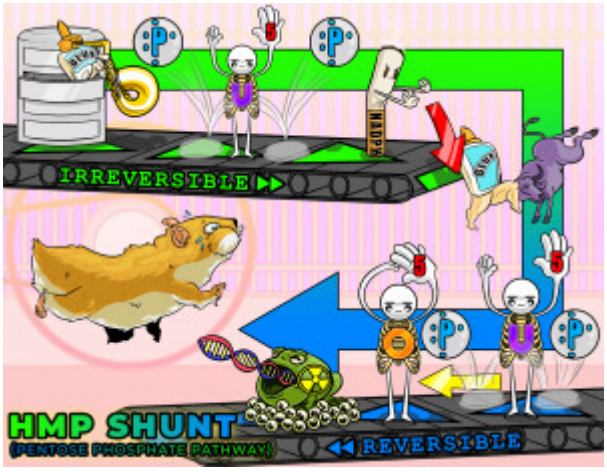
Hexose Monophosphate Shunt (Pentose Phosphate Pathway)

The hexose monophosphate (HMP) shunt, or pentose phosphate pathway, is a biochemical pathway responsible for the production of nucleotide precursors and NADPH. There are two phases, both in the cytoplasm: oxidative (irreversible) and non-oxidative (reversible).The oxidative phase begins with glucose-6-phosphate dehydrogenase, which catalyzes the rate limiting step of this pathway. The net effect of this pathway is the production of ribulose-5-phosphate from glucose-6-phosphate. Also generated is NADPH, which has multiple uses including reducing glutathione to protect the body's cells from oxidative stress. The non-oxidative phase begins with the enzyme ribulose-5-phosphate isomerase (phosphopentose isomerase), which forms ribose-5-phosphate. This molecule is crucial for nucleotide synthesis.



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Oxidative Phase (Irreversible)

Glucose-6-Phosphate Dehydrogenase

Glue-bottle (6) Sax Phosphate-P Dehydrator

Glucose-6-Phosphate Dehydrogenase is the first enzyme in the oxidative (irreversible) phase of the pentose phosphate pathway. The oxidative phase results in the production of NADPH and the formation of ribulose-5-phosphate. This enzyme catalyzes the rate-limiting step of the oxidative phase. NADPH is crucial for regenerating glutathione in red blood cells which protects against oxidative stress. Deficiency of glucose-6-phosphate dehydrogenase, therefore, results in hemolytic anemia.

Converts Glucose-6-Phosphate to Ribulose-5-Phosphate

Converts Glue-bottle (6) Sax Phosphate-P to Ribs-U (5) Hand Phosphate-P

The oxidative phase of the HMP shunt results in the conversion of Glucose-6-Phosphate to Ribulose-5-Phosphate, with the production of NADPH as well. The rate-limiting enzyme in this phase is Glucose-6-Phosphate Dehydrogenase.

Generates NADPH

Generates NADPH-cigarette

The oxidative (irreversible) phase of the hexose monophosphate pathway produces about 60% of the body's NADPH stores. NADPH is crucial for a number of biochemical reactions, including fatty acid and cholesterol synthesis, as well as the reduction of glutathione.

Reduces Glutathione

Down-arrow Glue-thigh

NADPH allows for the regeneration of glutathione, which functions as the body's main antioxidant. Glutathione, when reduced, is capable of neutralizing dangerous free radicals, preventing damage to cell membranes and DNA. After neutralizing a free radical, glutathione must be regenerated by being reduced again. This is done via the enzyme glutathione reductase, which requires NADPH as a cofactor.

Prevents Oxidative Damage

Blocking Oxidative-Ox from Causing Damage

Adequate glutathione stores in the body are integral to preventing free radical damage. Free radicals are molecules such as superoxide (O2-) that have an unpaired electron in their outermost shell. This enables them to destabilize and damage various cellular molecules and structures. RBCs are particularly susceptible to free radical damage. Thus, patients who are deficient in glucose-6-phosphate dehydrogenase have impaired glutathione production and will present with hemolytic anemia.

Non-Oxidative Phase (Reversible)

Ribulose-5-Phosphate to Ribose-5-Phosphate

Ribs-U (5) Hand Phosphate-P to Rib-O (5) Hand Phosphate-P

The second phase of the HMP shunt is the non-oxidative (reversible) phase. This phase uses the product from the first phase (ribulose-5-phosphate) to create ribose-5-phosphate, which can then be used for nucleotide synthesis. The enzyme ribulose-5-phosphate isomerase (phosphopentose isomerase) catalyzes this reaction.

Nucleotide Synthesis

Nuclear-toad Synthesized

Ribose-5-phosphate is a substrate in the synthesis of nucleotides. Nucleotides can then be used to create DNA and RNA. The body is constantly turning over new cells and replicating its genetic material, and thus having the appropriate reagents for nucleotide synthesis is crucial.
