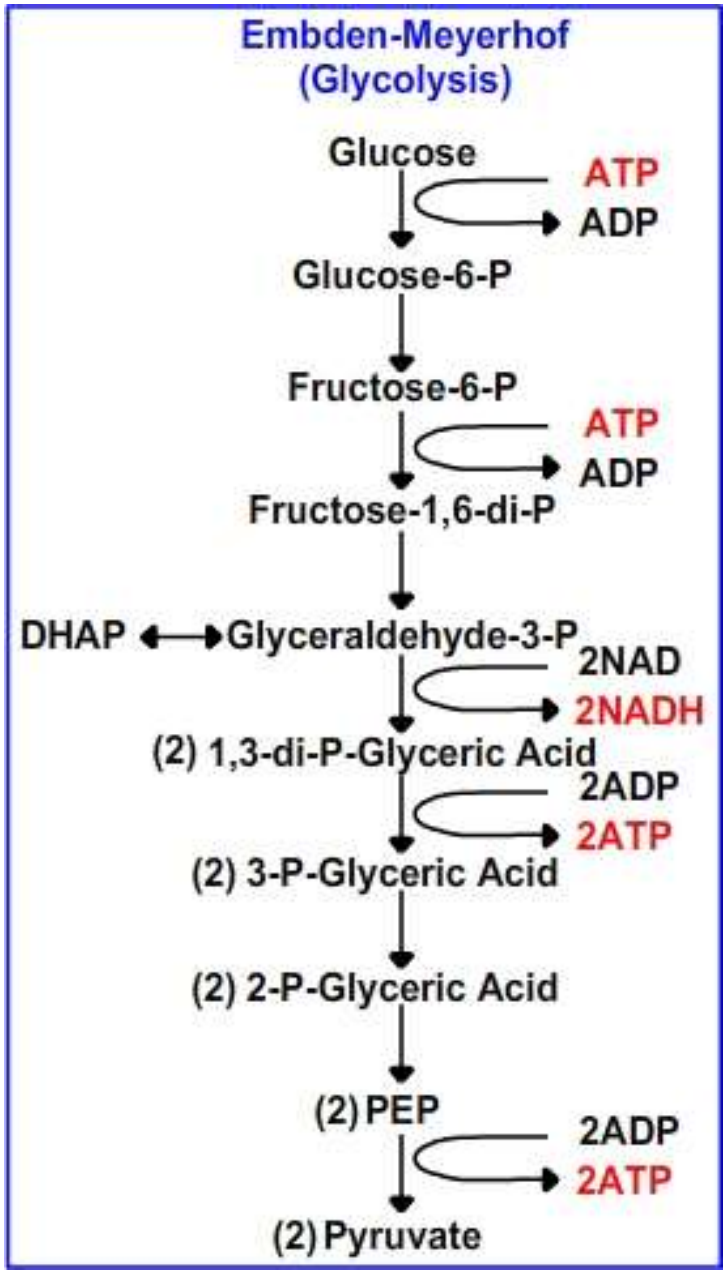
The most common pathway for the oxidation of glucose is glycolysis. Pyruvic acid is the end-product.

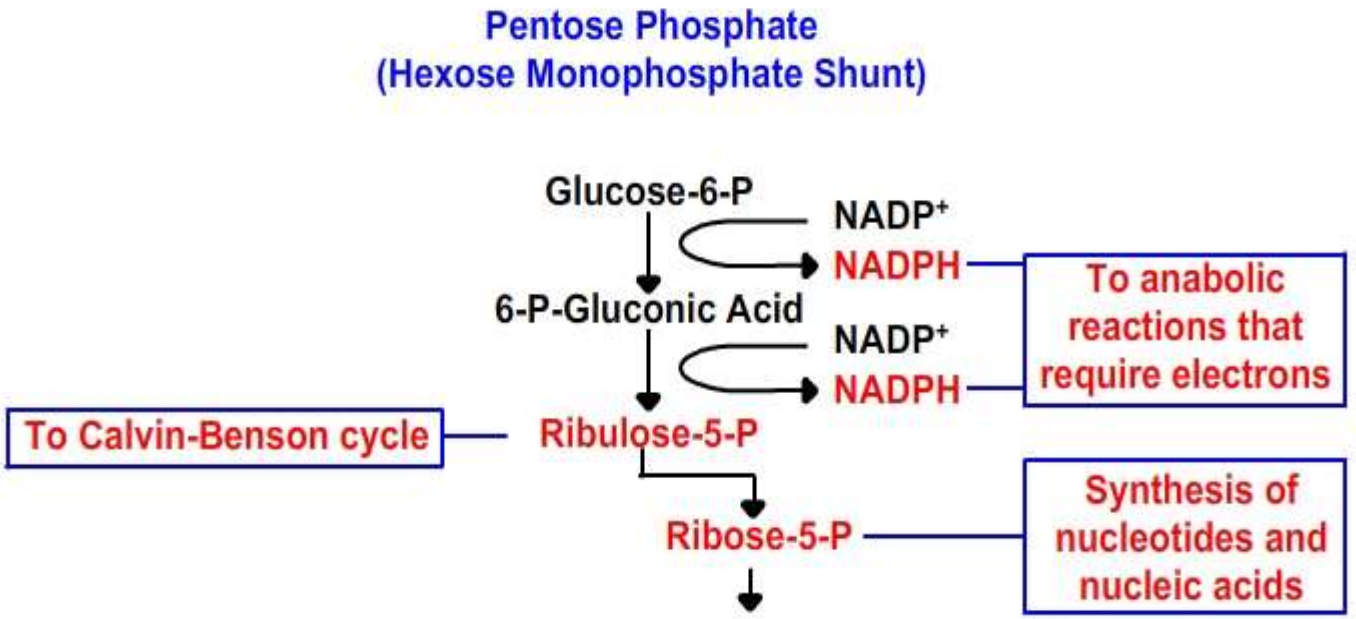
Two ATP and **two NADH** molecules are produced from one glucose molecule.



The **Pentose Phosphate** pathway (hexose monophosphate shunt) is used primarily to produce **five-carbon sugars** and **high energy electrons** for **anabolic reactions**.

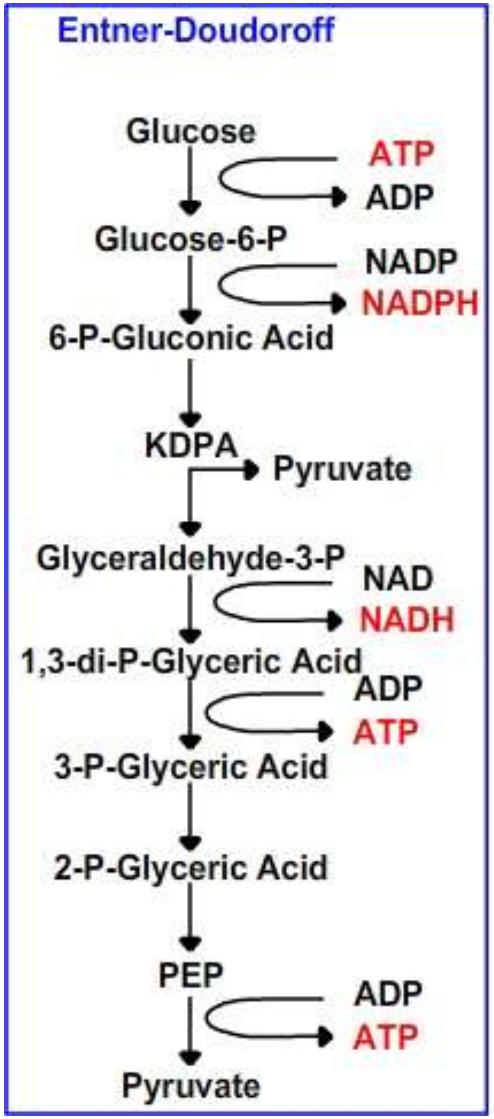
2 NADPH molecules are produced from oxidation of one glucose-6-P molecule, which may be "shunted" into the pentose phosphate pathway from both the Embden-Meyerhoff (glycolysis) and the Entner-Douderoff pathways.

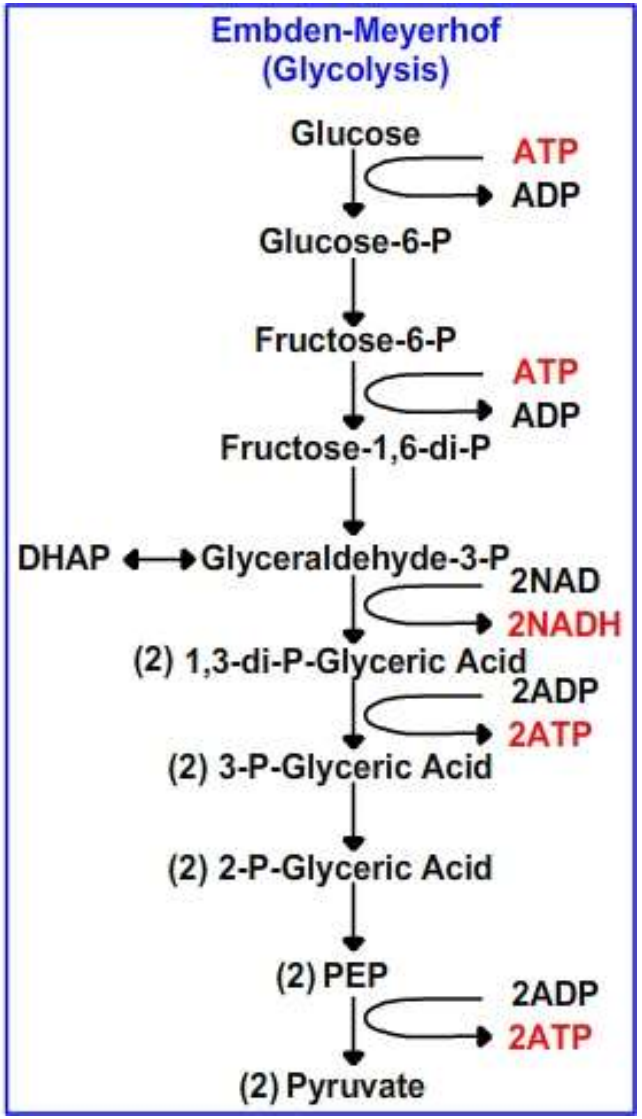
The pathway produces intermediates for nucleotide and nucleic acid synthesis, glucose synthesis from CO_2 in the Calvin-Benson cycle of photosynthesis, and some amino acids.



The **Entner-Doudoroff** pathway yields **one ATP**, **one NADPH**, and **one NADH** molecule from one glucose molecule.

Used by Gram negatives (e.g.*Rhizobium, Pseudomonas, Agrobacterium*), usually not by Gram positives.





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The Entner-Doudoroff Pathway Is Obligatory for Gluconate Utilization and Contributes to the Pathogenicity of *Vibrio cholerae*

Tapas Patra, Hemanta Koley, Thandavarayan Ramamurthy, Asoke C. Ghose, and Ranjan K. Nandy

National Institute of Cholera and Enteric Diseases, Kolkata, India

The Entner-Doudoroff (ED) pathway has recently been shown to play an important role in sugar catabolism for many organisms although very little information is available on the functionality of this pathway in *Vibrio cholerae*, the causative agent of cholera. In this study, activation of the genes *edd* and *eda*, encoding 6-phosphogluconate dehydratase and 2-keto-3-deoxy-6-phosphogluconate aldolase, was used as a marker of a functional ED pathway in *V. cholerae*. Transcriptional activation analyses and gene silencing experiments with cells grown in sugar-supplemented M9 medium demonstrated that the ED pathway is functional in *V. cholerae* and is obligatory for gluconate catabolism. Importantly, selective activation of the ED pathway led to concurrent elevation of transcripts of prime virulence genes (*ctxA* and *tcpA*) and their regulator (*toxT*). Further, lowering of these transcript levels and cholera toxin production *in vitro* by an ED pathway-defective mutant (strain N16961 with a Δ*edd* mutation [Δ*edd*$_{N16961}$ strain]) suggested the importance of this pathway in regulating *V. cholerae* virulence. The *in vivo* relevance of these data was established as the mutant failed to colonize in suckling mice intestine or to induce fluid accumulation in ligated rabbit ileal loops. Activation of the ED pathway in *V. cholerae* was shown to inhibit biofilm formation *in vitro* that could be reversed in the mutant. As further support for these results, comparative transcriptome analysis with cells grown in the presence of glucose or gluconate revealed that a functional ED pathway led to activation of a subset of previously reported *in vivo* expressed genes. All of these results suggest the importance of the ED pathway in *V. cholerae* pathogenesis.

Carbohydrates play an important role in the assimilation of energy by living cells and act as carbon sources for the synthesis of important metabolites. The breakdown of sugars through different catabolic pathways provides energy to the bacterial cells in the form of ATP and other reducing equivalents. The best-characterized pathways for sugar catabolism in bacteria are the Embden-Meyerhof-Parnas (EMP), the pentose phosphate (PP), and the Entner-Doudoroff (ED) pathways. These pathways are widespread in prokaryotes and are crucial for their physiology and nutrition. The overall schemes of the ED and EMP pathways are quite similar: 6-carbon sugars are primed by phosphorylation and subsequently cleaved by the aldolase enzyme into two 3-carbon intermediates (27). The two key enzymes distinctive to the ED pathway are (i) 6-phosphogluconate dehydratase (Edd) (EC 4.2.1.12), which catalyzes dehydration of 6-phosphogluconate to form 2-keto-3-deoxy-6-phosphogluconate (KDPG), and (ii) KDPG aldolase (Eda) (EC 4.1.2.14), which cleaves KDPG to pyruvate and glyceraldehyde 3-phosphate, the latter being further catabolized through the EMP pathway and tricarboxylic acid (TCA) cycle (6). The ED pathway was discovered in 1952 in *Pseudomonas saccharophila* (9) and several years later was shown to be present in *Escherichia coli* (8). Initially, the ED pathway was considered to be restricted to Gram-negative bacteria, but current studies indicate that it is widely distributed from *Archaea* to *Eukarya* (6). It is now believed that the ED pathway predates the EMP pathway in the evolution of microbes (30).

The enzymes Edd and Eda of the ED pathway play key roles in gluconate (Gnt) catabolism. Gnt, a sugar acid which is available in the intestinal milieu, can be utilized by various microorganisms as an energy source. The organism *E. coli* utilizes Gnt through the ED pathway (27). This bacterium has high-affinity (GntT) and low-affinity (GntU) Gnt transporters and a thermoresistant gluconokinase enzyme (GntK) (EC 2.7.1.12) involved in phosphorylation of Gnt. Catabolism of Gnt via the ED pathway in the organism is controlled by the repressor protein GntR. The *edd*, *eda*, *gntT*, *gntU*, and *gntK* genes are crucial for functioning of the ED pathway, and their expression is negatively regulated by *gntR*, whereas Gnt acts as a true inducer (26). Recent studies have suggested that the ED pathway may play an important role in the physiology of *E. coli* bacteria toward their adaptation specific for the intestinal milieu (4). Apart from *E. coli*, the ED pathway may be important in the survival of pathogenic organisms like *Salmonella enterica*, *Neisseria gonorrhoeae*, *Klebsiella pneumoniae*, *Helicobacter pylori*, *Pseudomonas aeruginosa*, *Legionella pneumophila*, *Pasteurella pestis*, *Xanthomonas campestris*, *Pectobacterium carotovorum*, etc. in their respective host systems (2, 3, 10, 15, 20, 21, 23, 24, 31, 33).

The Gram-negative gammaproteobacterium *Vibrio cholerae*, the etiological agent of the diarrheal disease cholera, has a life cycle that includes its existence in intestinal (in humans) as well as extraintestinal (marine aquatic) environments, preferably by forming biofilms (12). Clearly, the adaptation of the organism in such distinct environments would require appropriate metabolic pathways to be functional and efficient to derive energy from diverse nutrient sources. To date, our knowledge is quite limited in understanding the physiological changes that *V. cholerae* adopts during the transition between the two extreme environments and their pathological consequences. An analysis of genomic data of *V. cholerae* has revealed the presence of a Gnt utilization system in-

Received 2 March 2012 Accepted 16 April 2012 Published ahead of print 27 April 2012 Address correspondence to Ranjan K. Nandy, nandyrk@icmr.org.in. Supplemental material for this article may be found at http://jb.asm.org. doi:10.1128/JB.06379-11

Summary of Glycolysis and Alternatives