THE IRREVERSIBLE OXIDATIVE PHASE

1 oxidation of glucose 6 phosphate by glucose 6 phosphate dehydrogenase to produce 6 phosphogluconate and one NADPH molecule

2 oxidative decarboxylation of 6 phosphogluconate by 6 phosphogluconate dehydrogenase to produce ribulose 5 phosphate and one NADPH molecule and one CO_2 molecule

THE REVERSIBLE NON OXIDATIVE PHASE

1 isomerization of ribulose 5 phosphate by an isomerase to produce ribose 5 phosphate

2 epimerization of ribulose 5 phosphate by an epimerase to produce xylulose 5 phosphate

3 ribose 5 phosphate + xylulose 5 phosphate (transketolase) glyceraldehyde 3 phosphate + sedoheptulose 7 phosphate

4 glyceraldehyde 3 phosphate + sedoheptulose 7 phosphate (transaldolase) erythrose 4 phosphate + fructose 6 phosphate

5 erythrose 4 phosphate + xylulose 5 phosphate (transketolase) glyceraldehyde 3 phosphate + fructose 6 phosphate

NADPH FUNCTIONS:

biosynthesis of fatty acids

biosynthesis of steroid hormones

maintenance of glutathione in the reduced form

RIBOSE 5 PHOSPHATE FUNCTIONS:

biosynthesis of nucleotides

oxidation and reduction in NADH and NADPH occur at the nicotinamide

enzymes use NADH or NADPH

CATABOLIC RESERVOIR:

NAD^+ > NADH

ANABOLIC RESERVOIR:

$NADP^+$ < NADPH

endogenous sources of reactive oxygen species are normal and exogenous sources of reactive oxygen species are abnormal

ANTIOXIDANT REACTIONS:

1

glutathione consists of glycine, cysteine, and glutamate

2 GSH + H_2O_2 (glutathione peroxidase + selenium) GSSG + 2 H_2O

GSSG + NADPH + H^+ (glutathione reductase) 2 GSH + $NADP^+$

2

2 O_2^- + 2 H^+ (superoxide dismutase) O_2 + H_2O_2

2 H_2O_2 (catalase) O_2 + 2 H_2O

ANTIOXIDANTS:

vitamin C

vitamin E

carotenoids

GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY:

glucose 6 phosphate dehydrogenase gene is an insulin target gene

red blood cells cannot maintain glutathione in the reduced form due to NADPH deficiency that results in oxidative stress

oxidative stress leads to the senescence of red blood cells that results in hemolysis

hemolysis causes:

broad beans

oxidant drugs

infections

bilirubin

red blood cells are the most affected because they have neither nucleus nor mitochndria

glucose 6 phosphate dehydrogenase deficiency provides resistance to plasmodium falciparum

glucose 6 phosphate dehydrogenase deficiency classes:

class 1 > class 2 > class 3 > class 4

the activity of glucose 6 phosphate dehydrogenase decreases as the age of erythrocytes increases.

class 1 reaches zero

class 2 reaches zero

class 3 reaches zero

class 4 does not reach zero

oxidases produce reactive oxygen species and uses oxygen as the electron acceptor

monooxygenases produce reactive oxygen species and incorporate O in the product

dioxygenases produce reactive oxygen species and incorporate O_2 in the product

dioxygenases produce eicosanoids

coenzyme Q produce reactive oxygen species and uses oxygen as the electron acceptor

phagocytosis produce reactive oxygen species

ionizing radiation produce reactive oxygen species

cytochrome P450 enzymes are monooxygenases that contain heme

mitochondria:

synthesis of steroid hormones by hydroxylation

synthesis of bile acids by hydroxylation

activation of vitamin D by hydroxylation

smooth endoplasmic reticulum:

detoxification

activation of drugs

inactivation of drugs

solubilization

DESTRUCTION OF MICROORGANISMS:

conversion of oxygen to superoxide by NADPH oxidase

conversion of superoxide to hydrogen peroxide

conversion of hydrogen peroxide to hypochlorous acid by myeloperoxidase

nitric oxide is a gas that diffuses across cell membranes

the nitric oxide effect is concentration dependent

NITRIC OXIDE FUNCTIONS:

neurotransmitter

vasodilator

platelet aggregation inhibitor

nitric oxide produces reactive nitrogen oxygen species at high concentrations

reactive nitrogen oxygen species lead to neurodegenerative diseases and inflammatory diseases

NITRIC OXIDE SYNTHESIS:

L arginine + O_2 + NADPH (NO synthase) L citrulline + NO + $NADP^+$

neuronal NO synthase and endothelial NO synthase are constitutive and calcium dependent

inducible NO synthase is calcium independent

VASODILATION:

NO activate guanylyl cyclase to produce cGMP from GTP

cGMP activate protein kinase G

protein kinase G phosphorylate calcium channels