Pentose Phosphate Pathway-I

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INTRODUCTION

- In most animal tissues, the major catabolic fate of glucose 6-phosphate is glycolytic breakdown to pyruvate leading to the formation of ATP.

- Glucose 6-phosphate does have other catabolic fates, however, which lead to specialized products needed by the cell.

- The oxidation of glucose 6-phosphate to pentose phosphatesalso occurs by the **pentose phosphate pathway** OR **phosphogluconate pathway** OR **hexose monophosphate pathway.**

- In this oxidative pathway, NADP is the electron acceptor, yielding NADPH.

Significance of Pentose Phosphate Pathway

- Rapidly dividing cells, such as those of bone marrow, skin, and intestinal mucosa, use the pentoses to make RNA, DNA, and such coenzymes as ATP, NADH, $FADH_2$, and coenzyme A.

- In other tissues, the essential product of the pentose phosphate pathway is not the pentoses but the electron donor NADPH, needed for reductive biosynthesis or to counter the damaging effects of oxygen radicals.

- Tissues that carry out extensive fatty acid synthesis (liver, adipose, lactating mammary gland) or very active synthesis of cholesterol and steroid hormones (liver, adrenal gland, gonads) require the NADPH provided by the pathway.

- Erythrocytes and the cells of the lens and cornea are directly exposed to oxygen and thus to the damaging free radicals generated by oxygen.

General scheme of the pentose phosphate pathway

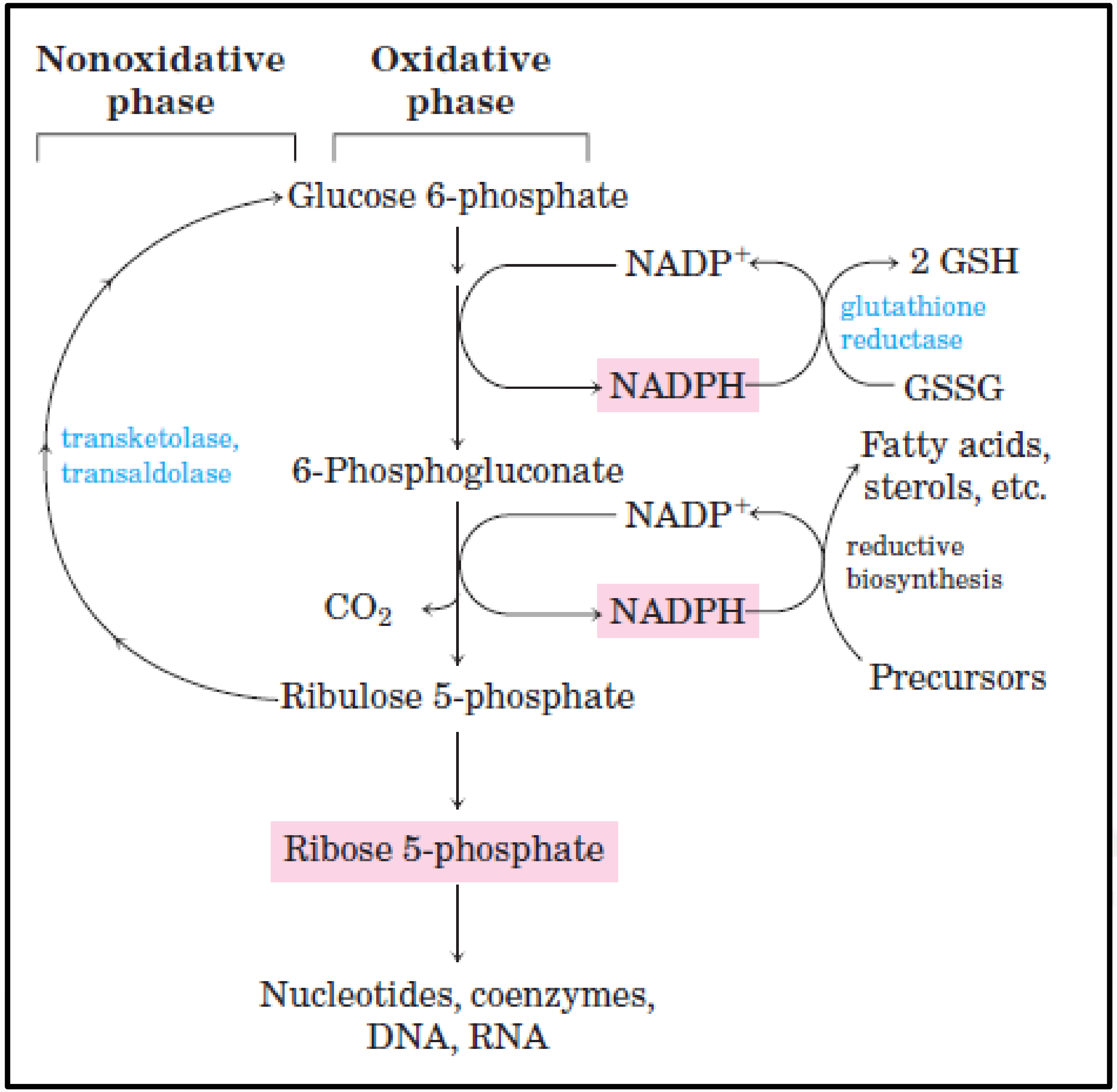


Image adapted from Lehninger

The pentose phosphate pathway

- **Oxidative phase**:

Ribose 5-phosphate and NADPH are produced.

- **Non-oxidative phase:**

Ribose 5-phosphate recycles six molecules of the pentose into five molecules of the hexose glucose 6-phosphate,

Allowing continued production of NADPH and converting glucose 6-phosphate

The Oxidative Phase

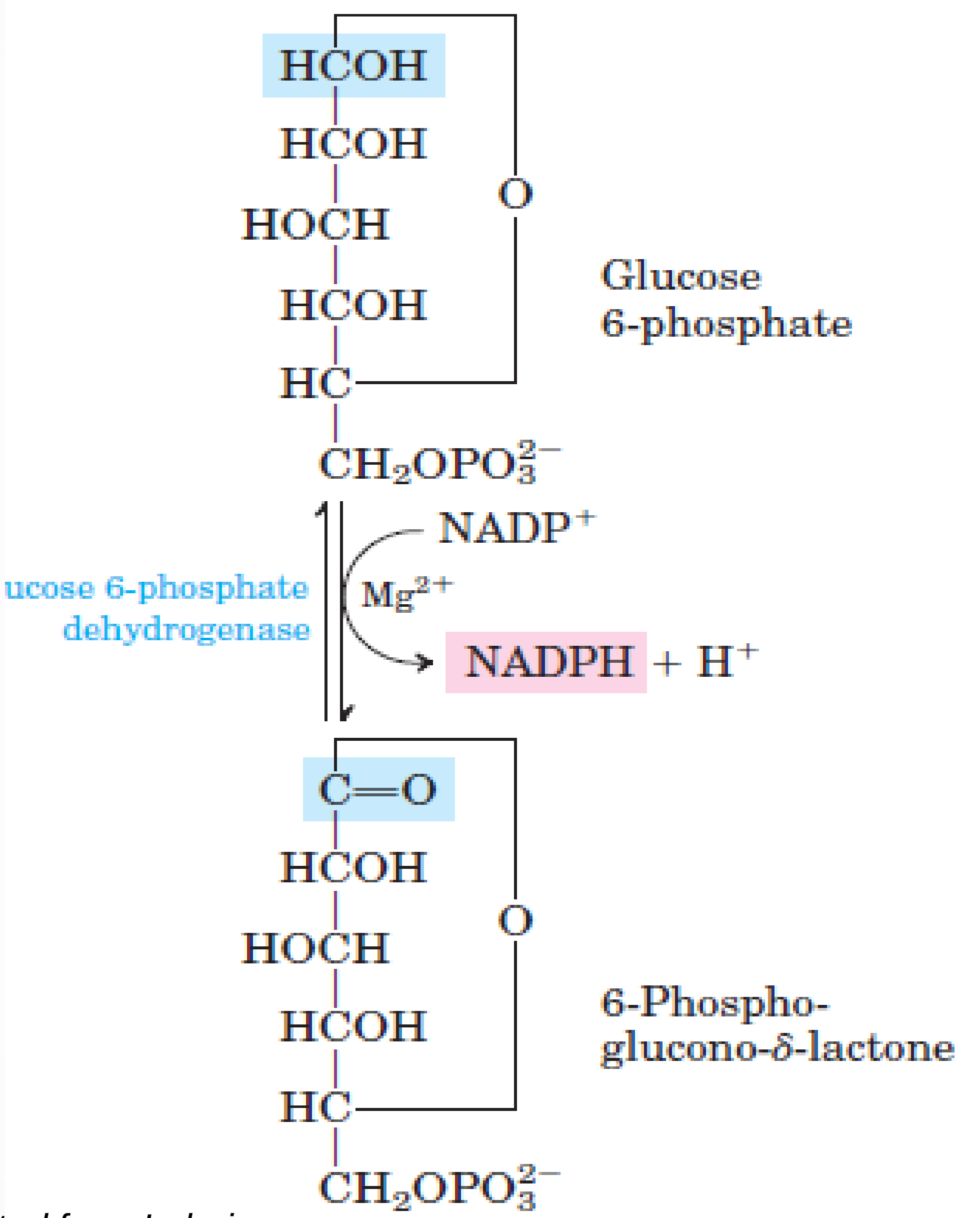
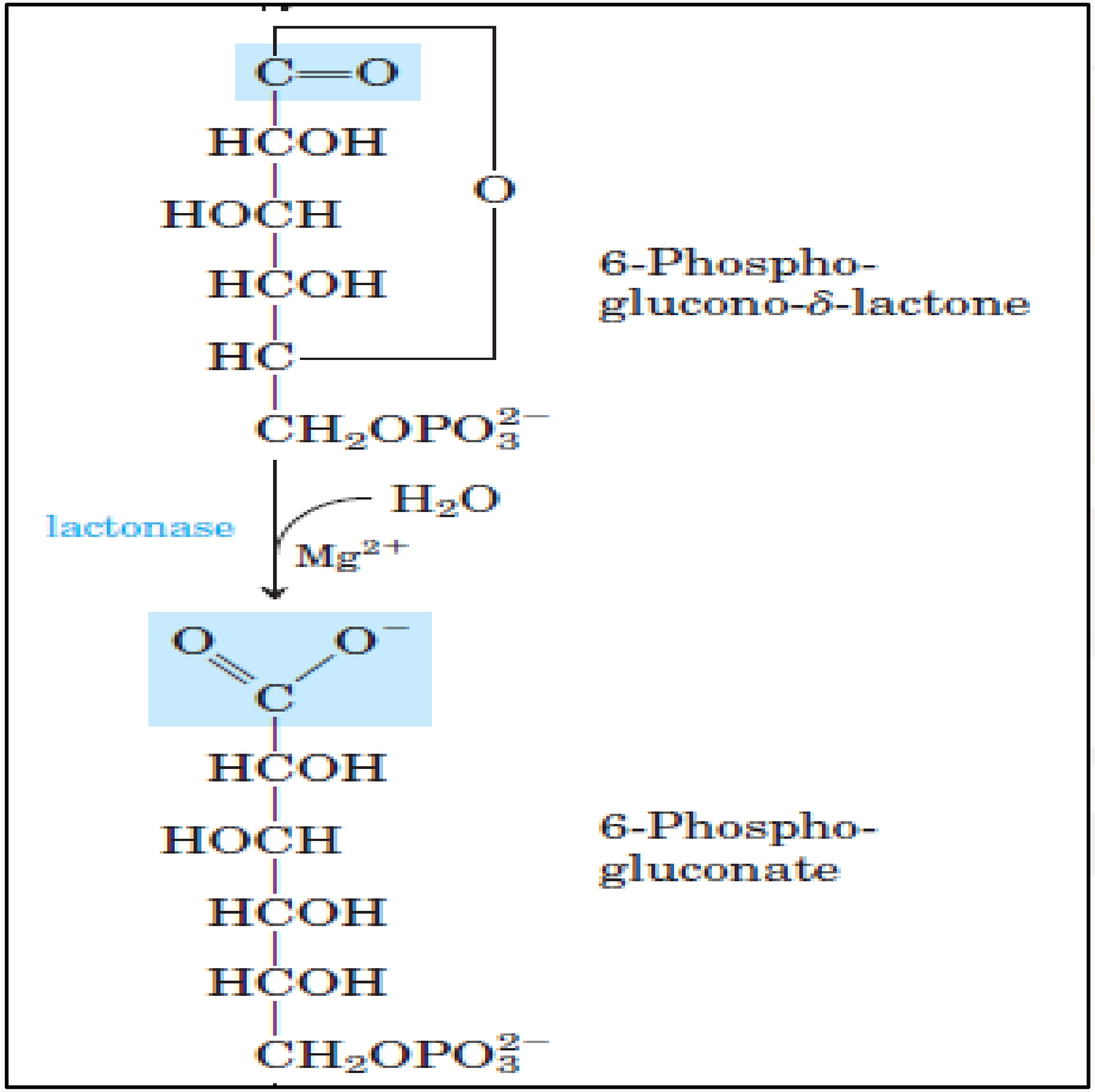


Image adapted from Lehninger

- The first reaction of the pentose phosphate pathway is the oxidation of glucose 6-phosphate by **glucose 6-phosphate dehydrogenase (G6PD)** to form 6-phosphoglucono—lactone.

- NADP is the electron acceptor, and the formation of NADPH occur.

Formation of 6-phosphogluconate dehydrogenase



- The lactone is hydrolyzed to the free acid 6-phosphogluconate by a specific **lactonase.**

- 6-phosphogluconate undergoes oxidation and decarboxylation by **6-phosphogluconate dehydrogenase** to form the ketopentose ribulose 5-phosphate.

Image adapted from Lehninger

Formation of Ribulose-5-Phosphate

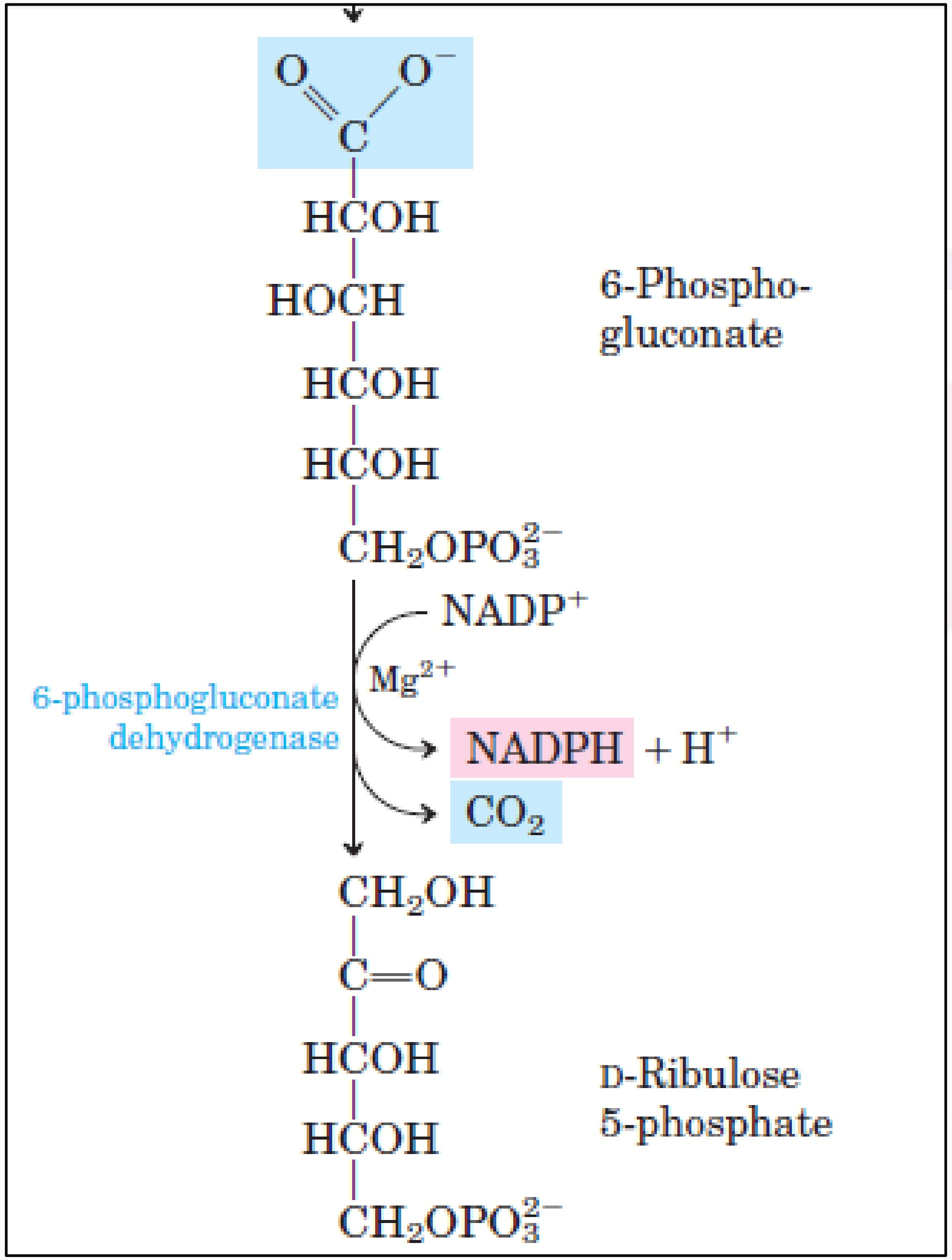


Image adapted from Lehninger

Phosphopentose isomerase converts ribulose 5-phosphate to its aldose isomer, ribose 5-phosphate.

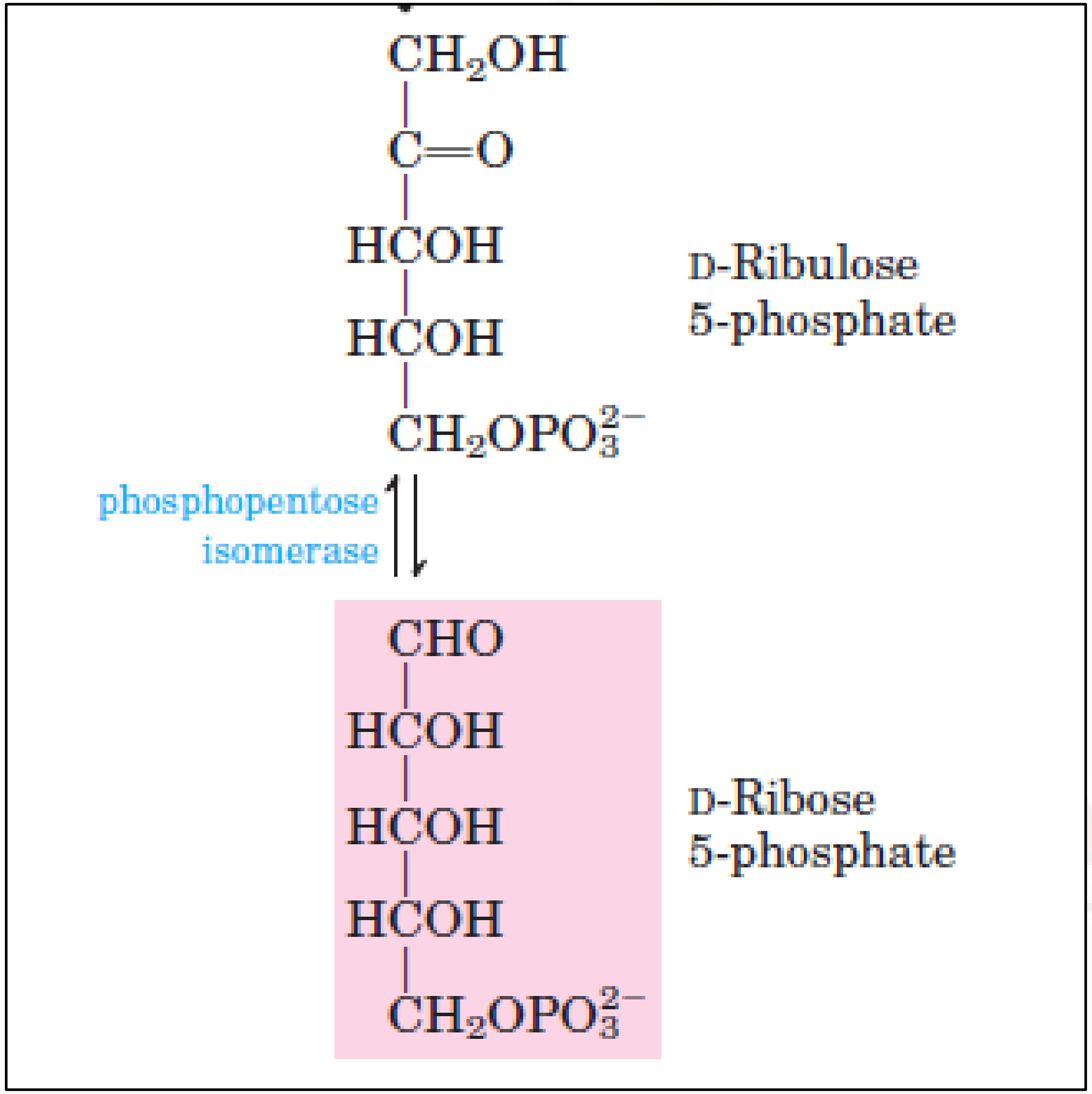


Image adapted from Lehninger

In some tissues, the pentose phosphate pathway ends at this point, and its overall equation is:

$$\text{Glucose 6-phosphate} + 2NADP^+ + H_2O \longrightarrow \text{ribose 5-phosphate} + CO_2 + 2NADPH + 2H^+$$

The net result is:

- The production of NADPH, a reductant for biosynthetic reactions,
- Ribose 5-phosphate, a precursor for nucleotide synthesis.

References:

Lehninger, Albert L., Cox, Michael M.Nelson, David L.Lehninger Principles Of Biochemistry. New York : W.H. Freeman, 2008.

Biochemistry (9th Edition). Author(s):. Jeremy M. Berg, Lubert Stryer, John Tymoczko, Gregory Gatto. Publisher: WH Freeman.


Thank you