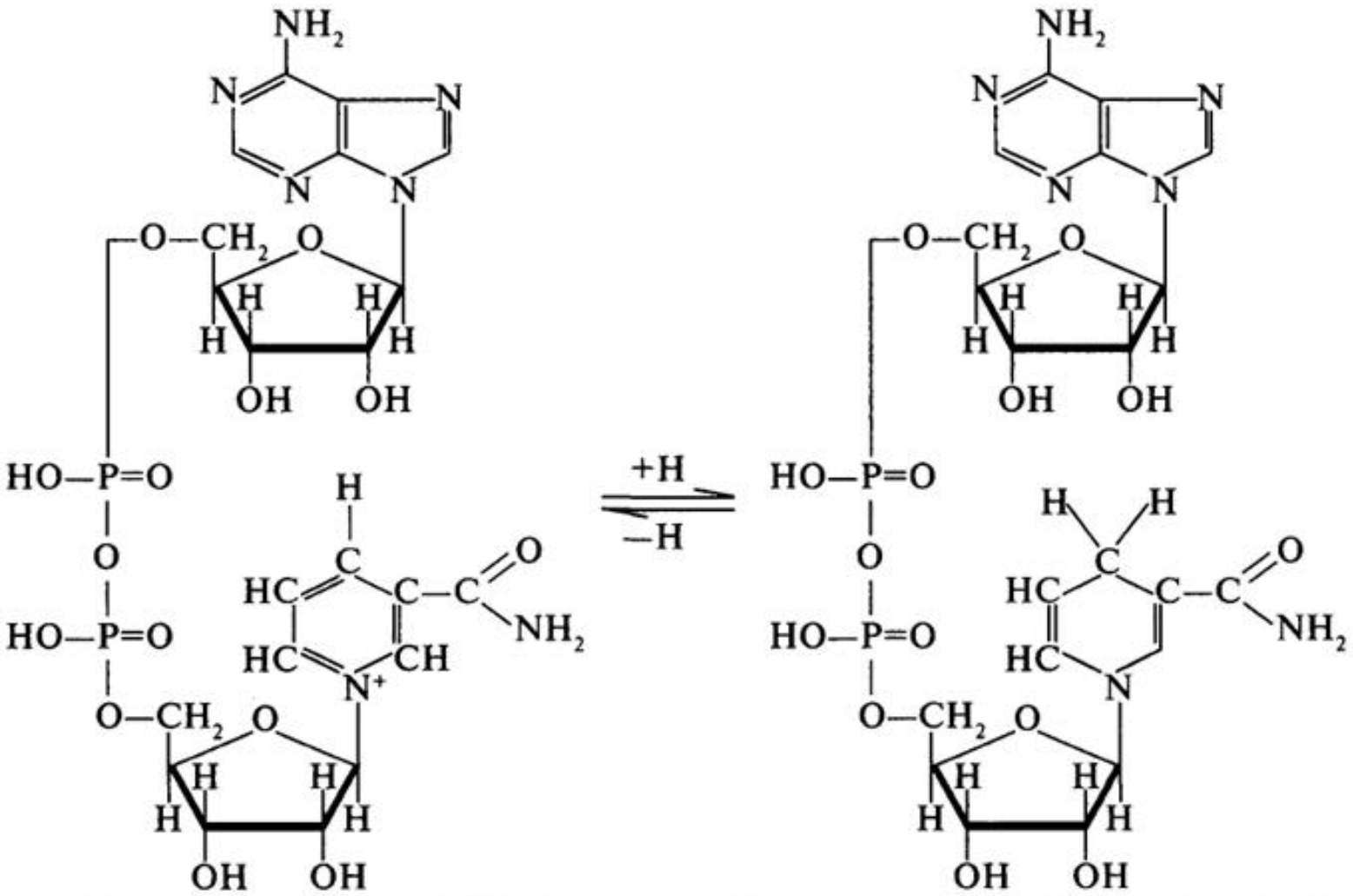
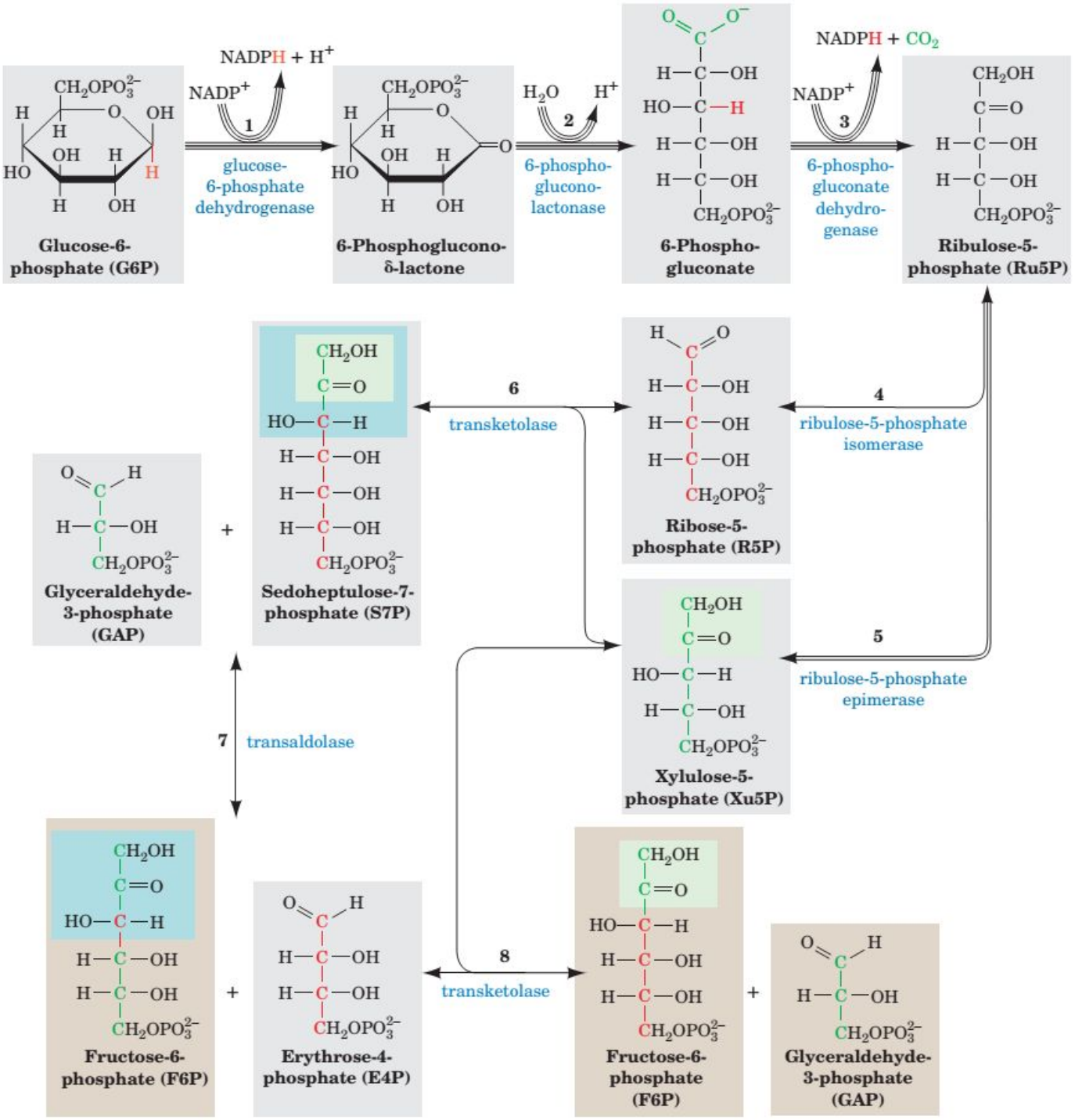
Пентозофосфатный путь (ПФП) окисления глюкозы. Обмен других моносахаридов. Регуляция и патология углеводного обмена

ПЕНТОЗОФОСФАТНЫЙ ПУТЬ ПРЕВРАЩЕНИЯ ГЛЮКОЗЫ

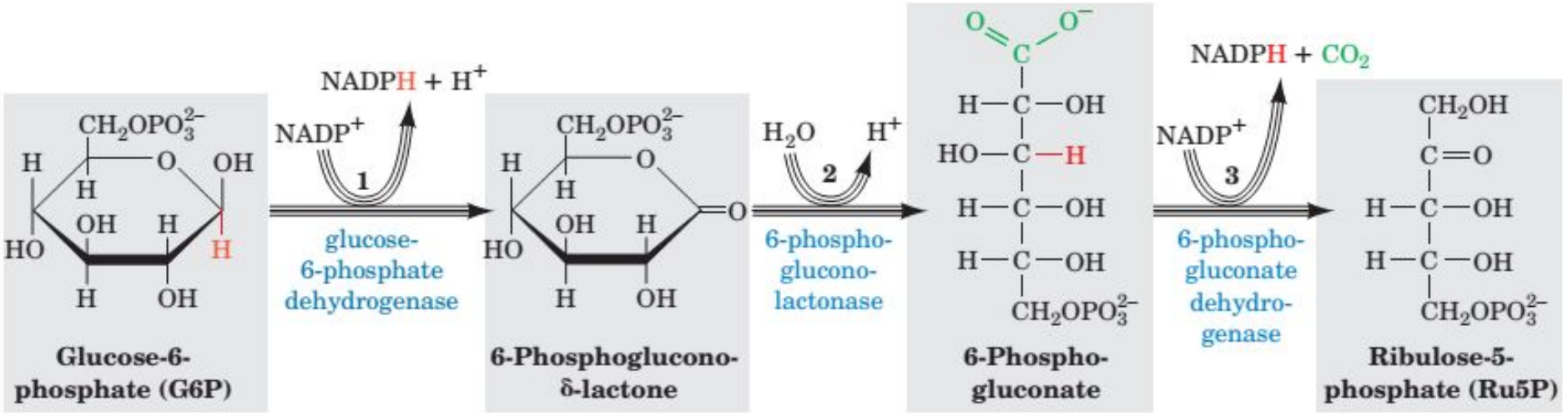


Окисленная форма НАД-НАД⁺

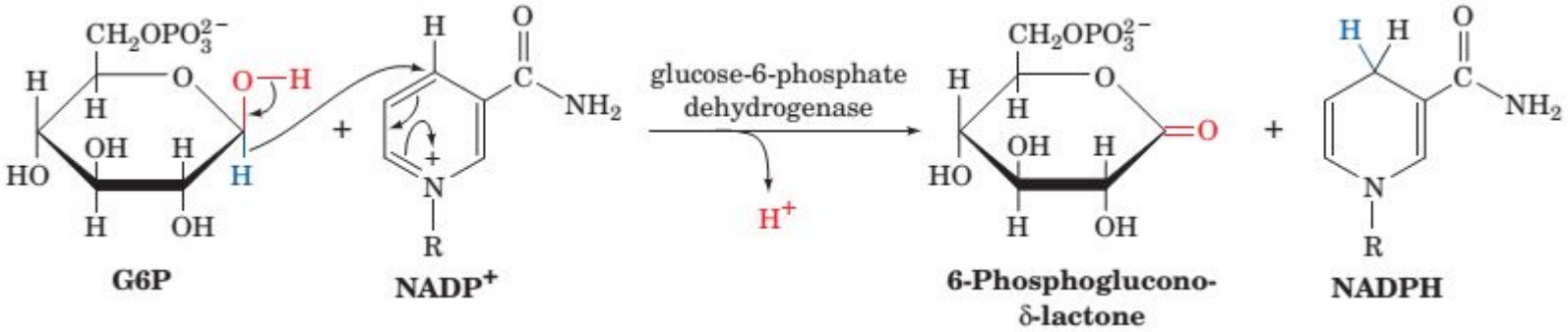
Восстановленная форма НАД-НАДН


Glucose-6-phosphate (G6P)
NADPH + H+
NADP+
1
glucose-6-phosphate dehydrogenase
6-Phosphoglucono-δ-lactone
H2O
H+
2
6-phospho-gluconolactonase
6-Phospho-gluconate
NADPH + CO2
NADP+
3
6-phospho-gluconate dehydro-genase
Ribulose-5-phosphate (Ru5P)
4
ribulose-5-phosphate isomerase
Ribose-5-phosphate (R5P)
6
transketolase
Glyceraldehyde-3-phosphate (GAP)
Sedoheptulose-7-phosphate (S7P)
5
ribulose-5-phosphate epimerase
Xylulose-5-phosphate (Xu5P)
7
transaldolase
Fructose-6-phosphate (F6P)
Erythrose-4-phosphate (E4P)
8
transketolase
Fructose-6-phosphate (F6P)
Glyceraldehyde-3-phosphate (GAP)

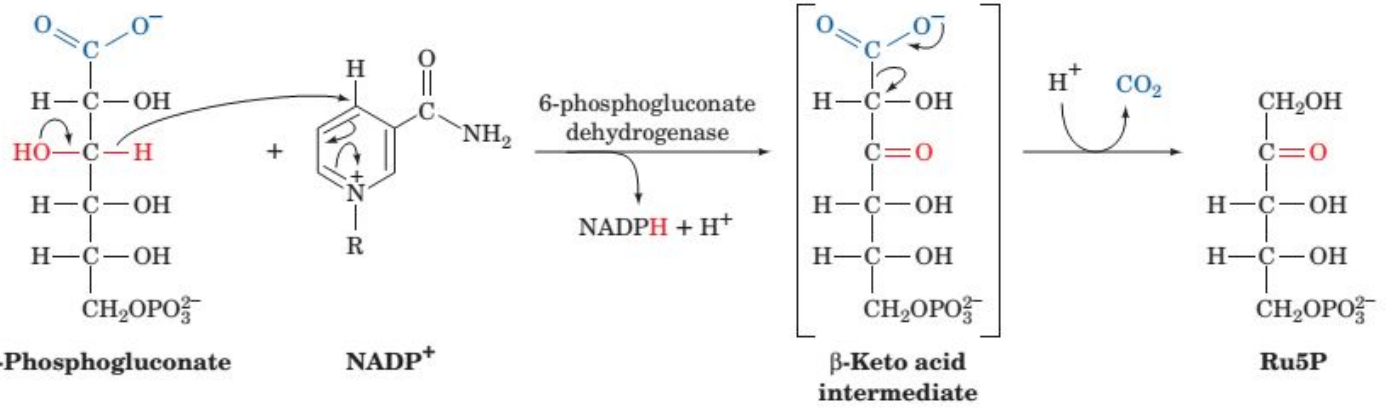
Окислительный этап

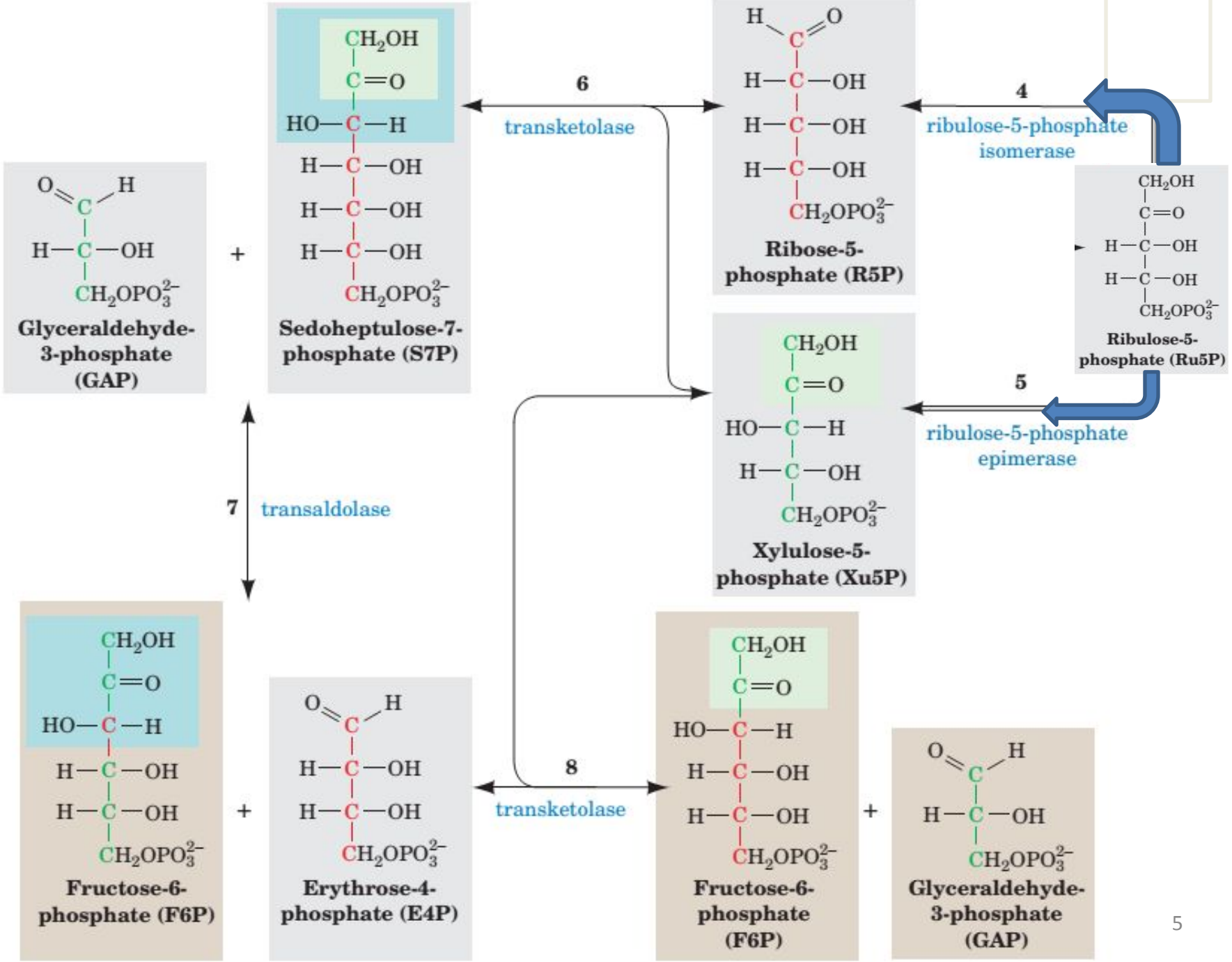


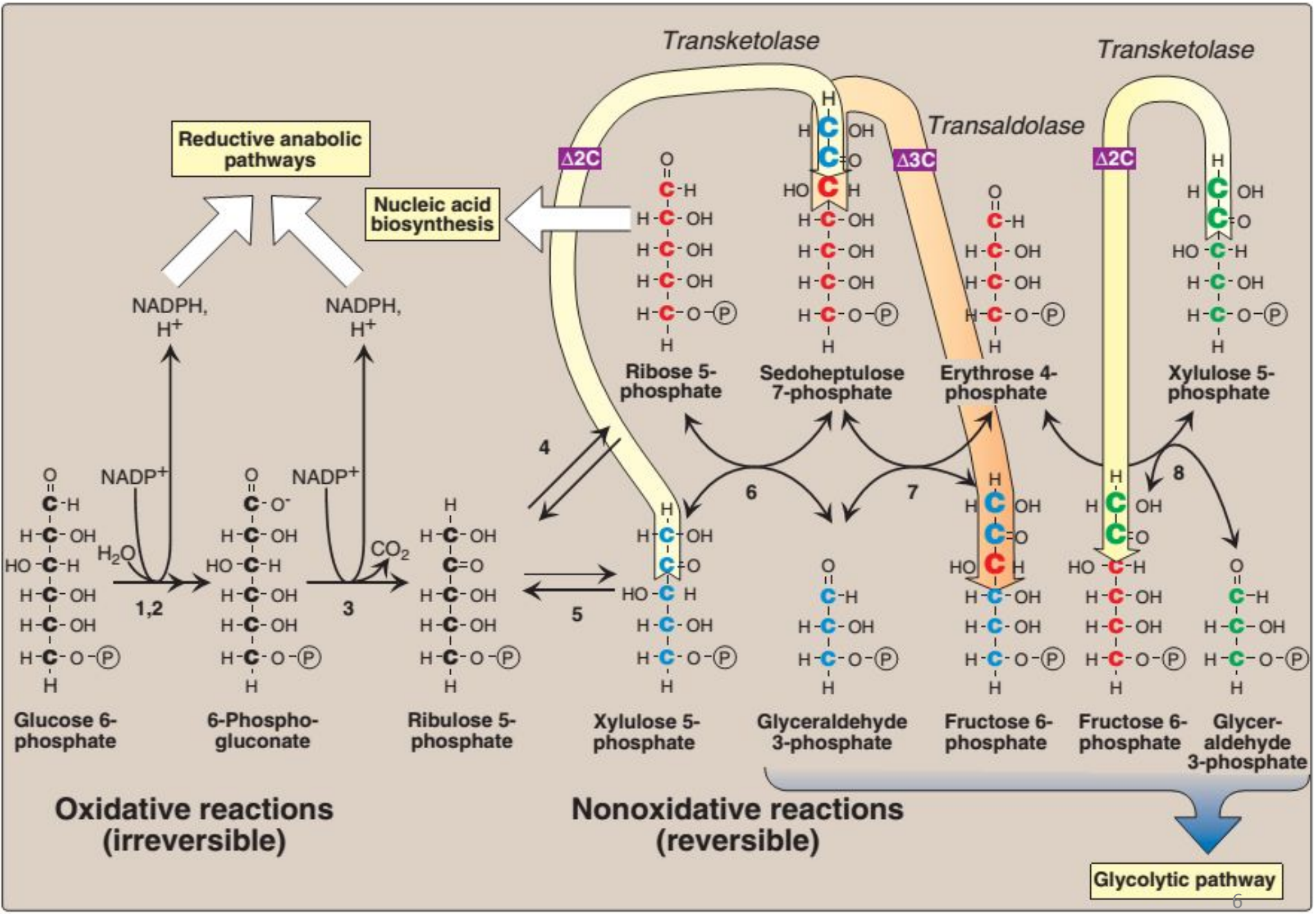
I реакция

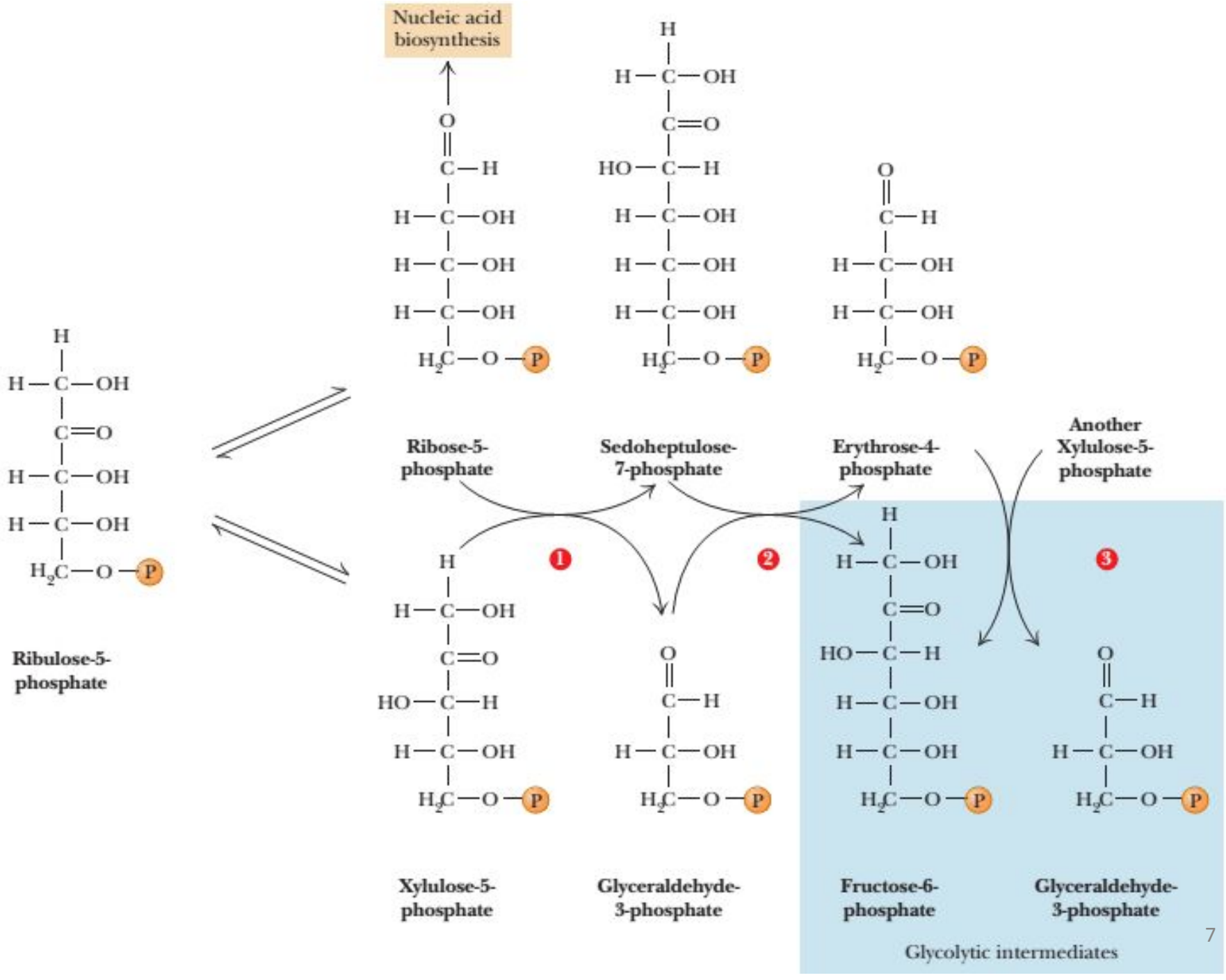


III реакция

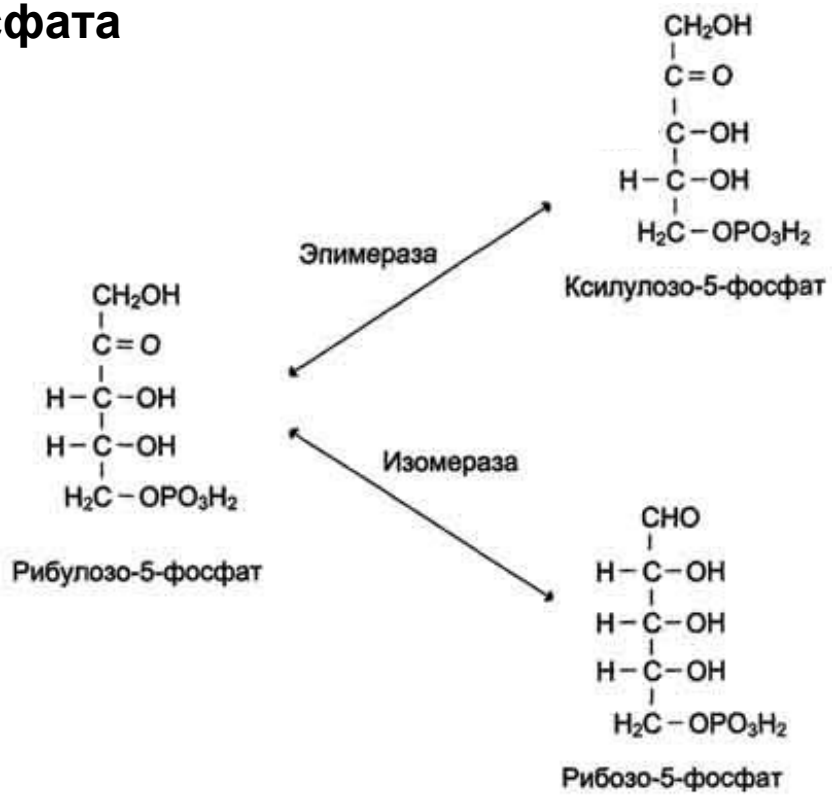



Glyceraldehyde-3-phosphate (GAP)
+
Sedoheptulose-7-phosphate (S7P)
6
transketolase
Ribose-5-phosphate (R5P)
4
ribulose-5-phosphate isomerase
Ribulose-5-phosphate (Ru5P)
5
ribulose-5-phosphate epimerase
Xylulose-5-phosphate (Xu5P)
7
transaldolase
Fructose-6-phosphate (F6P)
+
Erythrose-4-phosphate (E4P)
8
transketolase
Fructose-6-phosphate (F6P)
+
Glyceraldehyde-3-phosphate (GAP)

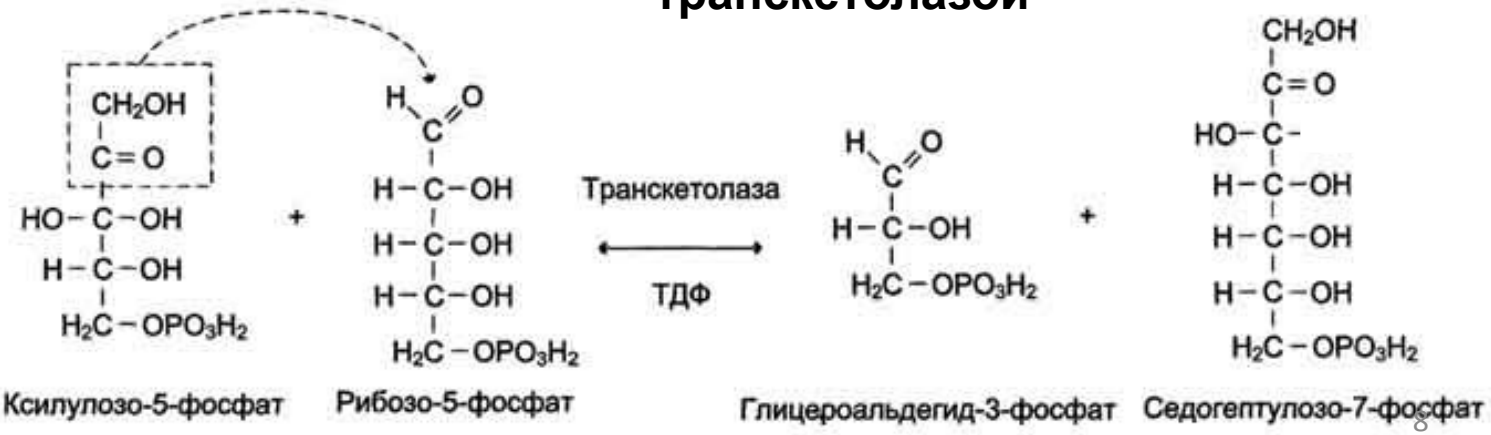

Transketolase
Transketolase
Transaldolase
Reductive anabolic pathways
Nucleic acid biosynthesis
Δ2C
Δ3C
Δ2C
NADPH, H+
NADPH, H+
NADP+
NADP+
H2O
CO2
1,2
3
4
5
6
7
8
Ribose 5-phosphate
Sedoheptulose 7-phosphate
Erythrose 4-phosphate
Xylulose 5-phosphate
Glucose 6-phosphate
6-Phospho-gluconate
Ribulose 5-phosphate
Xylulose 5-phosphate
Glyceraldehyde 3-phosphate
Fructose 6-phosphate
Fructose 6-phosphate
Glycer-aldehyde 3-phosphate
Oxidative reactions (irreversible)
Nonoxidative reactions (reversible)
Glycolytic pathway


Nucleic acid biosynthesis
Ribulose-5-phosphate
Ribose-5-phosphate
Sedoheptulose-7-phosphate
Erythrose-4-phosphate
Another Xylulose-5-phosphate
1
2
3
Xylulose-5-phosphate
Glyceraldehyde-3-phosphate
Fructose-6-phosphate
Glyceraldehyde-3-phosphate
Glycolytic intermediates

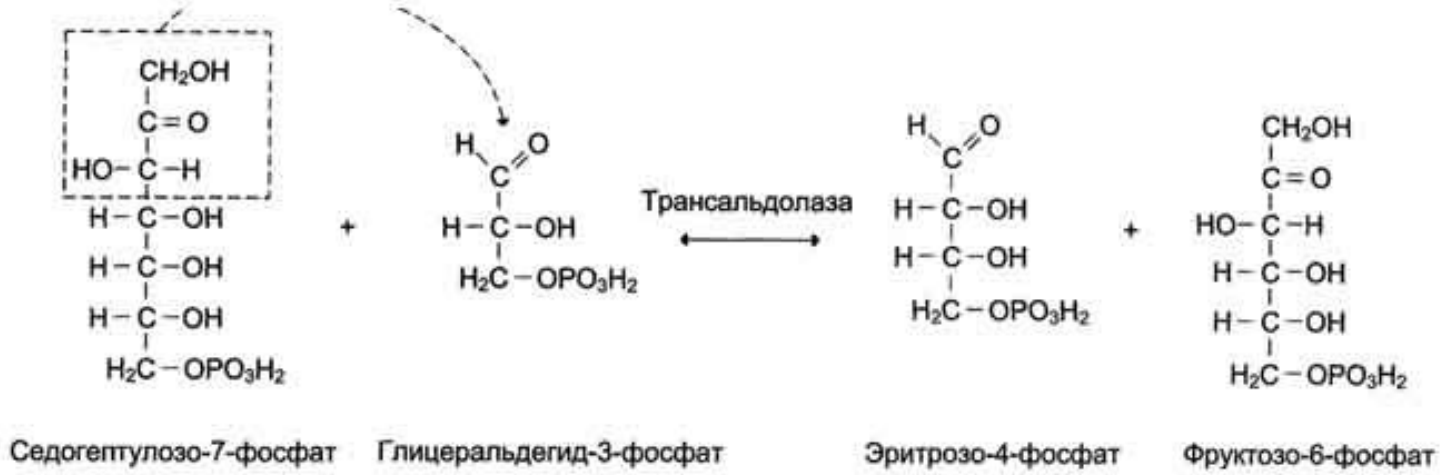
Превращения рибулозо-5-фосфата



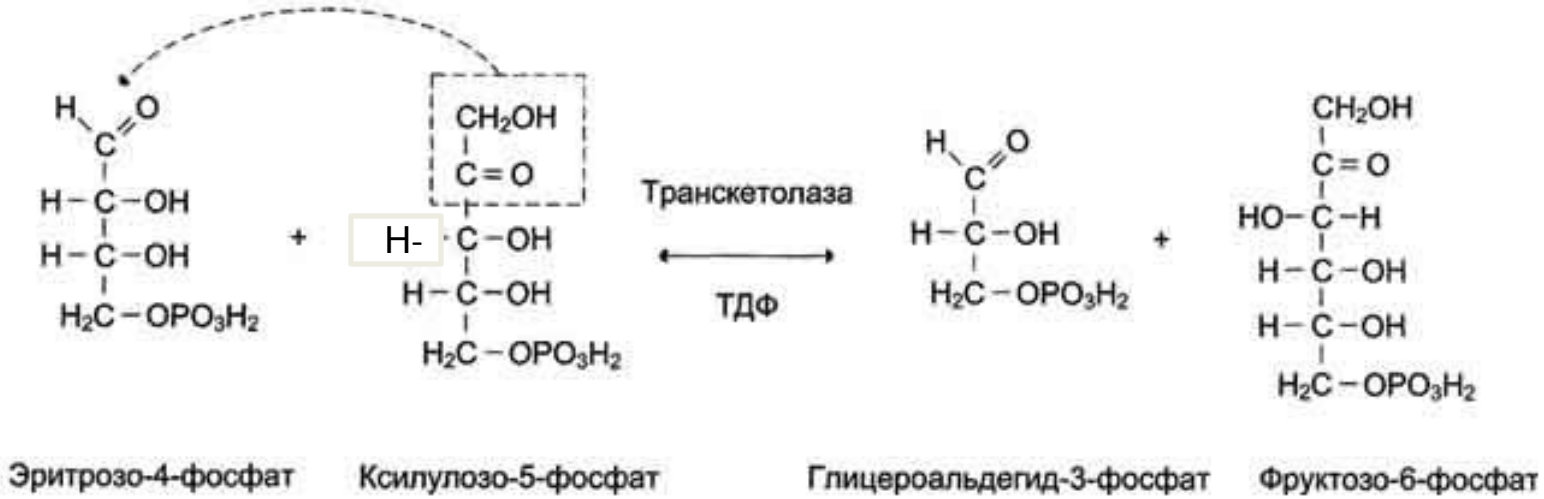
Реакция переноса двухуглеродного фрагмента, катализируемая транскетолазой

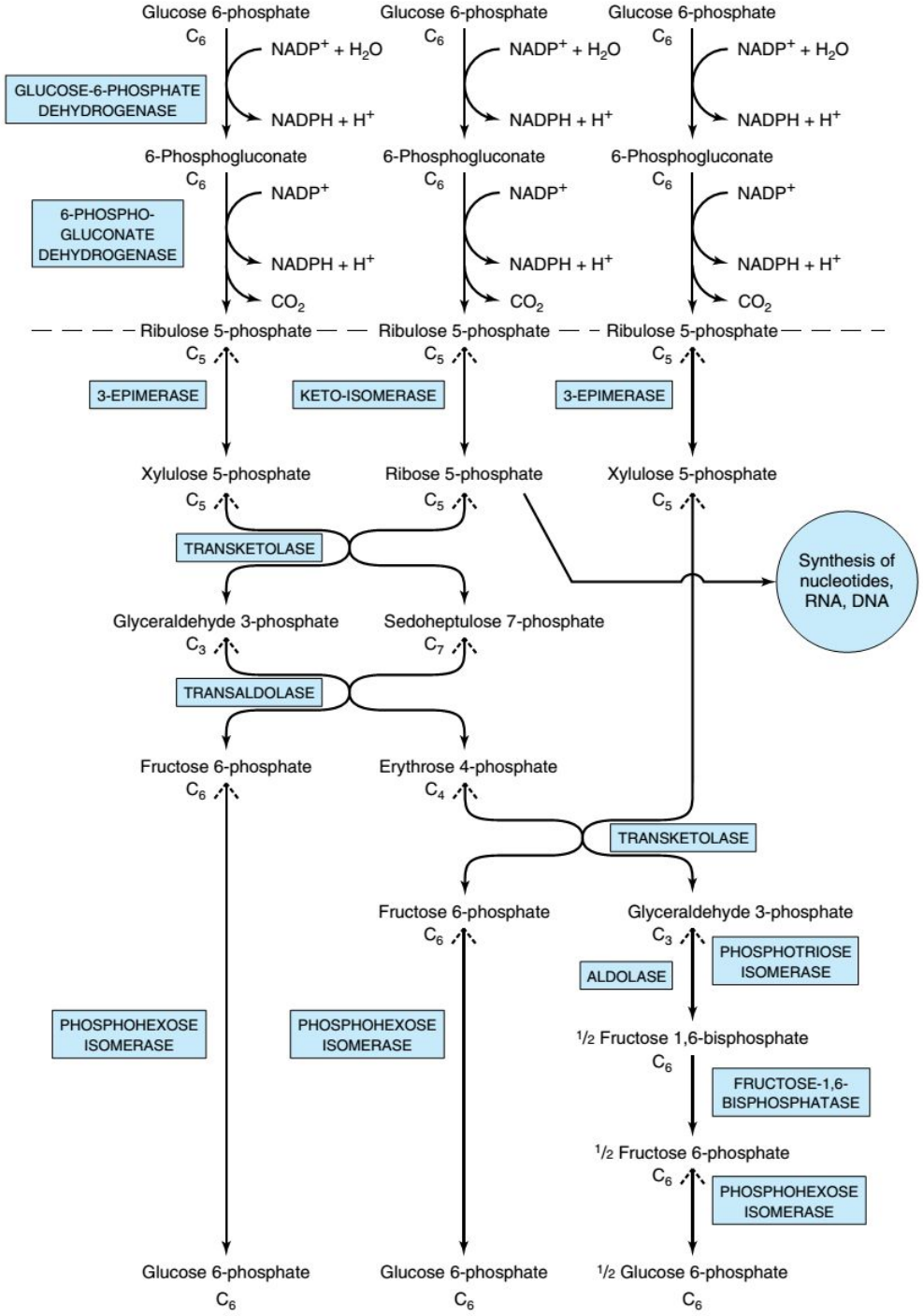


Реакция, катализируемая трансальдолазой



Реакция, катализируемая транскетолазой




Glucose 6-phosphate
C6
NADP+ + H2O
NADPH + H+
GLUCOSE-6-PHOSPHATE DEHYDROGENASE
6-Phosphogluconate
C6
NADP+
NADPH + H+
CO2
6-PHOSPHO-GLUCONATE DEHYDROGENASE
Ribulose 5-phosphate
C5
3-EPIMERASE
KETO-ISOMERASE
Xylulose 5-phosphate
Ribose 5-phosphate
TRANSKETOLASE
Synthesis of nucleotides, RNA, DNA
Glyceraldehyde 3-phosphate
C3
Sedoheptulose 7-phosphate
C7
TRANSALDOLASE
Fructose 6-phosphate
C6
Erythrose 4-phosphate
C4
PHOSPHOHEXOSE ISOMERASE
ALDOLASE
PHOSPHOTRIOSE ISOMERASE
1/2 Fructose 1,6-bisphosphate
FRUCTOSE-1,6-BISPHOSPHATASE
1/2 Fructose 6-phosphate
1/2 Glucose 6-phosphate

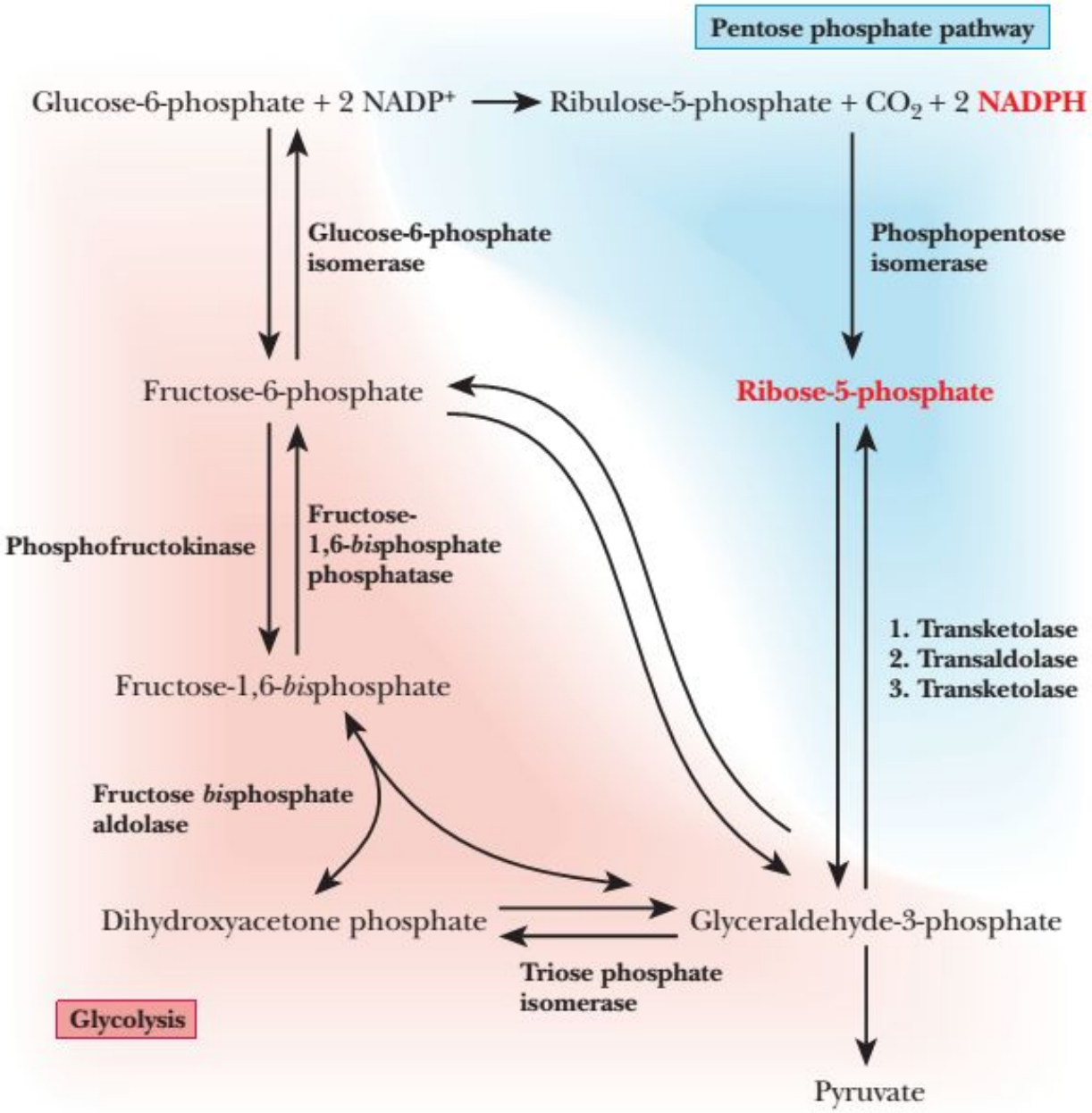
Пентозофосфатный цикл. Окислительный этап синтеза пентоз и этап возвращения пентоз в гексозы (неокислительный этап в обратном направлении) вместе составляют циклический процесс (пентозофосфатный цикл) - за один оборот цикла полностью распадается одна молекула глюкозы. Пентозофосфатный цикл функционирует в основном только в жировой ткани и печени. Суммарное уравнение пентозофосфатного цикла

$$6\ \text{глюкозо-6-фосфат} + 12NADP^+ + 2H_2O \rightarrow 12\ (NADPH + H^+) \rightarrow$$
$$\rightarrow 5\ \text{глюкозо-6-фосфат} + 6CO_2 .$$

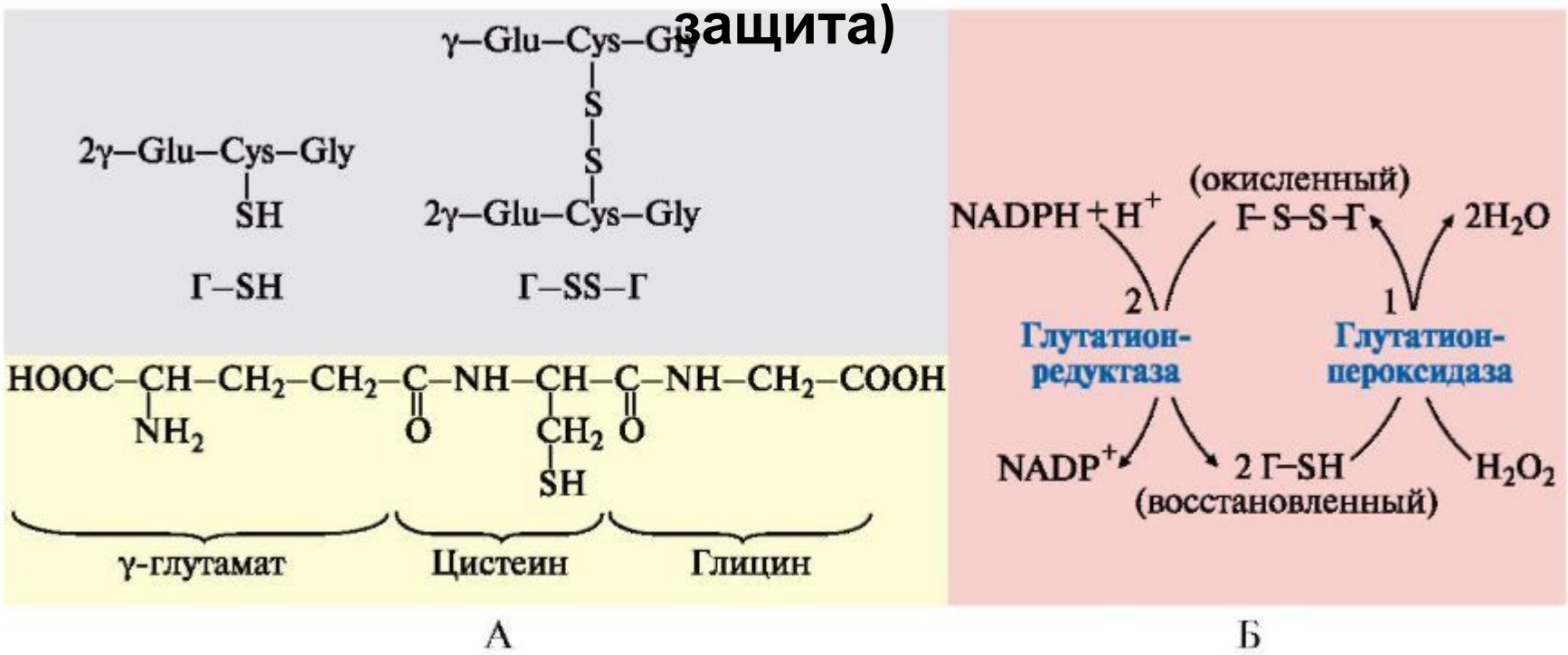
Промежуточные продукты пентозофосфатного пути превращения глюкозы (фруктозо-6-фосфат, глицеральдегид-3-фосфат) могут включаться в пути аэробного и анаэробного окисления и служить источником энергии для синтеза АТР.

У растений реакции пентозофосфатного пути составляют часть процесса образования гексоз из CO_2 при фотосинтезе.

Взаимосвязь ПФП и гликолиза



Механизм действия глутатиона (антирадикальная защита)



Восстановление глутатиона с участием NADPH+H$^+$:

А - **Строение глутатиона:**

Г-SH - восстановленная форма; Г-S-S-Г - окисленная форма;

Б - **Участие глутатиона в обезвреживании пероксида водорода и его регенерация:**

1 - взаимодействие глутатиона с H_2O_2 с образованием воды и окисленной формы глутатиона;

2 - регенерация глутатиона с использованием в качестве донора водорода NADPH+H$^+$, образуемой на окислительном этапе пентозофосфатного пути превращения глюкозы

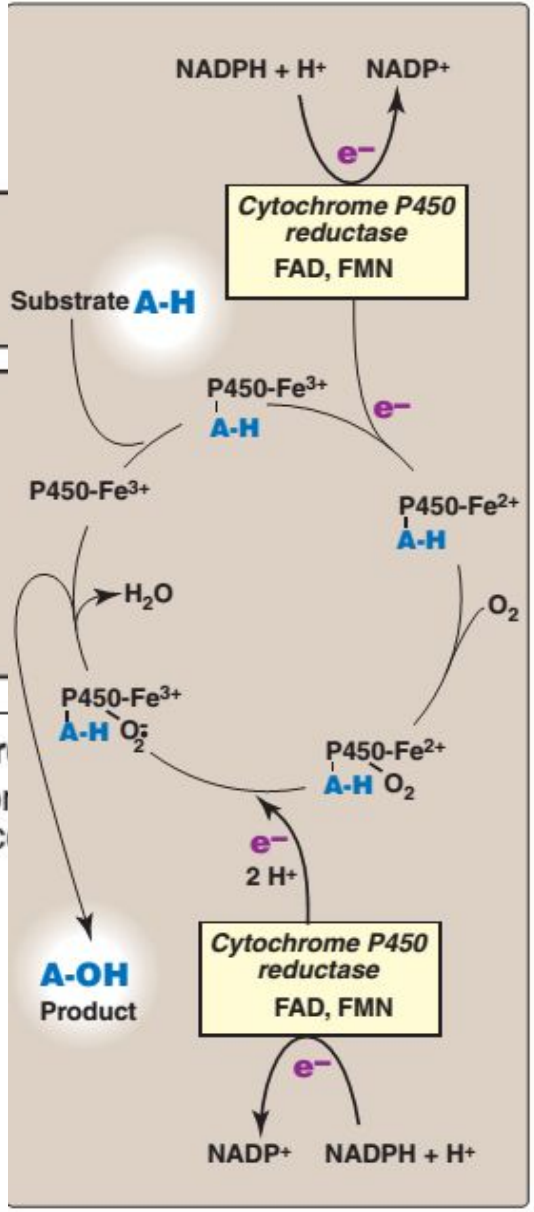
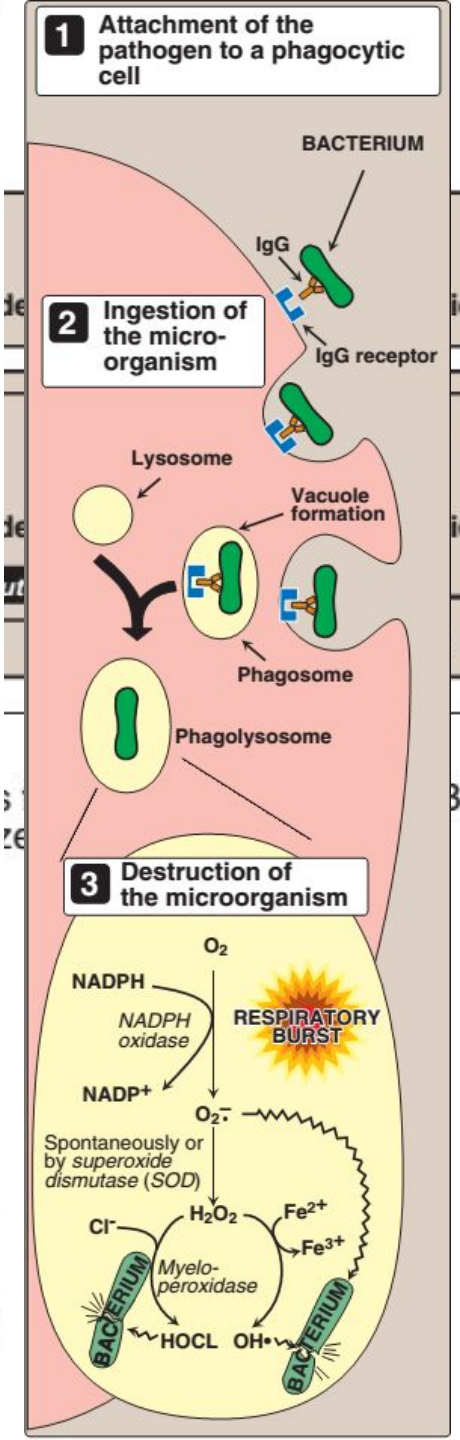
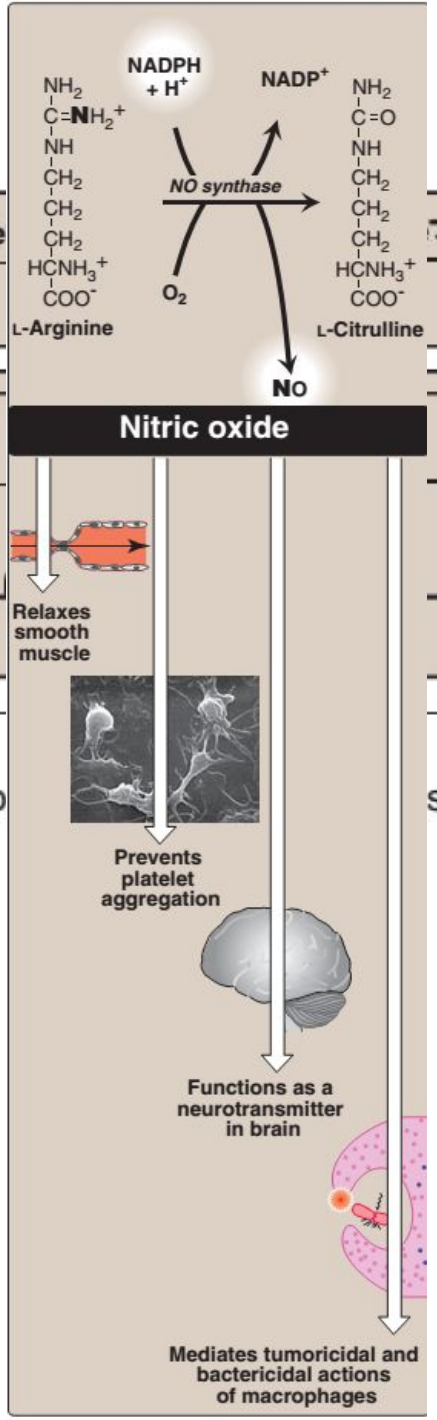
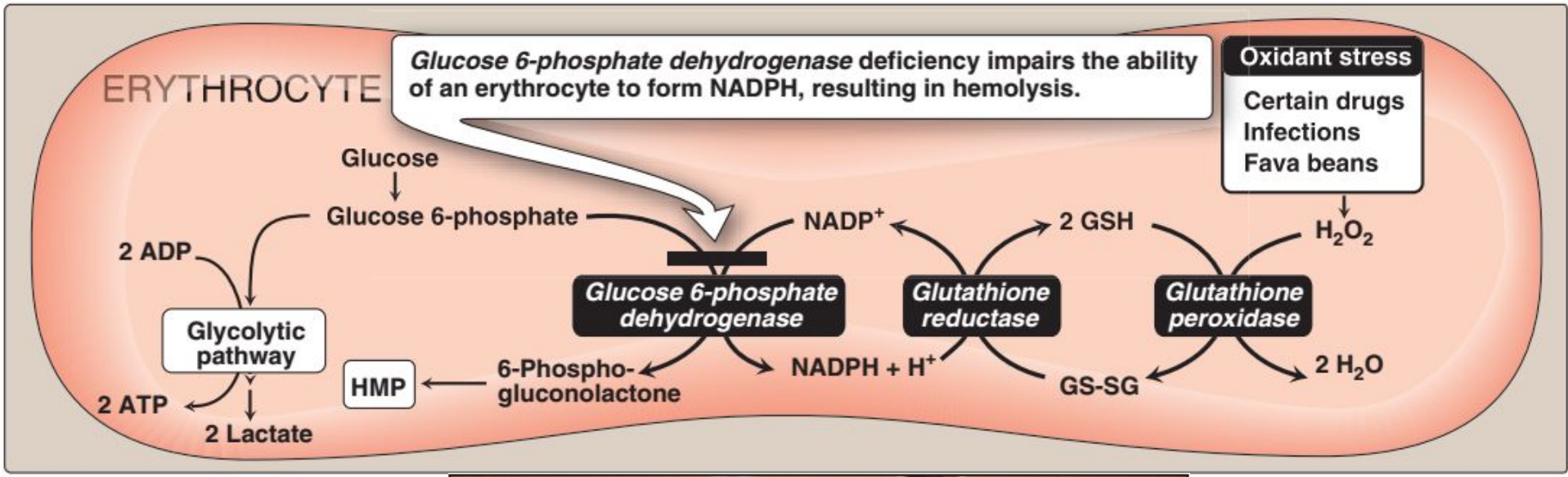


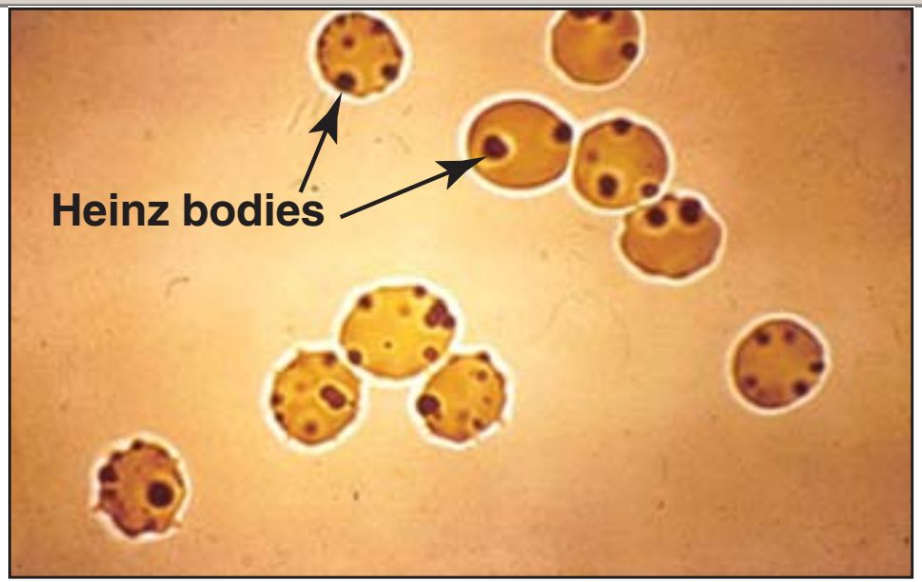
Figure 13.7
Cytochrome P450 monooxygenase cycle. Electrons move from NADPH to FAD to FMN and then to the heme iron.

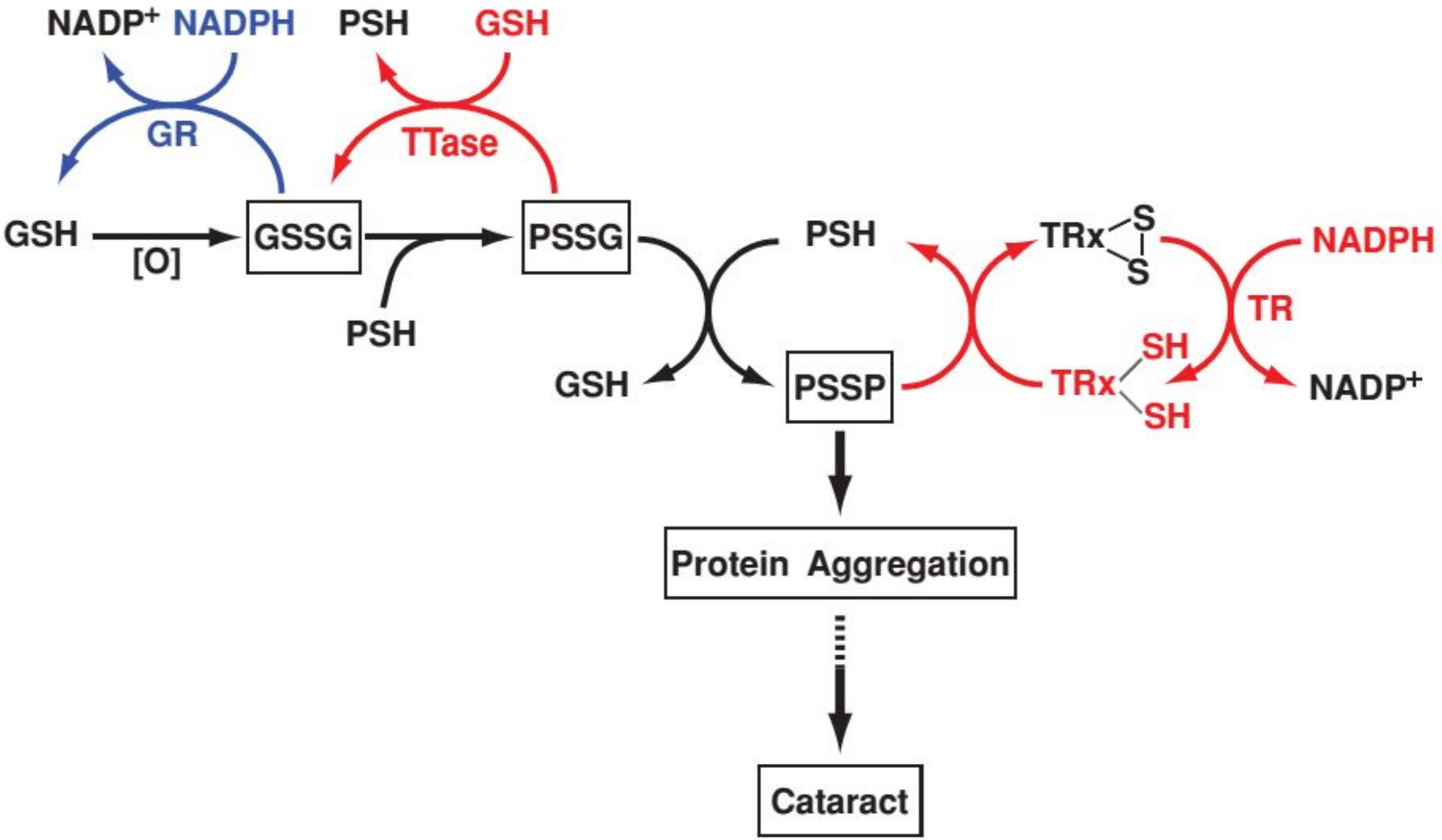




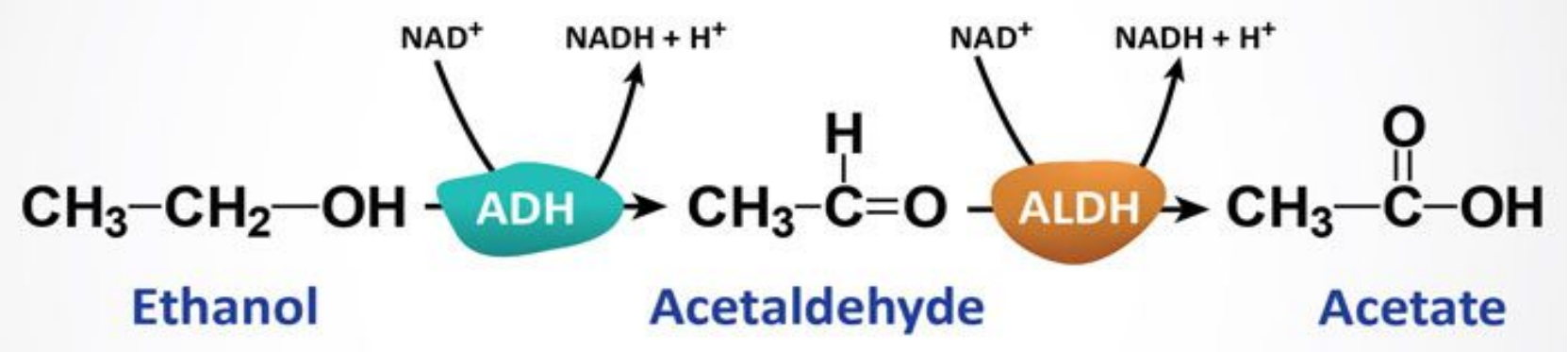
Метаболизм в эритроците

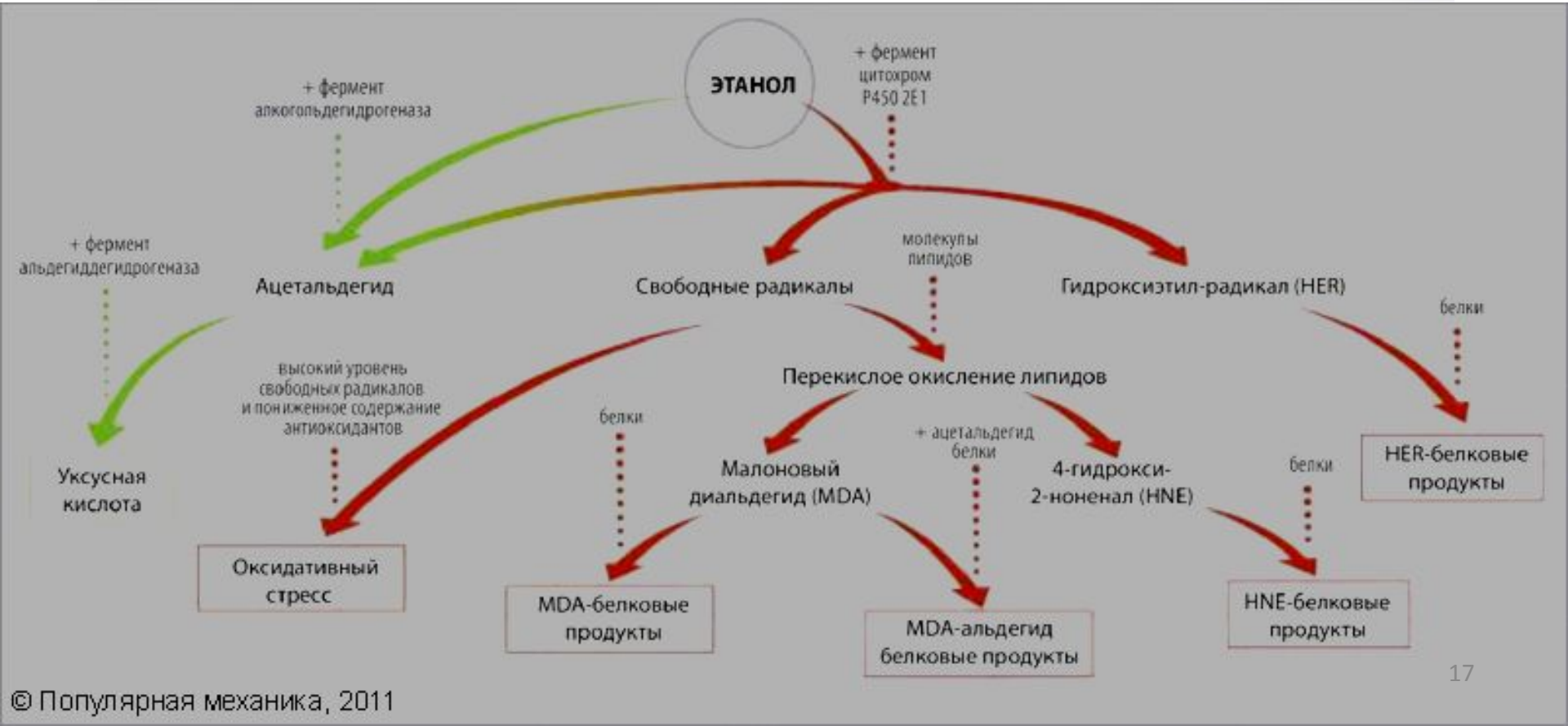


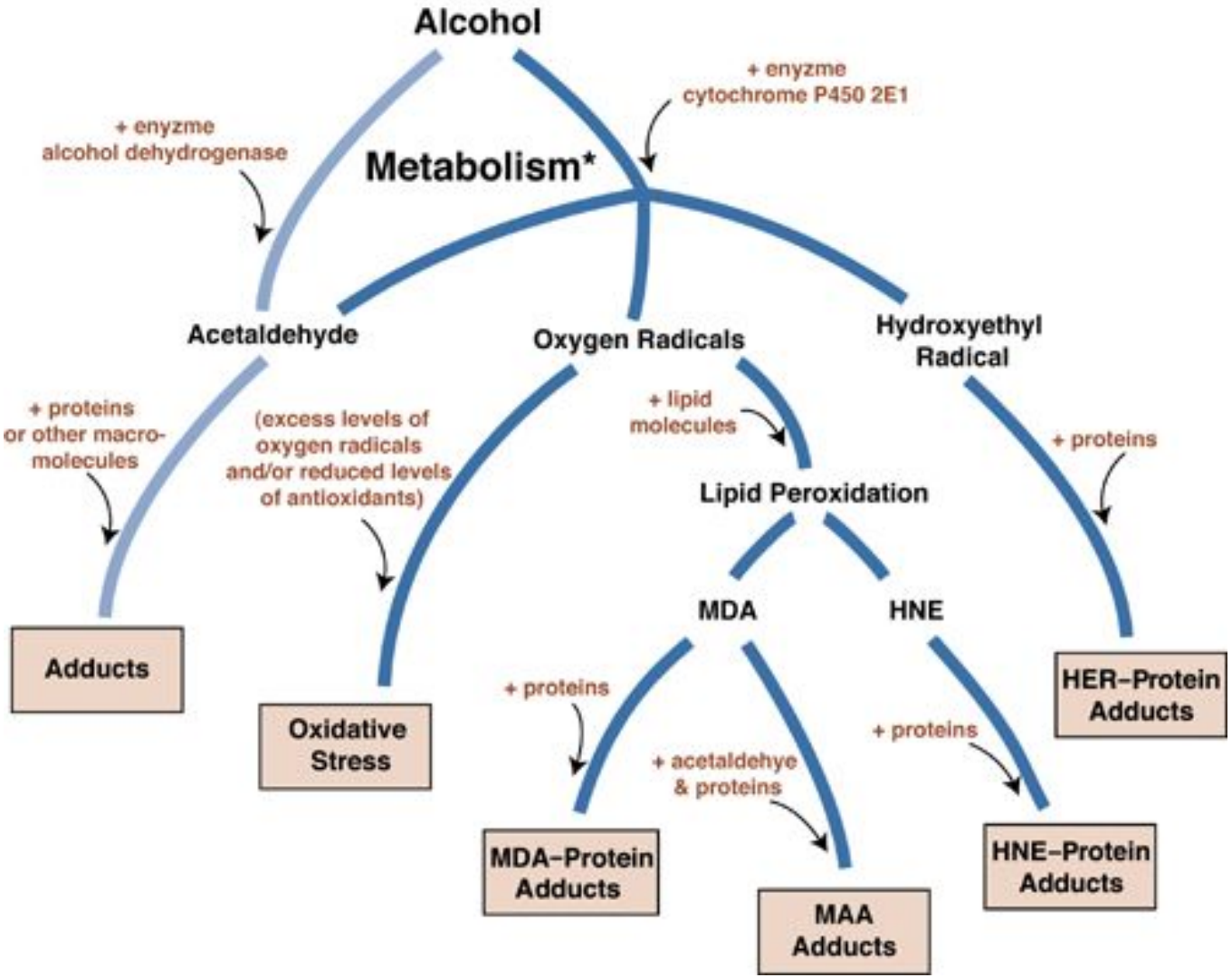


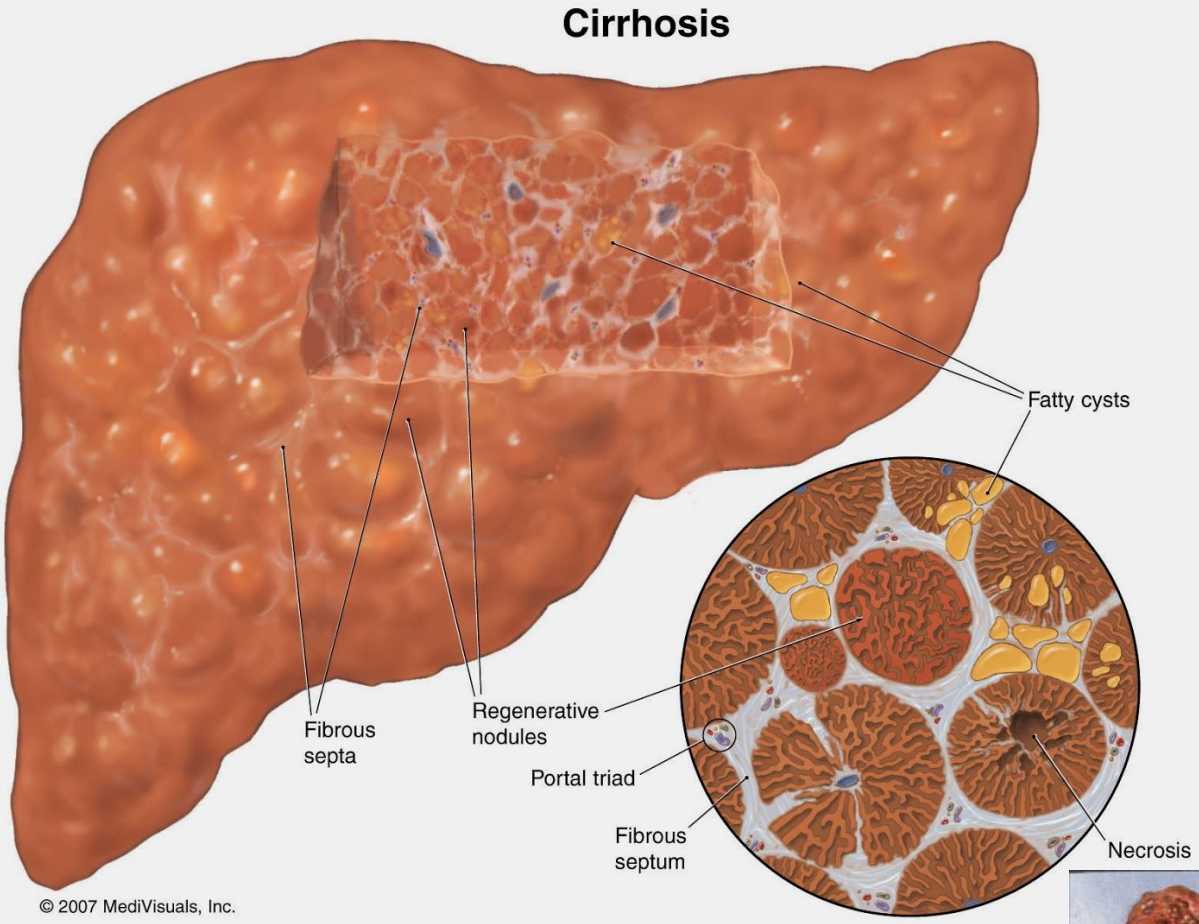

NADP+ NADPH
PSH
GSH
GR
TTase
GSH
[O]
GSSG
PSSG
PSH
PSH
GSH
PSSP
TRx
S
S
NADPH
TR
SH
TRx
SH
NADP+
Protein Aggregation
Cataract

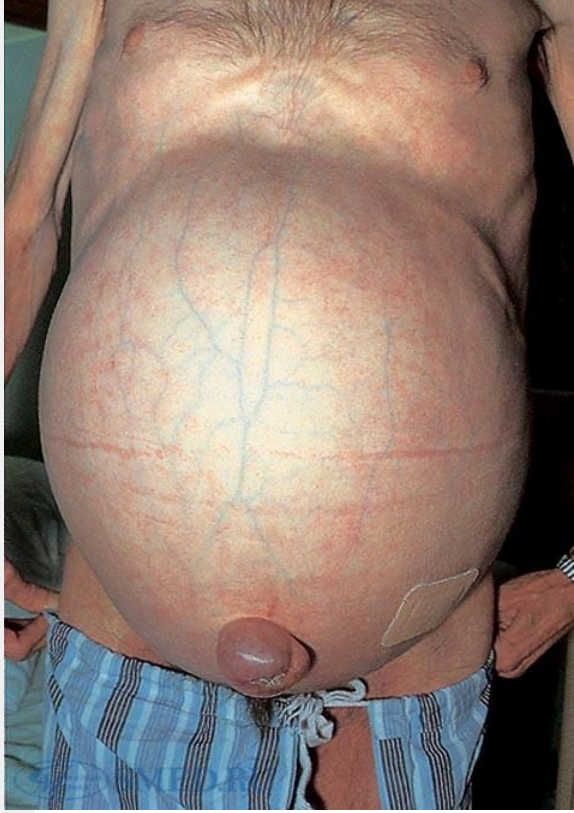
Метаболизм этанола

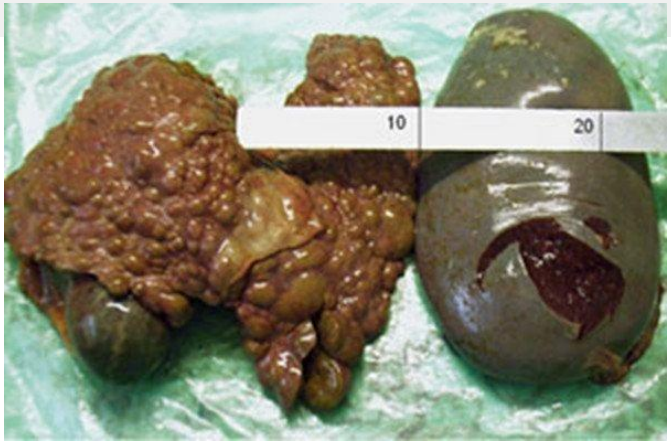


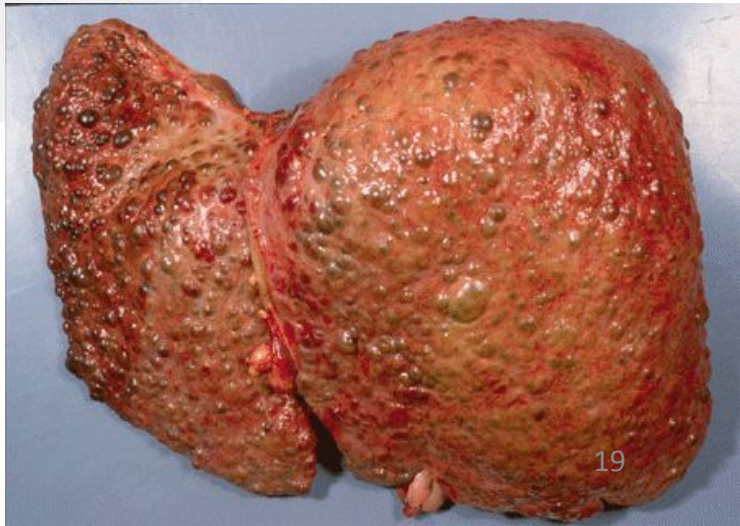



Alcohol
+ enyzme
cytochrome P450 2E1
+ enyzme
alcohol dehydrogenase
Metabolism*
Acetaldehyde
Oxygen Radicals
Hydroxyethyl
Radical
+ proteins
or other macro-
molecules
(excess levels of
oxygen radicals
and/or reduced levels
of antioxidants)
+ lipid
molecules
+ proteins
Lipid Peroxidation
MDA
HNE
Adducts
Oxidative
Stress
+ proteins
+ acetaldehye
& proteins
+ proteins
HER-Protein
Adducts
MDA-Protein
Adducts
MAA
Adducts
HNE-Protein
Adducts

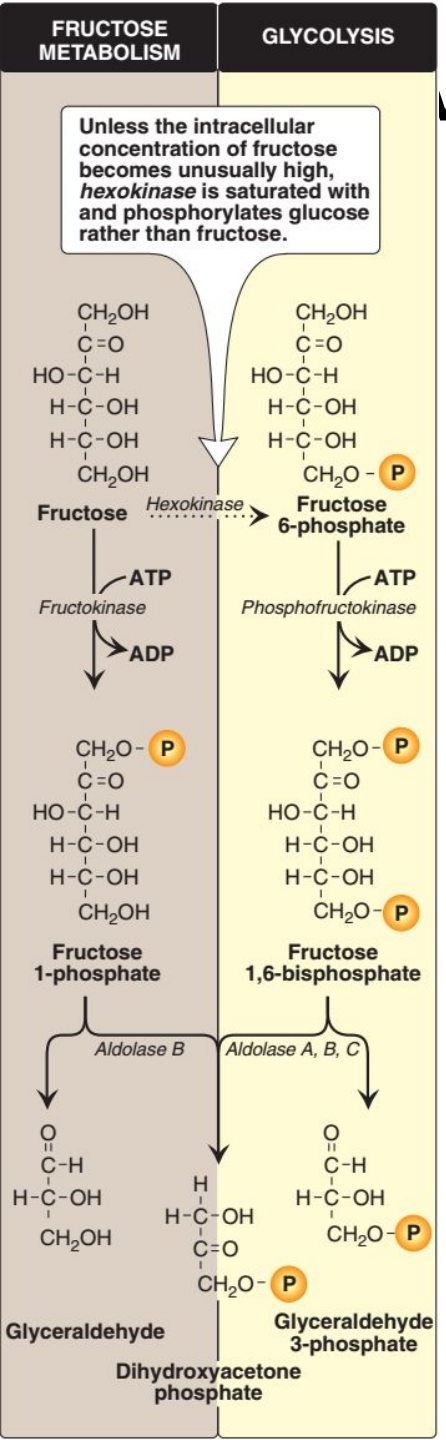

Cirrhosis
Fatty cysts
Fibrous septa
Regenerative nodules
Portal triad
Fibrous septum
Necrosis
© 2007 MediVisuals, Inc.

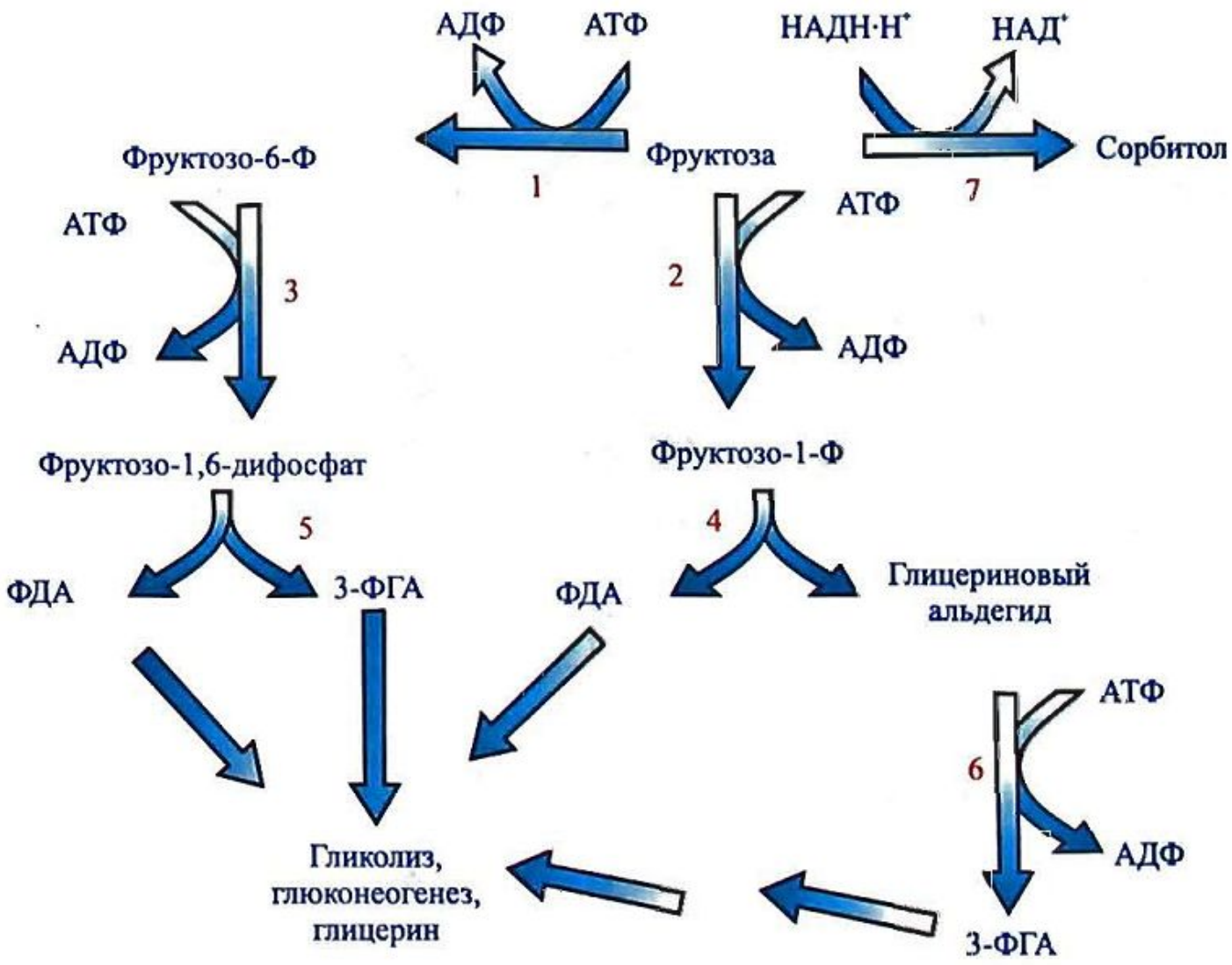



10
20

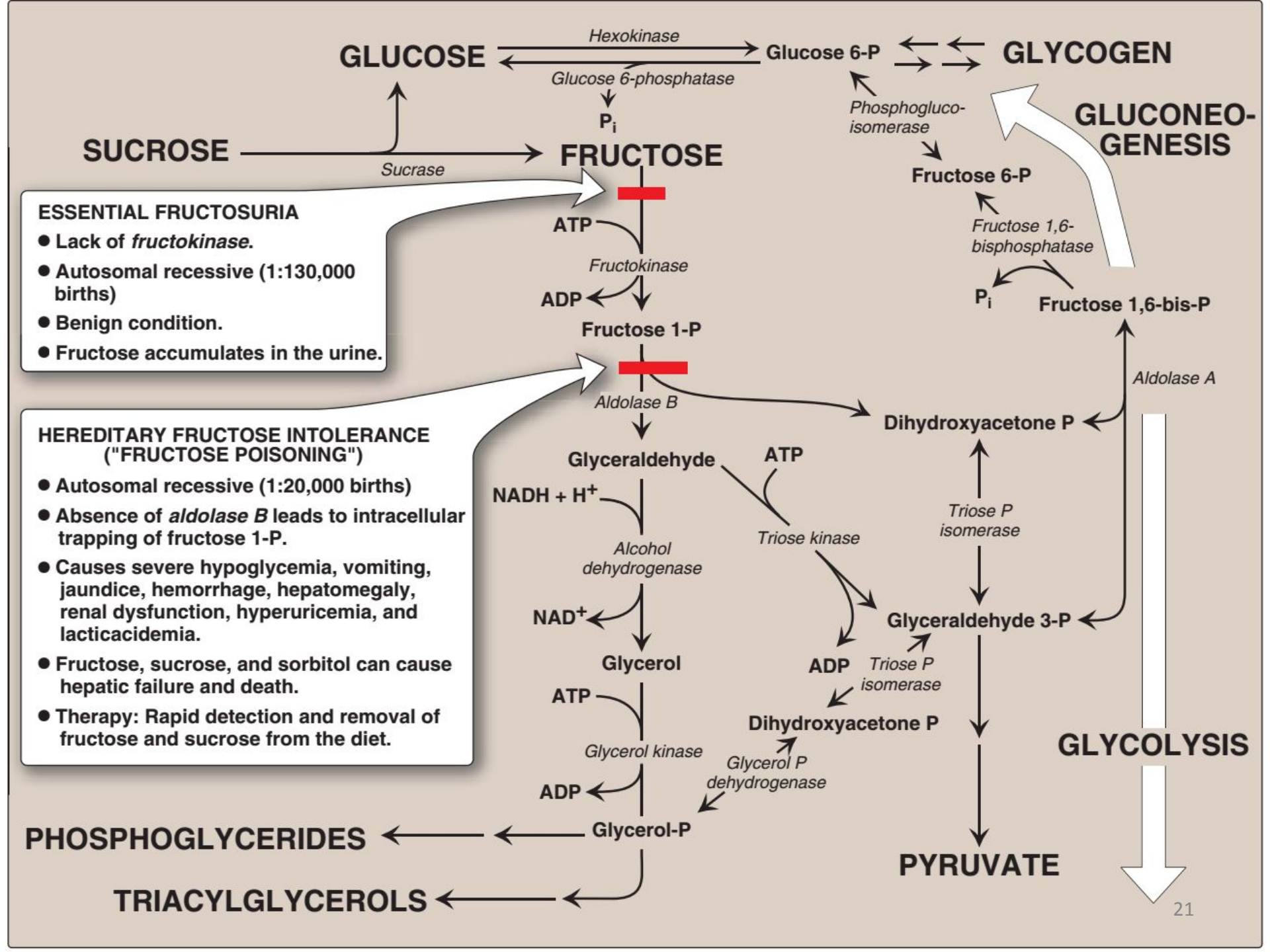


Метаболизм фруктозы

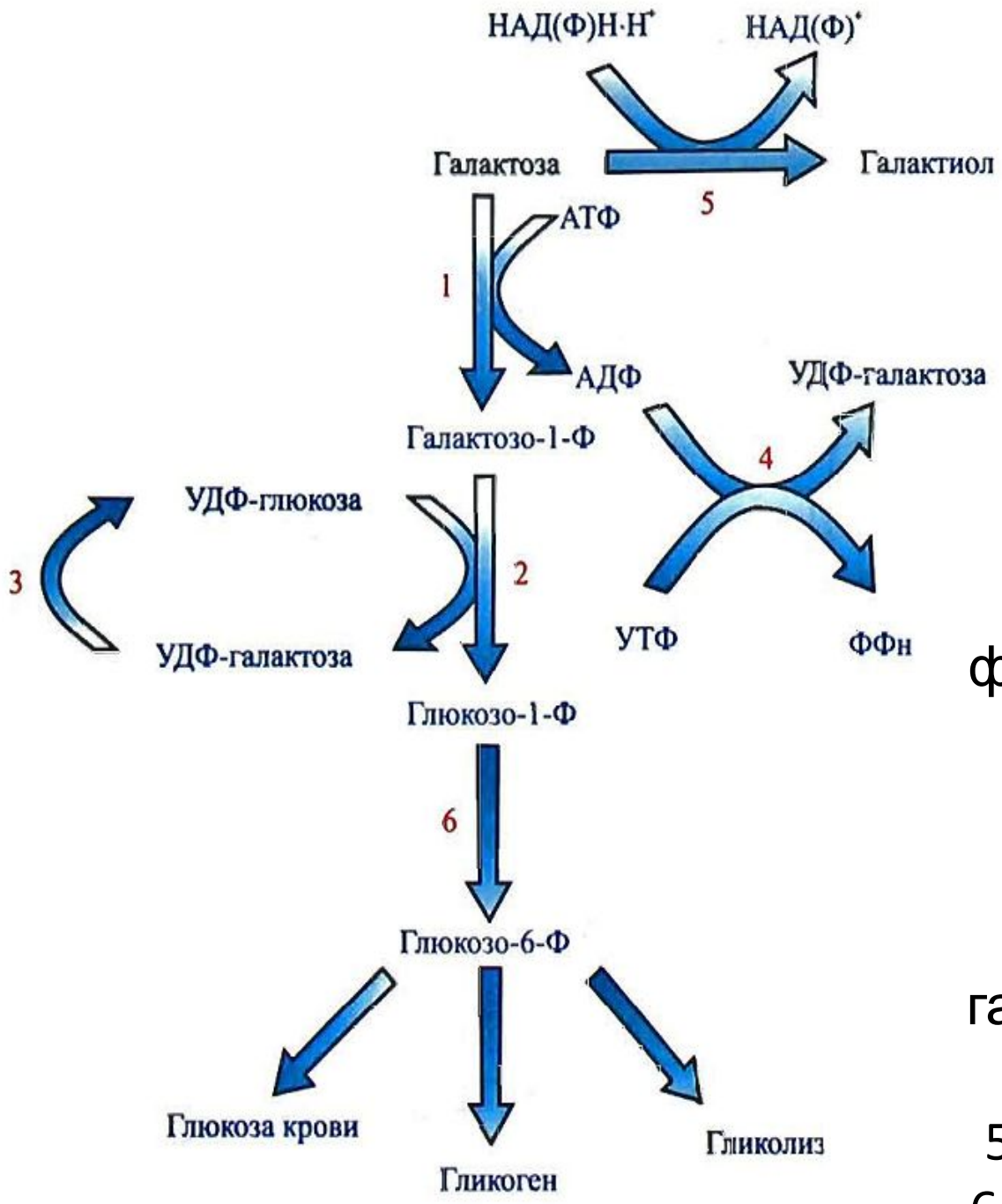




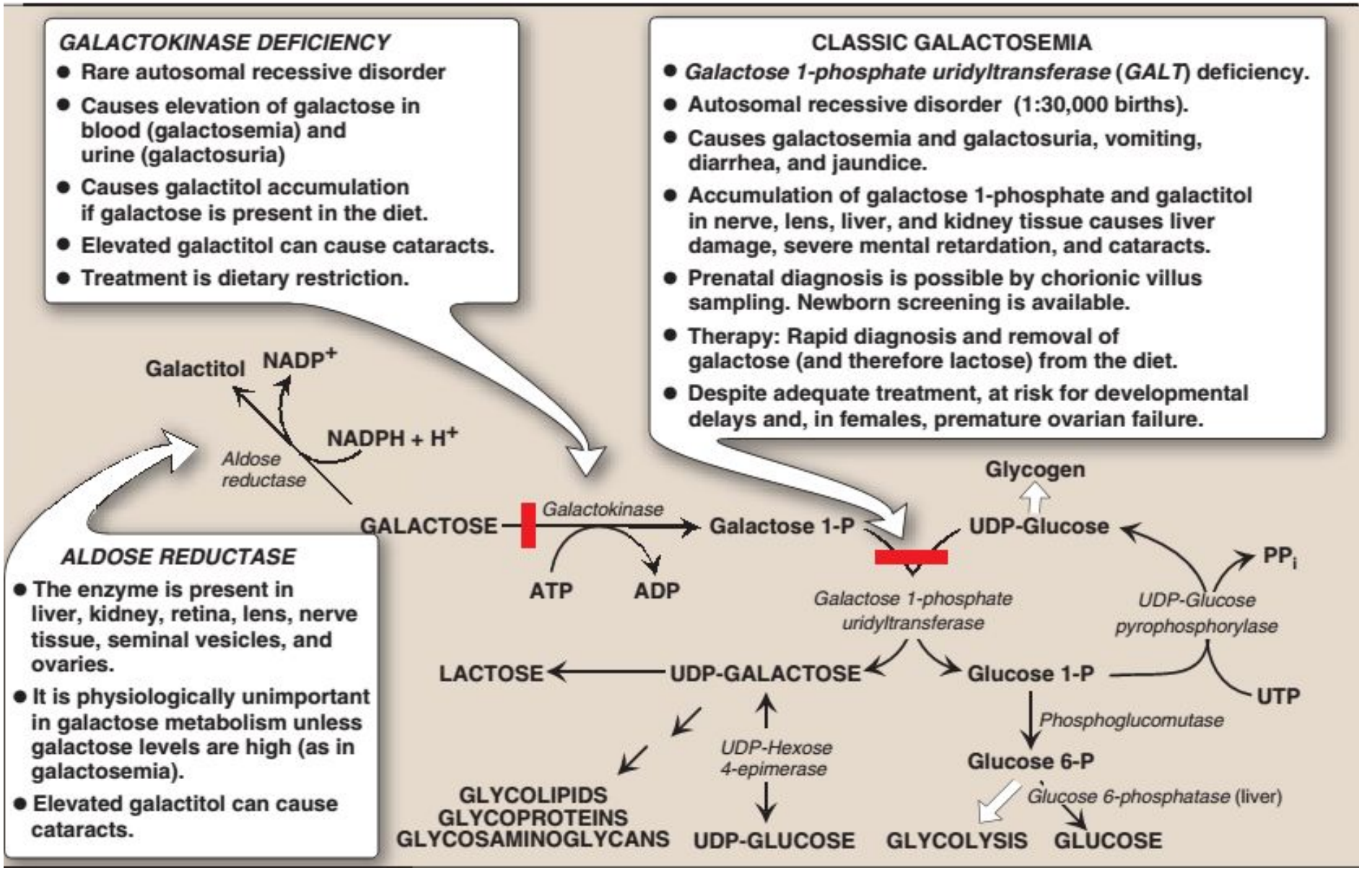
1. Гексокиназа; 2. Фруктокиназа; 3. ФФК; 4. Альдолаза В; 5. Альдолаза А; 6. Триозокиназа; 7. Альдозоредуктаза.


GLUCOSE
Hexokinase
Glucose 6-P
GLYCOGEN
Glucose 6-phosphatase
P_i
Phosphogluco-isomerase
GLUCONEO-GENESIS
SUCROSE
Sucrase
FRUCTOSE
Fructose 6-P
ESSENTIAL FRUCTOSURIA
● Lack of fructokinase.
● Autosomal recessive (1:130,000 births)
● Benign condition.
● Fructose accumulates in the urine.
ATP
Fructokinase
Fructose 1,6-bisphosphatase
ADP
P_i
Fructose 1,6-bis-P
Fructose 1-P
Aldolase A
HEREDITARY FRUCTOSE INTOLERANCE ("FRUCTOSE POISONING")
● Autosomal recessive (1:20,000 births)
● Absence of aldolase B leads to intracellular trapping of fructose 1-P.
● Causes severe hypoglycemia, vomiting, jaundice, hemorrhage, hepatomegaly, renal dysfunction, hyperuricemia, and lacticacidemia.
● Fructose, sucrose, and sorbitol can cause hepatic failure and death.
● Therapy: Rapid detection and removal of fructose and sucrose from the diet.
Aldolase B
Dihydroxyacetone P
Glyceraldehyde
ATP
$NADH + H^+$
Triose kinase
Triose P isomerase
Alcohol dehydrogenase
NAD^+
Glyceraldehyde 3-P
Glycerol
ADP
Triose P isomerase
ATP
Dihydroxyacetone P
GLYCOLYSIS
Glycerol kinase
Glycerol P dehydrogenase
ADP
PHOSPHOGLYCERIDES
Glycerol-P
PYRUVATE
TRIACYLGLYCEROLS

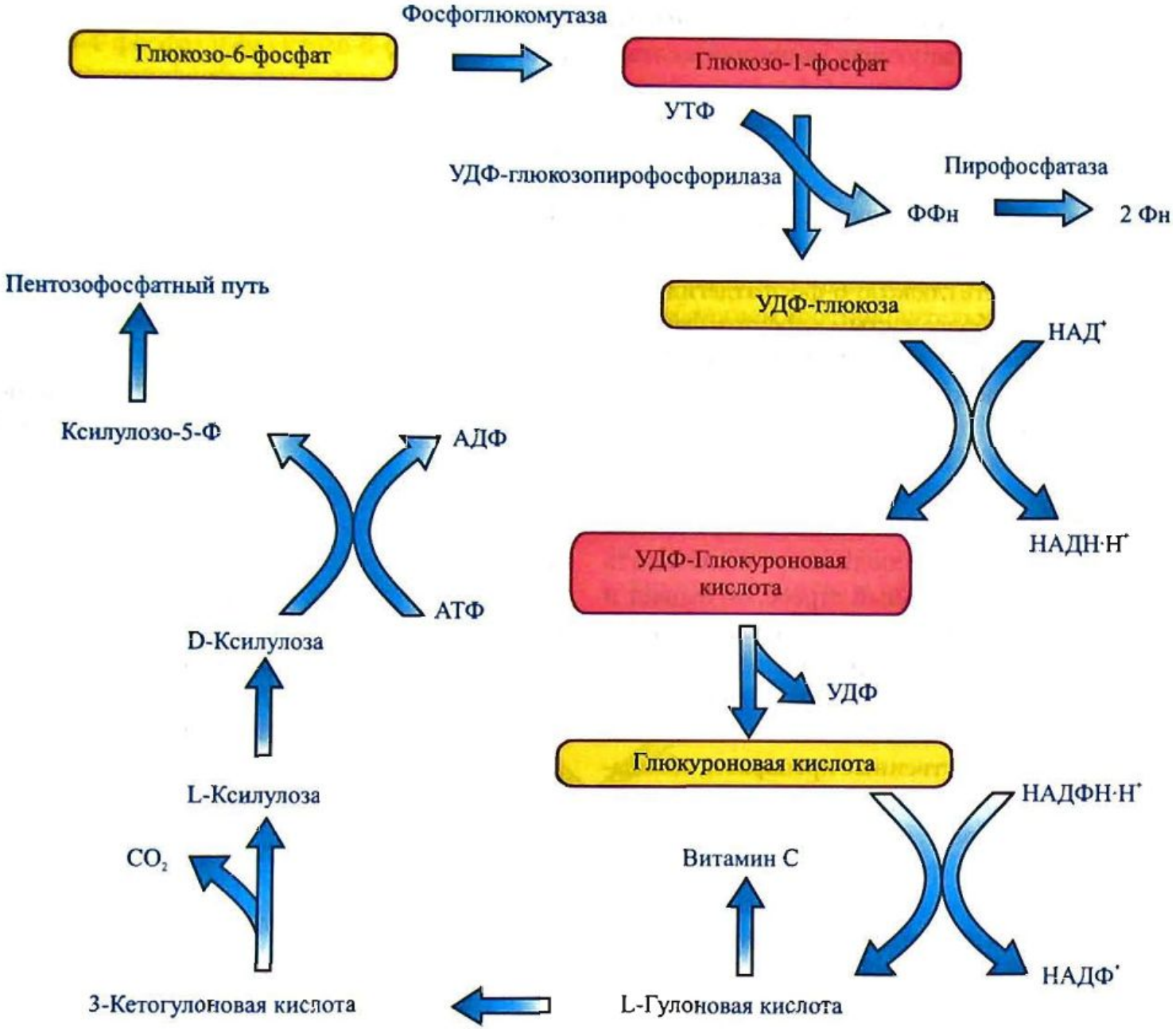
Обмен галактозы



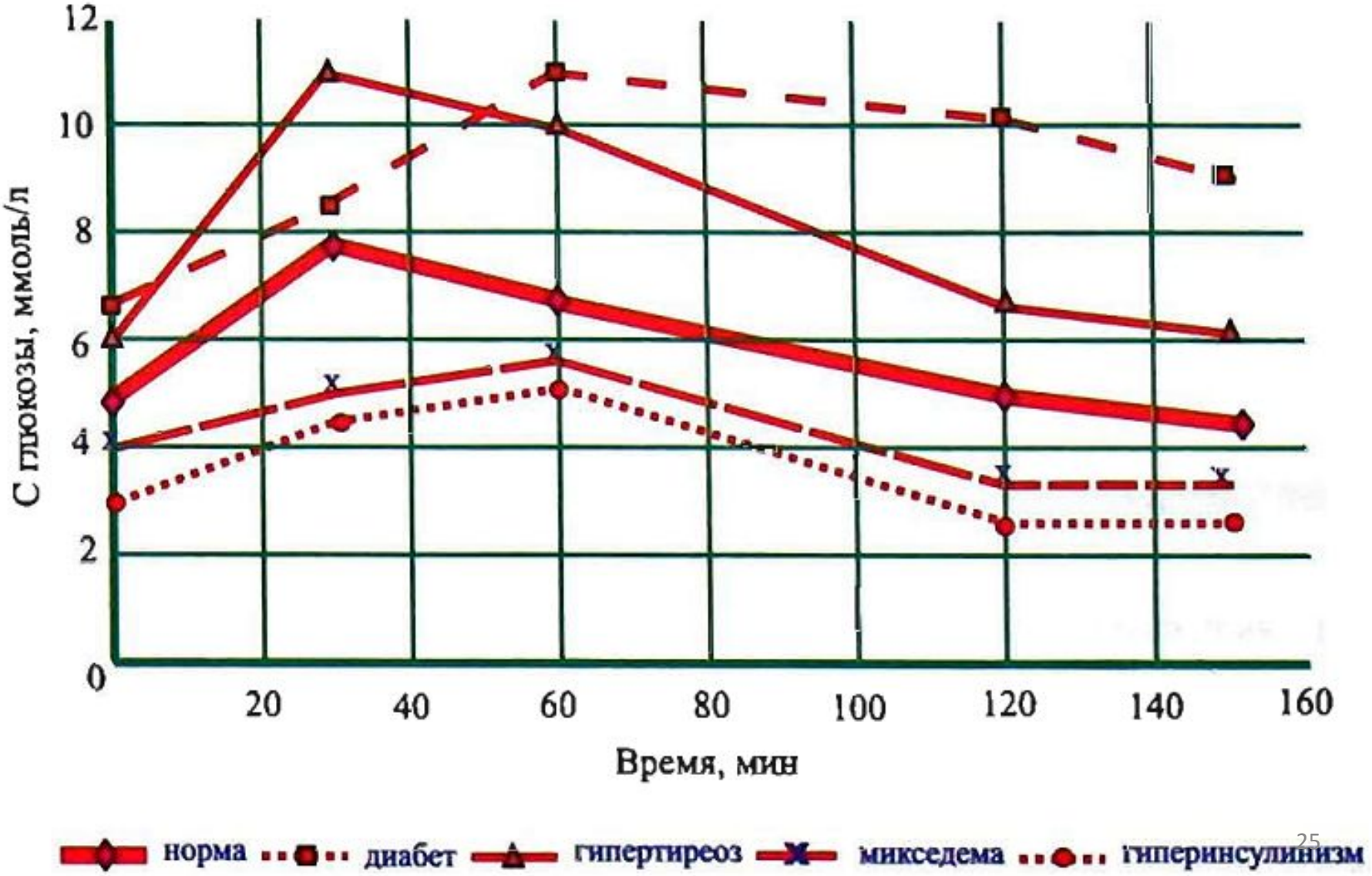
1. Галактокиназа;
2. Галактозо-1-фосфатуридилтрансфераза;
3. УДФ-галактозо-4-эпимераза;
4. УДФ-галактозопирофосфорилаза;
5. Альдозоредуктаза;
6. Фосфоглюкомутаза.


GALACTOKINASE DEFICIENCY
Rare autosomal recessive disorder
Causes elevation of galactose in blood (galactosemia) and urine (galactosuria)
Causes galactitol accumulation if galactose is present in the diet.
Elevated galactitol can cause cataracts.
Treatment is dietary restriction.
CLASSIC GALACTOSEMIA
Galactose 1-phosphate uridyltransferase (GALT) deficiency.
Autosomal recessive disorder (1:30,000 births).
Causes galactosemia and galactosuria, vomiting, diarrhea, and jaundice.
Accumulation of galactose 1-phosphate and galactitol in nerve, lens, liver, and kidney tissue causes liver damage, severe mental retardation, and cataracts.
Prenatal diagnosis is possible by chorionic villus sampling. Newborn screening is available.
Therapy: Rapid diagnosis and removal of galactose (and therefore lactose) from the diet.
Despite adequate treatment, at risk for developmental delays and, in females, premature ovarian failure.
Galactitol
NADP+
NADPH + H+
Aldose reductase
GALACTOSE
Galactokinase
ATP
ADP
Galactose 1-P
Glycogen
UDP-Glucose
PPi
Galactose 1-phosphate uridyltransferase
UDP-Glucose pyrophosphorylase
UTP
LACTOSE
UDP-GALACTOSE
Glucose 1-P
Phosphoglucomutase
Glucose 6-P
UDP-Hexose 4-epimerase
GLYCOLIPIDS
GLYCOPROTEINS
GLYCOSAMINOGLYCANS
UDP-GLUCOSE
Glucose 6-phosphatase (liver)
GLYCOLYSIS
GLUCOSE
ALDOSE REDUCTASE
The enzyme is present in liver, kidney, retina, lens, nerve tissue, seminal vesicles, and ovaries.
It is physiologically unimportant in galactose metabolism unless galactose levels are high (as in galactosemia).
Elevated galactitol can cause cataracts.

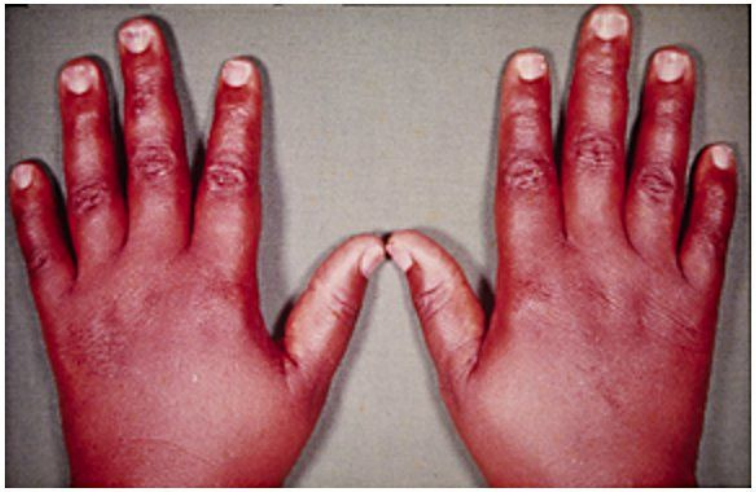
Глюкуроновый путь обмена глюкозы

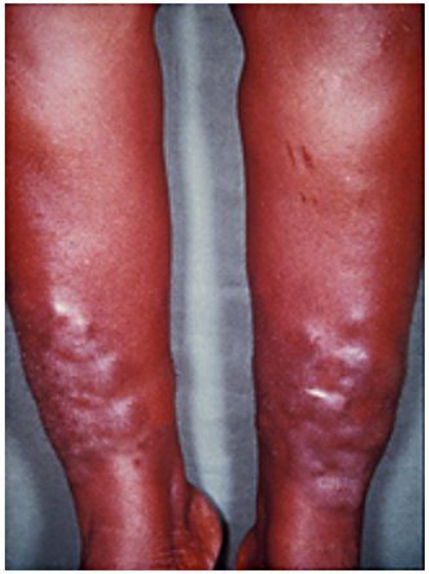


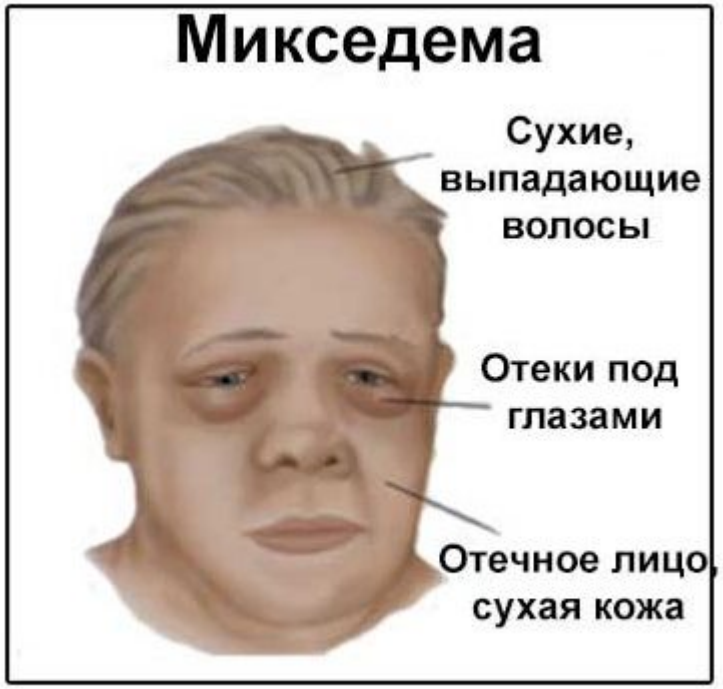
Изменение концентрации глюкозы в норме и при патологиях

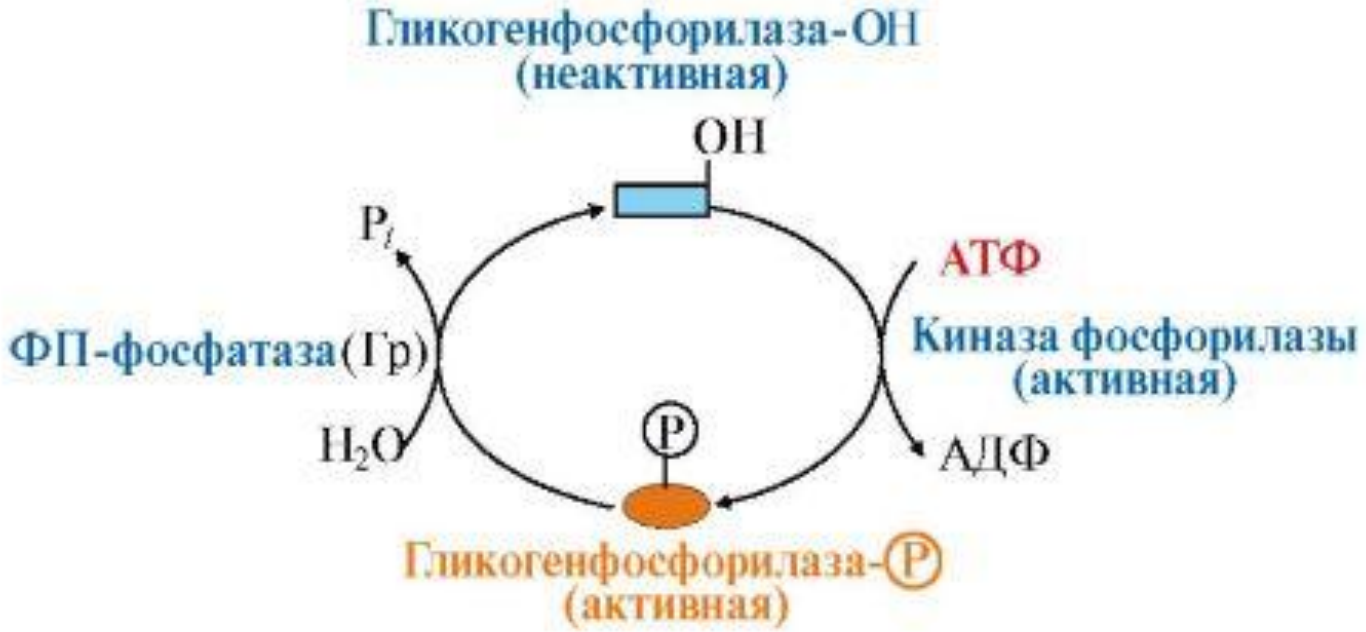


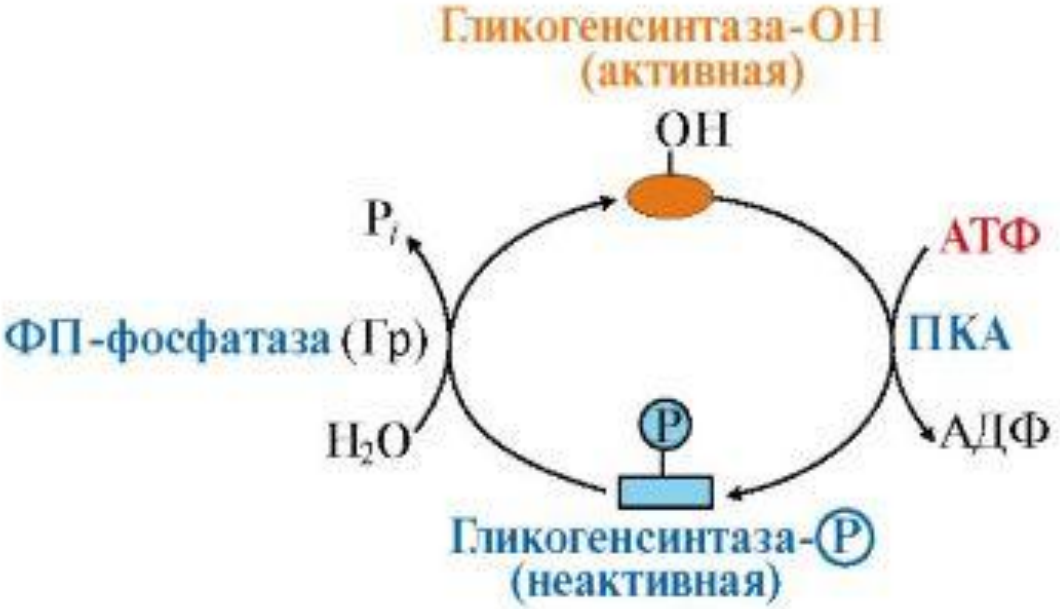
Микседема






Микседема
Сухие, выпадающие волосы
Отеки под глазами
Отечное лицо, сухая кожа

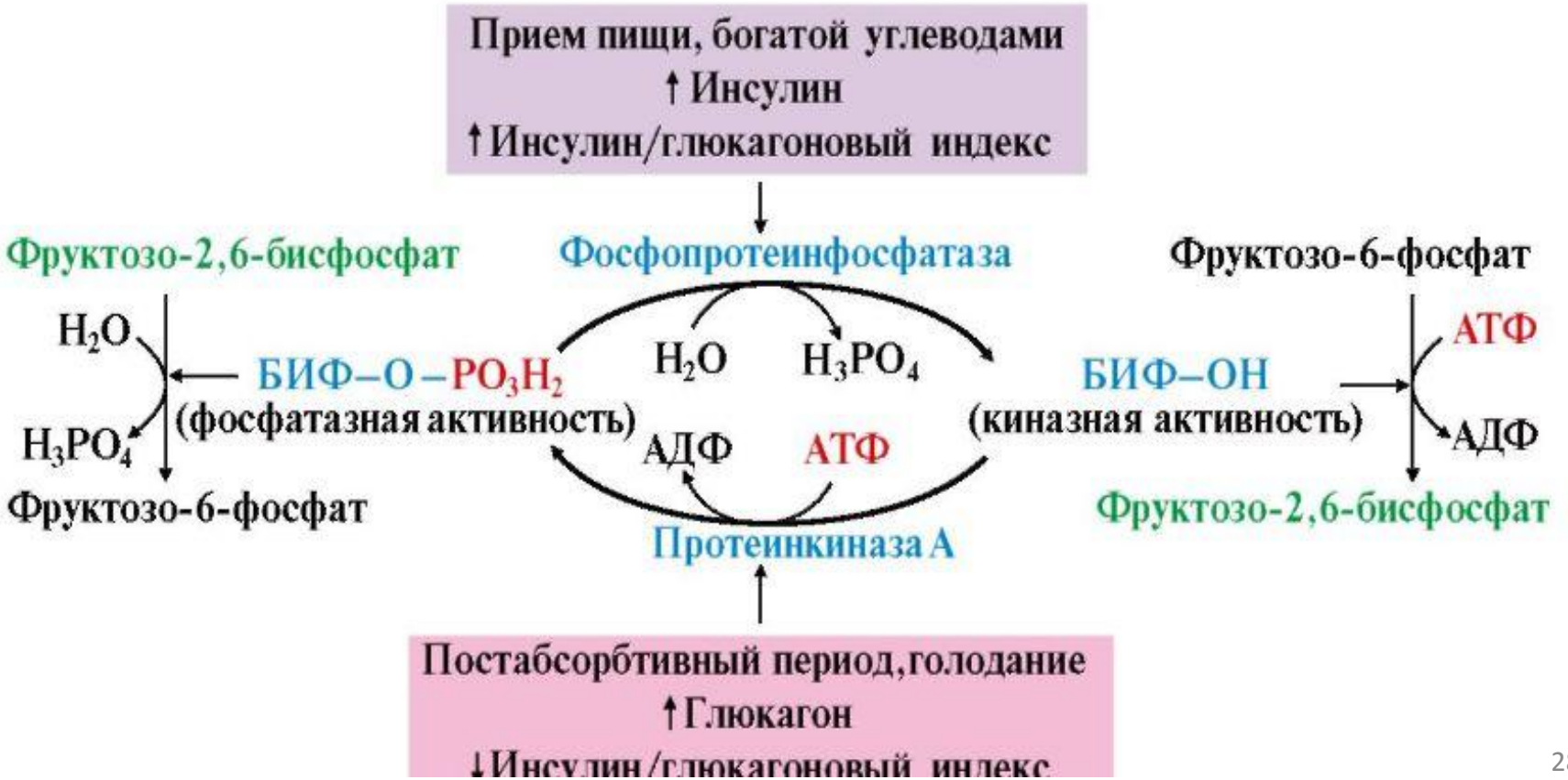

Гликогенфосфорилаза-ОН
(неактивная)
OH
P_i
АТФ
ФП-фосфатаза (Гр)
Киназа фосфорилазы
(активная)
H_2O
Р
АДФ
Гликогенфосфорилаза-Р
(активная)

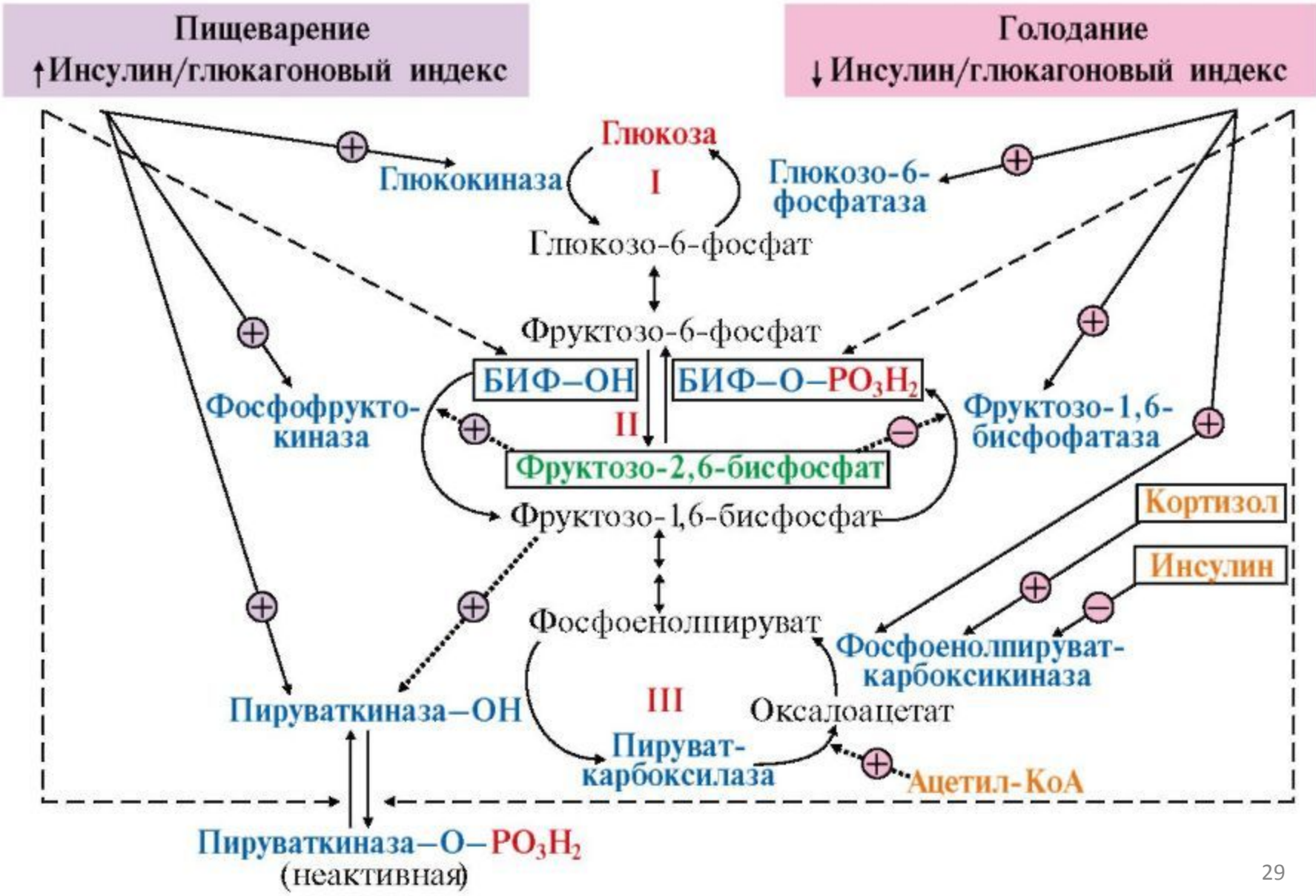

Гликогенсинтаза-ОН
(активная)
OH
P_i
АТФ
ФП-фосфатаза (Гр)
ПКА
H_2O
Р
АДФ
Гликогенсинтаза-Р
(неактивная)

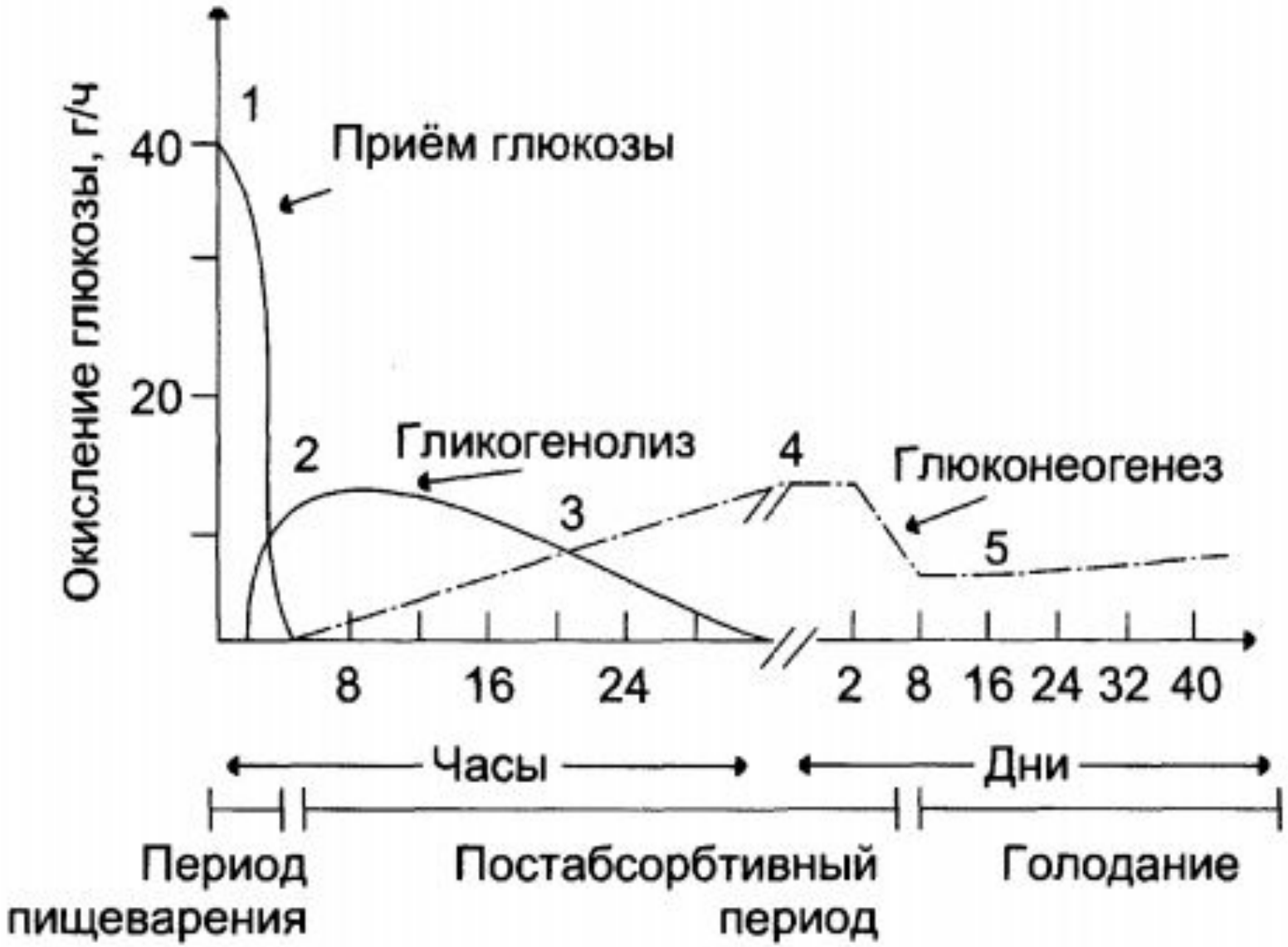
РЕГУЛЯЦИЯ ГЛИКОЛИЗА И ГЛЮКОНЕОГЕНЕЗА В ПЕЧЕНИ

1. Переключение метаболизма печени с гликолиза на глюконеогенез и наоборот происходит при помощи:

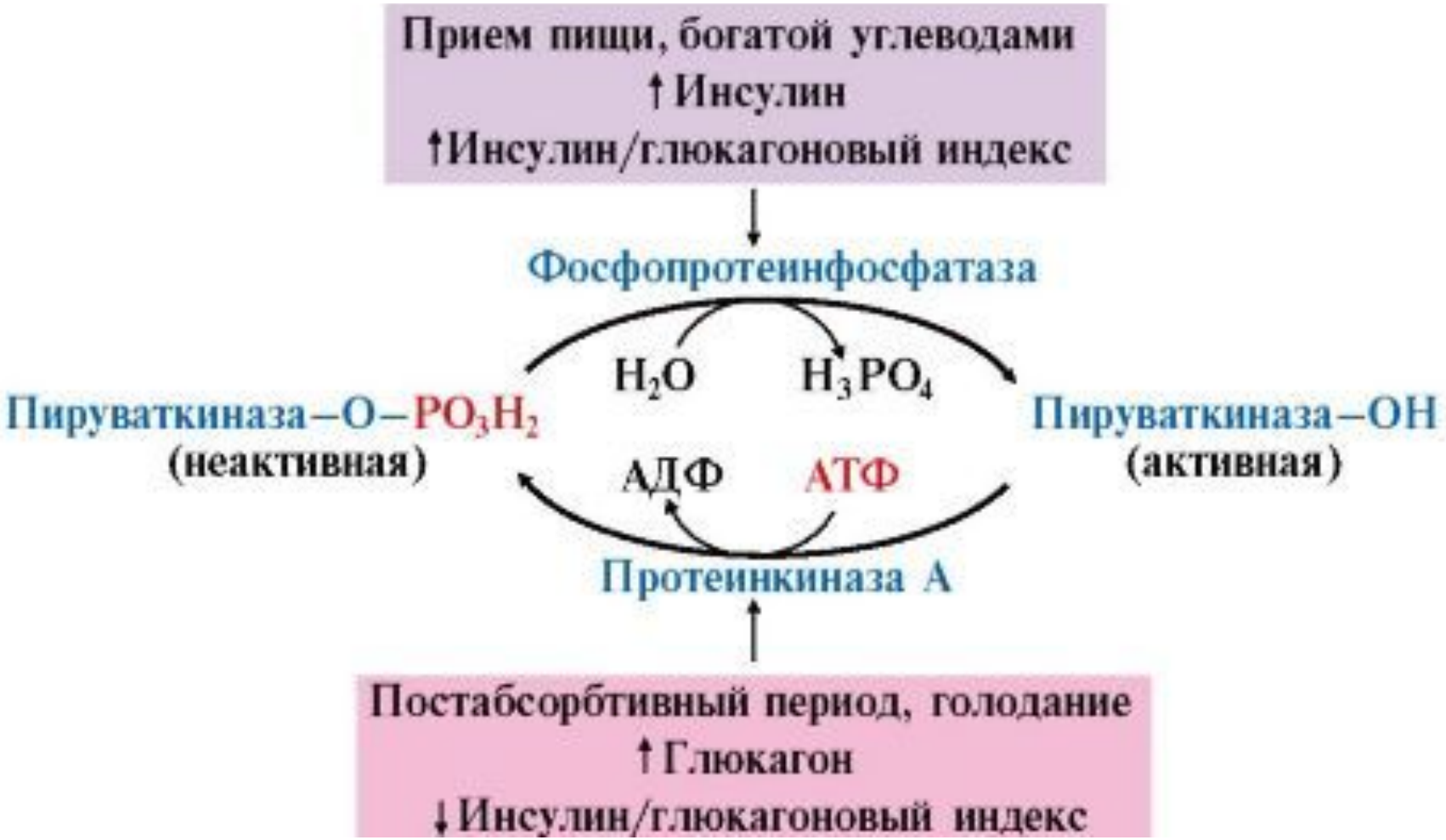
- аллостерических механизмов регуляции активности ключевых ферментов;
- ковалентной модификации ферментов путем фосфорилирования (дефосфорилирования) с участием инсулина и глюкагона;
- индукции (репрессии) синтеза ключевых ферментов, катализирующих реакции субстратных циклов.




Пищеварение
↑Инсулин/глюкагоновый индекс
Голодание
↓Инсулин/глюкагоновый индекс
Глюкоза
Глюкокиназа
I
Глюкозо-6-фосфатаза
Глюкозо-6-фосфат
Фруктозо-6-фосфат
БИФ–ОН
БИФ–О–PO3H2
II
Фосфофруктокиназа
Фруктозо-1,6-бисфосфатаза
Фруктозо-2,6-бисфосфат
Фруктозо-1,6-бисфосфат
Кортизол
Инсулин
Фосфоенолпируват
Фосфоенолпируват-карбоксикиназа
Пируваткиназа–ОН
III
Оксалоацетат
Пируват-карбоксилаза
Ацетил-КоА
Пируваткиназа–О–PO3H2
(неактивная)


Окисление глюкозы, г/ч
40
20
1
Приём глюкозы
2
Гликогенолиз
3
4
Глюконеогенез
5
8
16
24
2
8
16
24
32
40
Часы
Дни
Период пищеварения
Постабсорбтивный период
Голодание

Регуляция пируваткиназы в печени



Механизм действия глюкагона адреналина

Структурные компоненты ГАГ

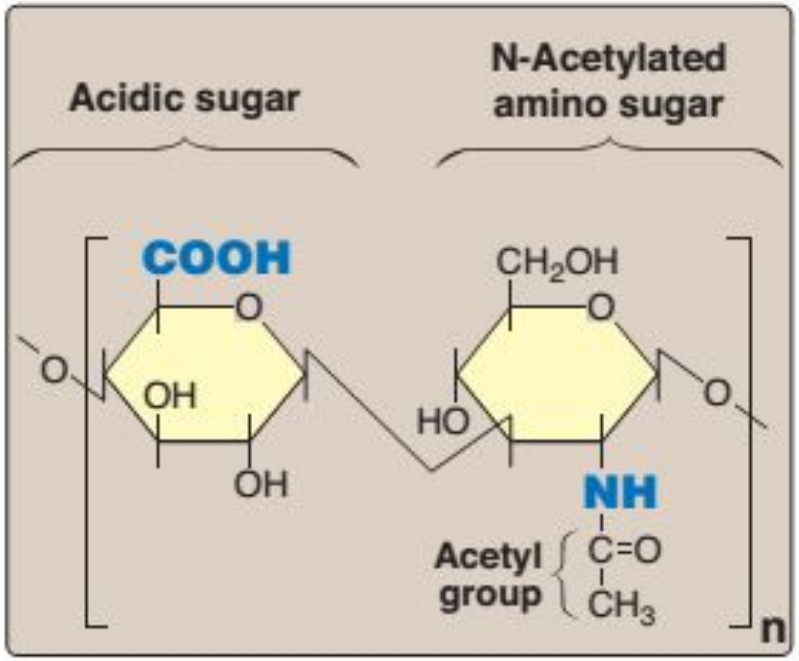


Figure 14.1
Repeating disaccharide unit.

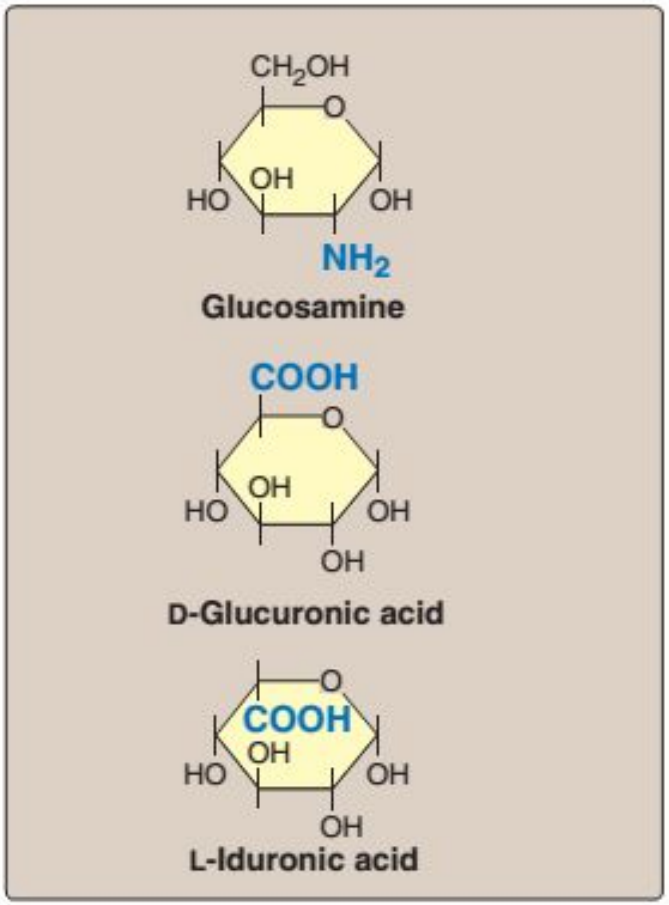
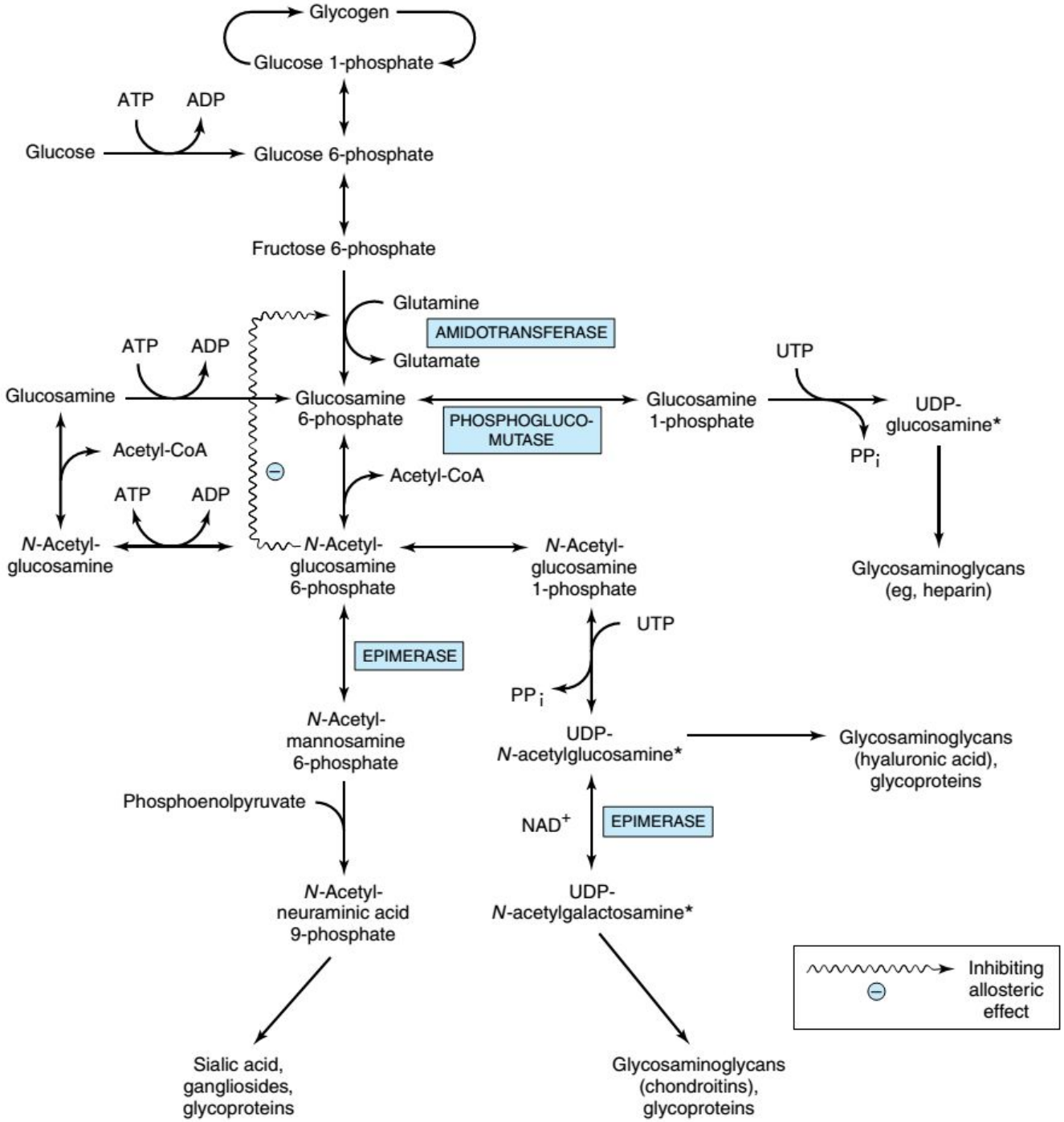
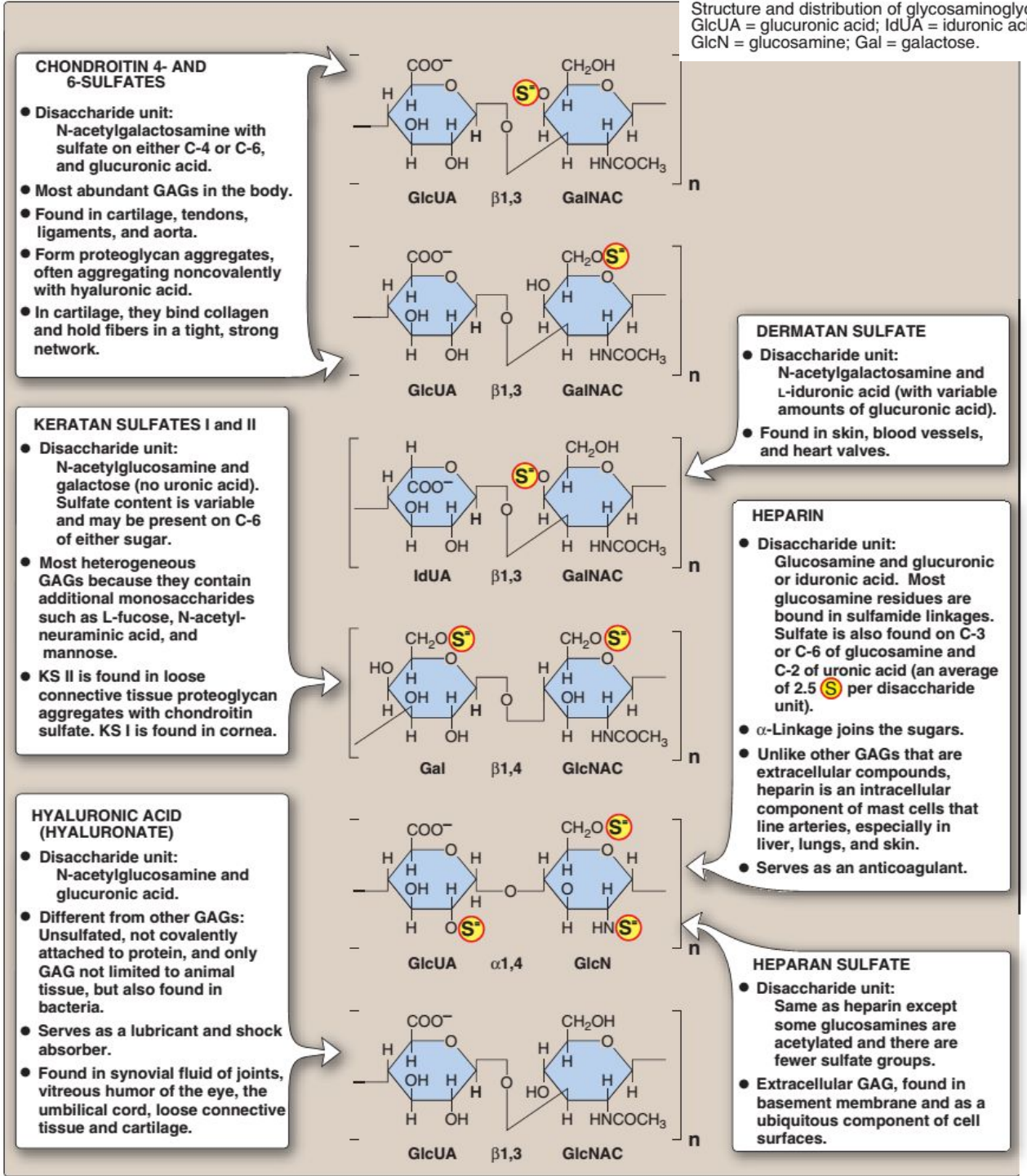
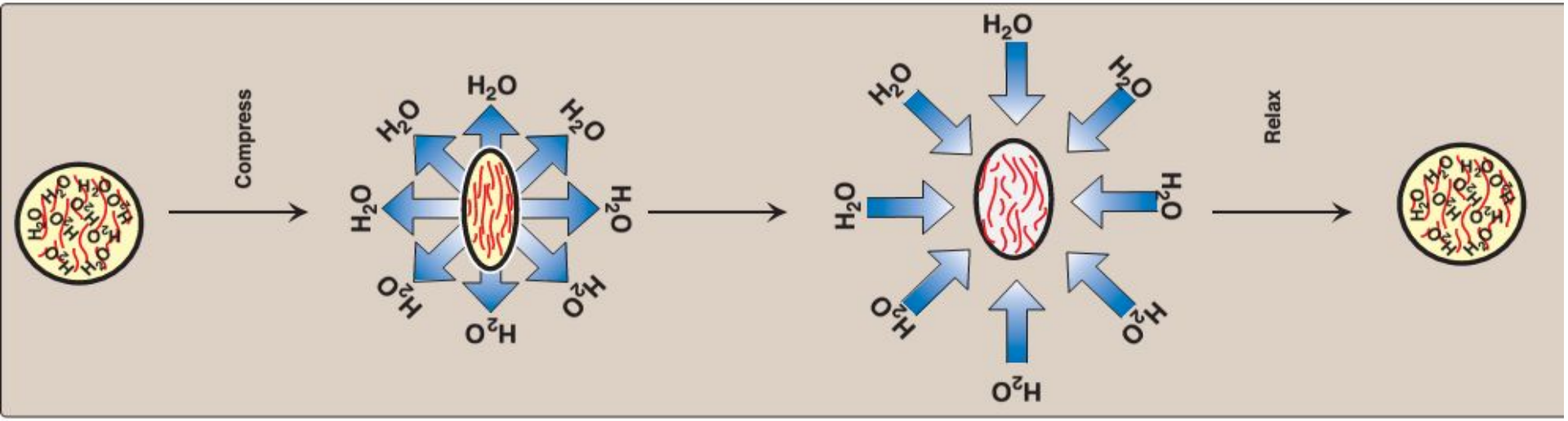


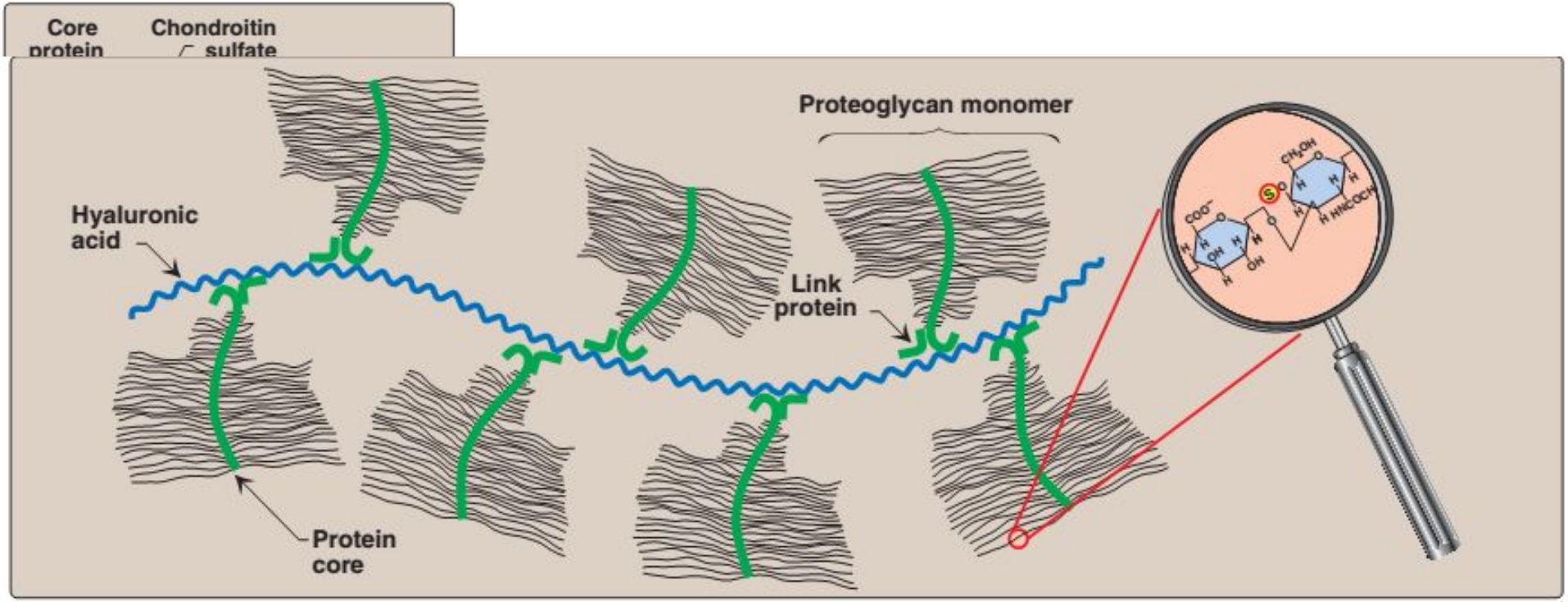
Figure 14.2
Some monosaccharide units found in glycosaminoglycans.


Glycogen
Glucose 1-phosphate
ATP
ADP
Glucose
Glucose 6-phosphate
Fructose 6-phosphate
Glutamine
AMIDOTRANSFERASE
Glutamate
ATP
ADP
Glucosamine
Glucosamine 6-phosphate
PHOSPHOGLUCO-MUTASE
Glucosamine 1-phosphate
UTP
UDP-glucosamine*
PPi
Acetyl-CoA
Acetyl-CoA
ATP
ADP
N-Acetyl-glucosamine
N-Acetyl-glucosamine 6-phosphate
N-Acetyl-glucosamine 1-phosphate
Glycosaminoglycans (eg, heparin)
EPIMERASE
UTP
PPi
N-Acetyl-mannosamine 6-phosphate
UDP-N-acetylglucosamine*
Glycosaminoglycans (hyaluronic acid), glycoproteins
Phosphoenolpyruvate
NAD+
EPIMERASE
N-Acetyl-neuraminic acid 9-phosphate
UDP-N-acetylgalactosamine*
Inhibiting allosteric effect
Sialic acid, gangliosides, glycoproteins
Glycosaminoglycans (chondroitins), glycoproteins

Structure and distribution of glycosaminoglycans (GAGs). Sulfate groups (Ⓢ) are shown in all possible positions. GlcUA = glucuronic acid; IdUA = iduronic acid; GalNAC = N-acetylgalactosamine; GlcNAC = N-acetylglucosamine; GlcN = glucosamine; Gal = galactose.




Compress
Relax
H_2O


Core protein
Chondroitin sulfate
Proteoglycan monomer
Hyaluronic acid
Link protein
Protein core

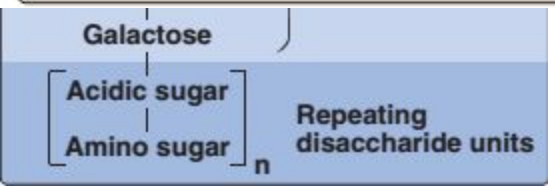
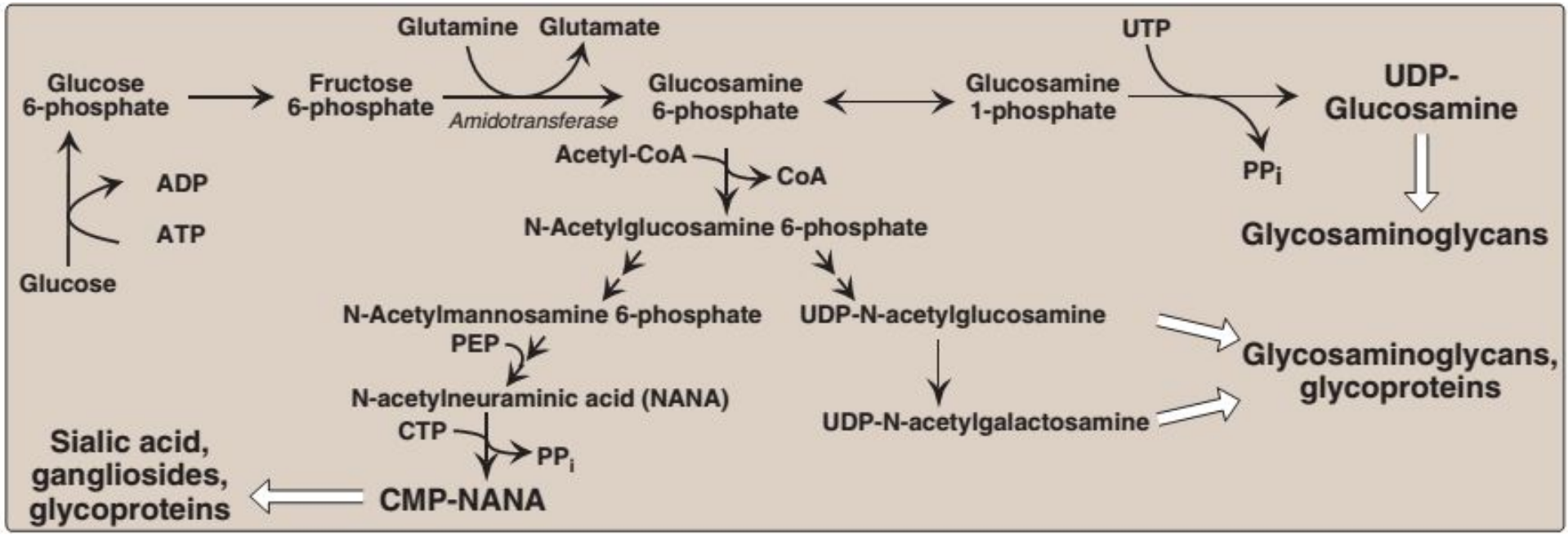

Galactose
Acidic sugar
Amino sugar
n
Repeating disaccharide units

Схема синтеза ГАГ



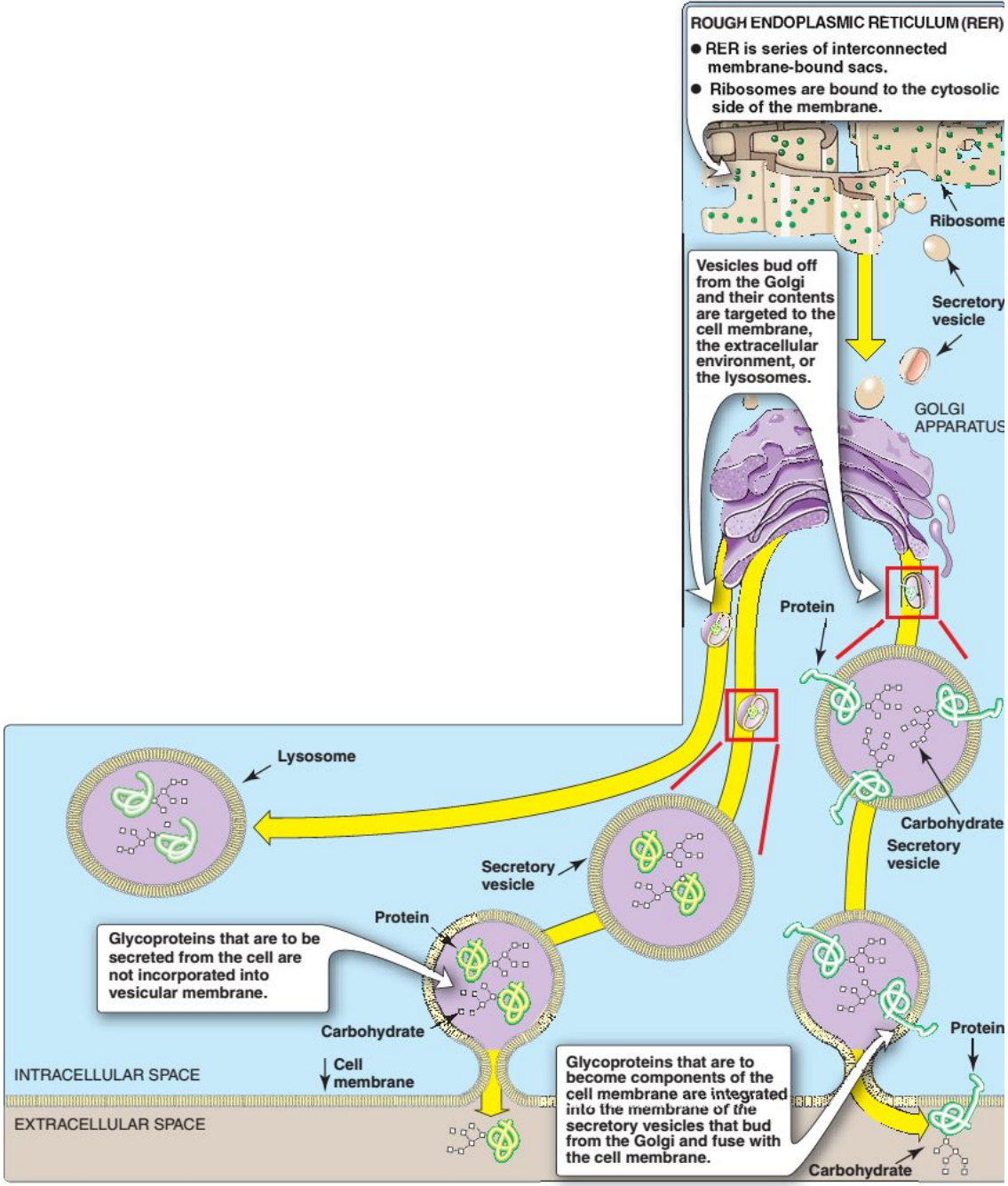


Figure 14.15
Transport of glycoproteins through the Golgi apparatus and their subsequent release or incorporation into a lysosome or the cell membrane.