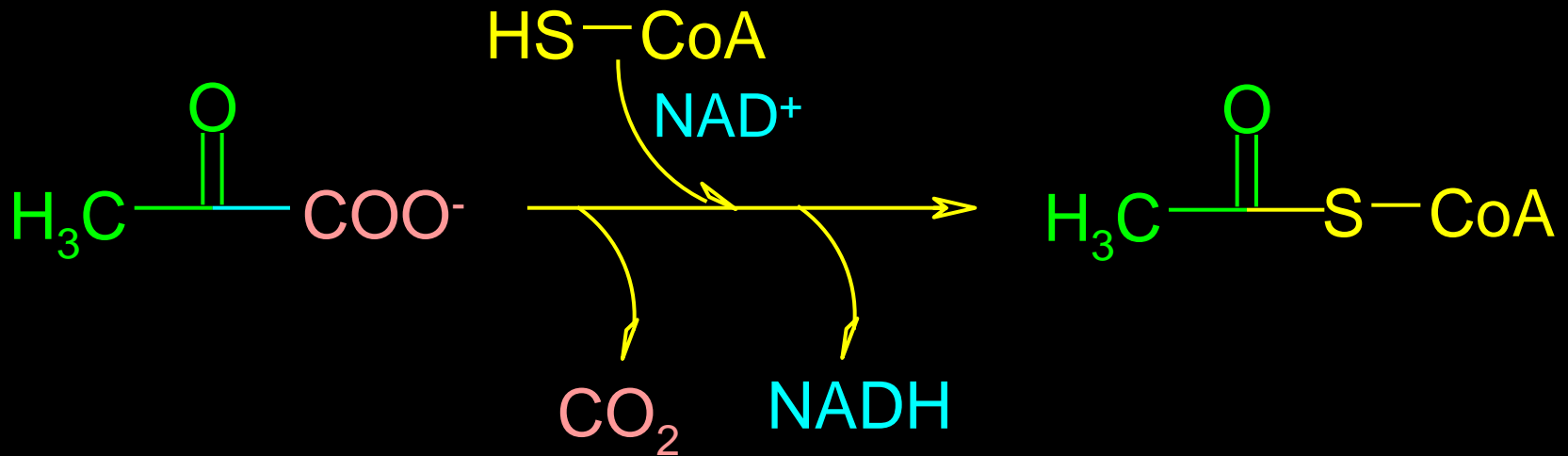
1. Glycolytic enzymes are cytosolic.  
PDH and TCA cycle enzymes are mitochondrial.
2. Fate of cytosolic pyruvate is lactate or alanine.  
Sole fate of mitochondrial pyruvate is the TCA cycle (Acetyl-CoA, Oxaloacetate).

# Pyruvate Dehydrogenase

## -role of vitamins

# Pyruvate Dehydrogenase Complex

- links glycolysis & TCA cycle



PDH

# Role of Vitamins & Cofactors in PDH

1. Thiamine → Thiamine Pyrophosphate
2. Niacin → NAD<sup>+</sup>
3. Riboflavin → FAD (Flavin Adenine Dinucleotide)
4. Panthothenic Acid → Coenzyme A
5. Lipoic Acid → Lipoamide

# Discovery of thiamine (and vitamins)

TABLE 1-1

*Japanese naval records of deaths from beriberi*

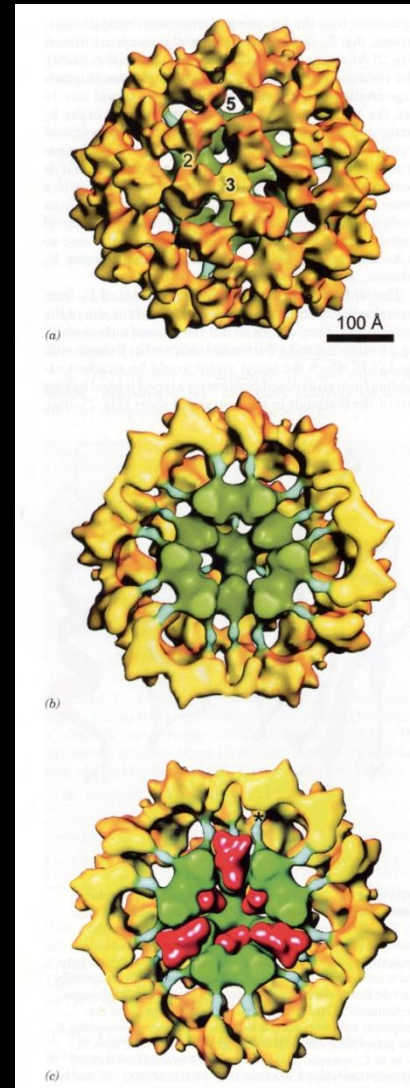
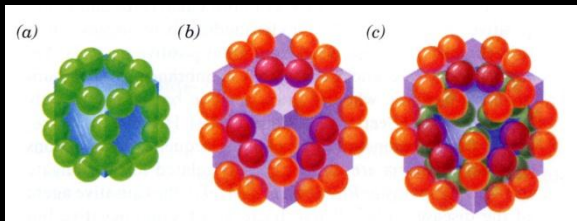
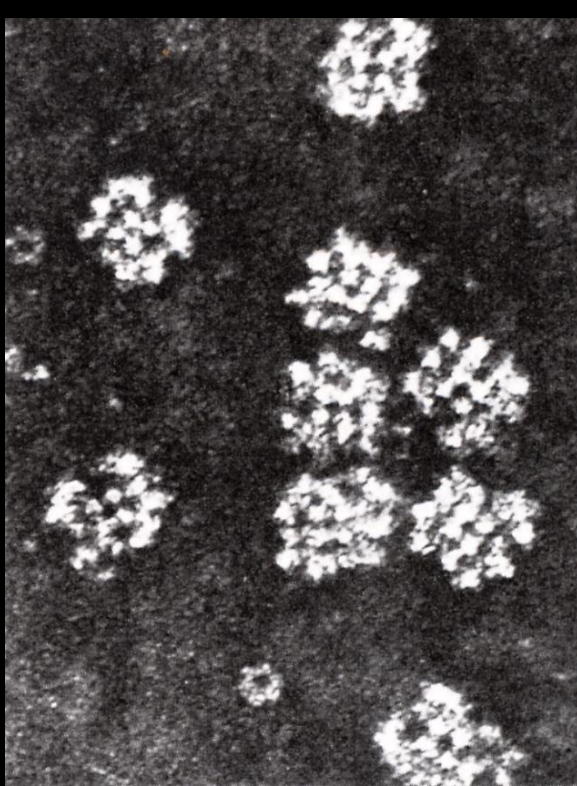
| Year | Diet               | Total navy personnel | Deaths from beriberi |
|------|--------------------|----------------------|----------------------|
| 1880 | Rice diet          | 4,956                | 1,725                |
| 1881 | Rice diet          | 4,641                | 1,165                |
| 1882 | Rice diet          | 4,769                | 1,929                |
| 1883 | Rice diet          | 5,346                | 1,236                |
| 1884 | Change to new diet | 5,638                | 718                  |
| 1885 | New diet           | 6,918                | 41                   |
| 1886 | New diet           | 8,475                | 3                    |
| 1887 | New diet           | 9,106                | 0                    |
| 1888 | New diet           | 9,184                | 0                    |



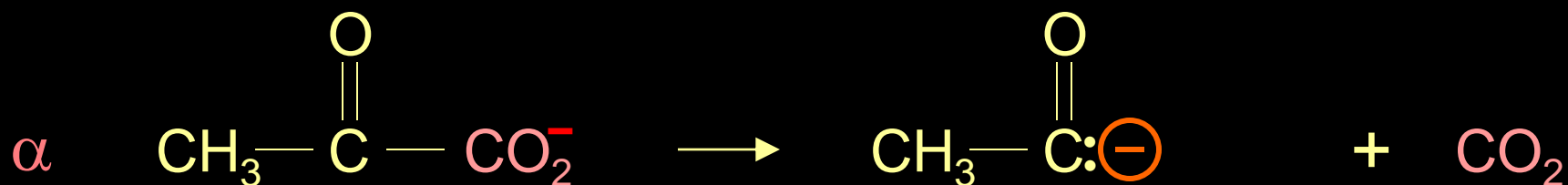
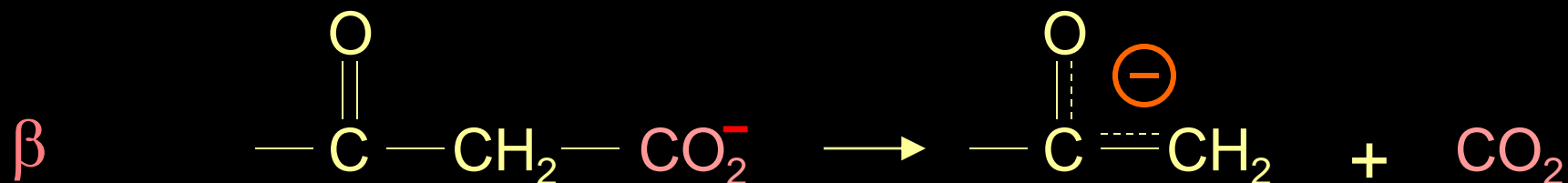
**TABLE 17.1** Pyruvate dehydrogenase complex of *E. coli*

| Enzyme                           | Abbreviation   | Number of chains | Prosthetic group | Reaction catalyzed                             |
|----------------------------------|----------------|------------------|------------------|--|
| Pyruvate dehydrogenase component | E <sub>1</sub> | 24               | TPP              | Oxidative decarboxylation of pyruvate          |
| Dihydrolipoyl transacetylase     | E <sub>2</sub> | 24               | Lipoamide        | Transfer of the acetyl group to CoA            |
| Dihydrolipoyl dehydrogenase      | E <sub>3</sub> | 12               | FAD              | Regeneration of the oxidized form of lipoamide |

# 3D Imaging of PDH Complex

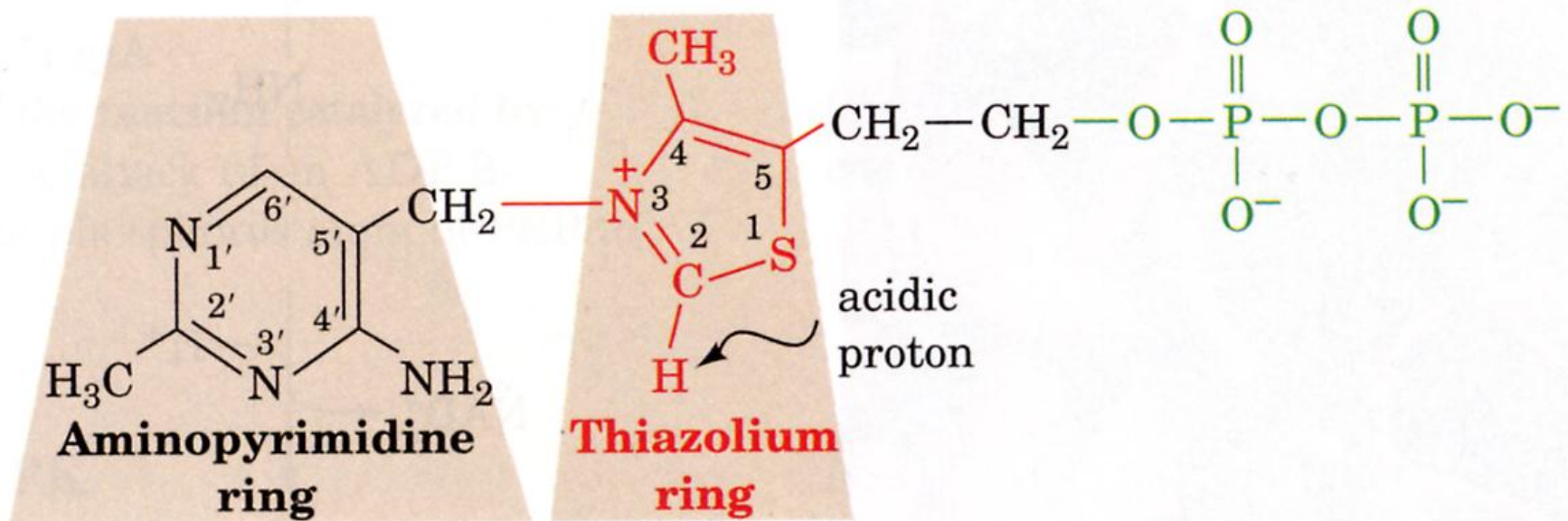


## General Decarboxylation

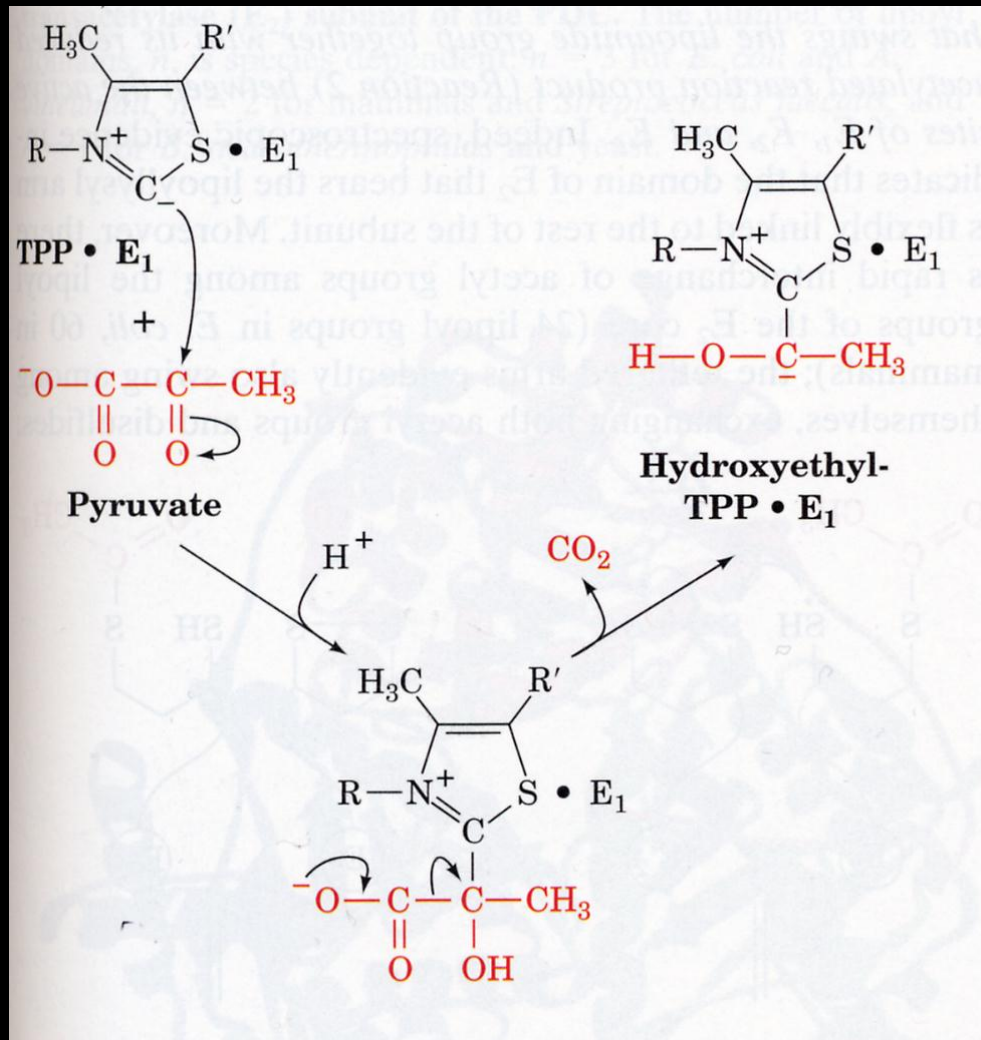


pyruvate

# Thiamine Pyrophosphate



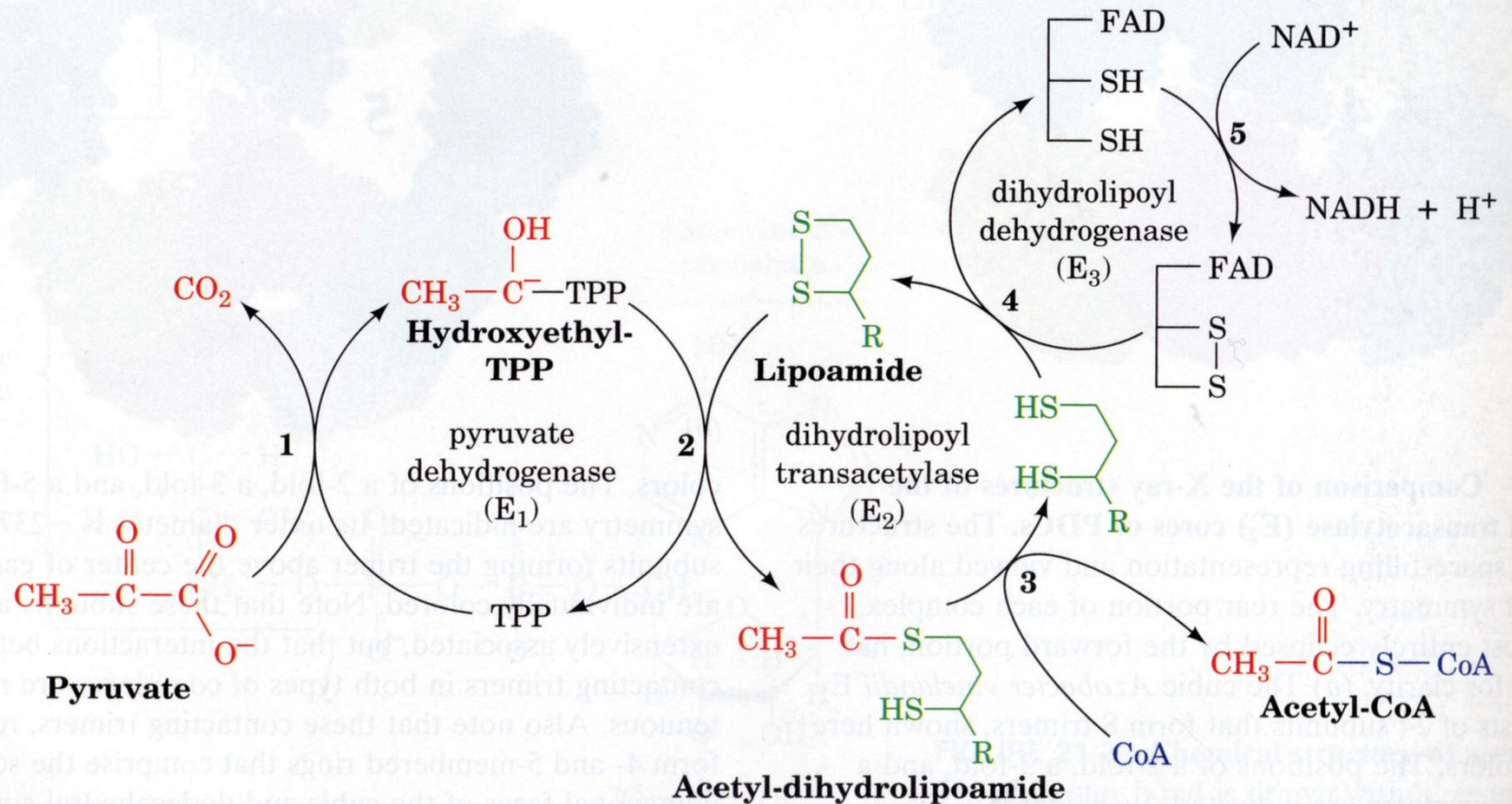
# Mechanism of pyruvate decarboxylation and oxidation by PDH



**Step 1:**  
**TPP-dependent  
 $\alpha$ -decarboxylation**



# Complete PDH mechanism



**FIGURE 21-6 The five reactions of the PDC.** E<sub>1</sub> (pyruvate dehydrogenase) contains TPP and catalyzes Reactions 1 and 2. E<sub>2</sub> (dihydrolipoyl transacetylase) contains lipoamide and

catalyzes Reaction 3. E<sub>3</sub> (dihydrolipoyl dehydrogenase) contains FAD and a redox-active disulfide and catalyzes Reactions 4 and 5.

# Pyruvate Dehydrogenase

