

Exercise 12

Corrections

BIO-213

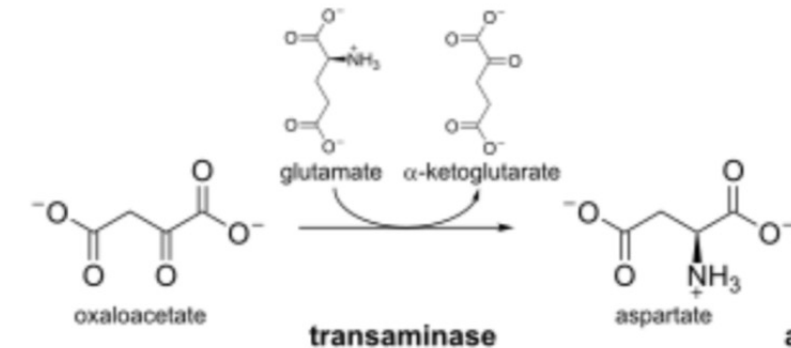
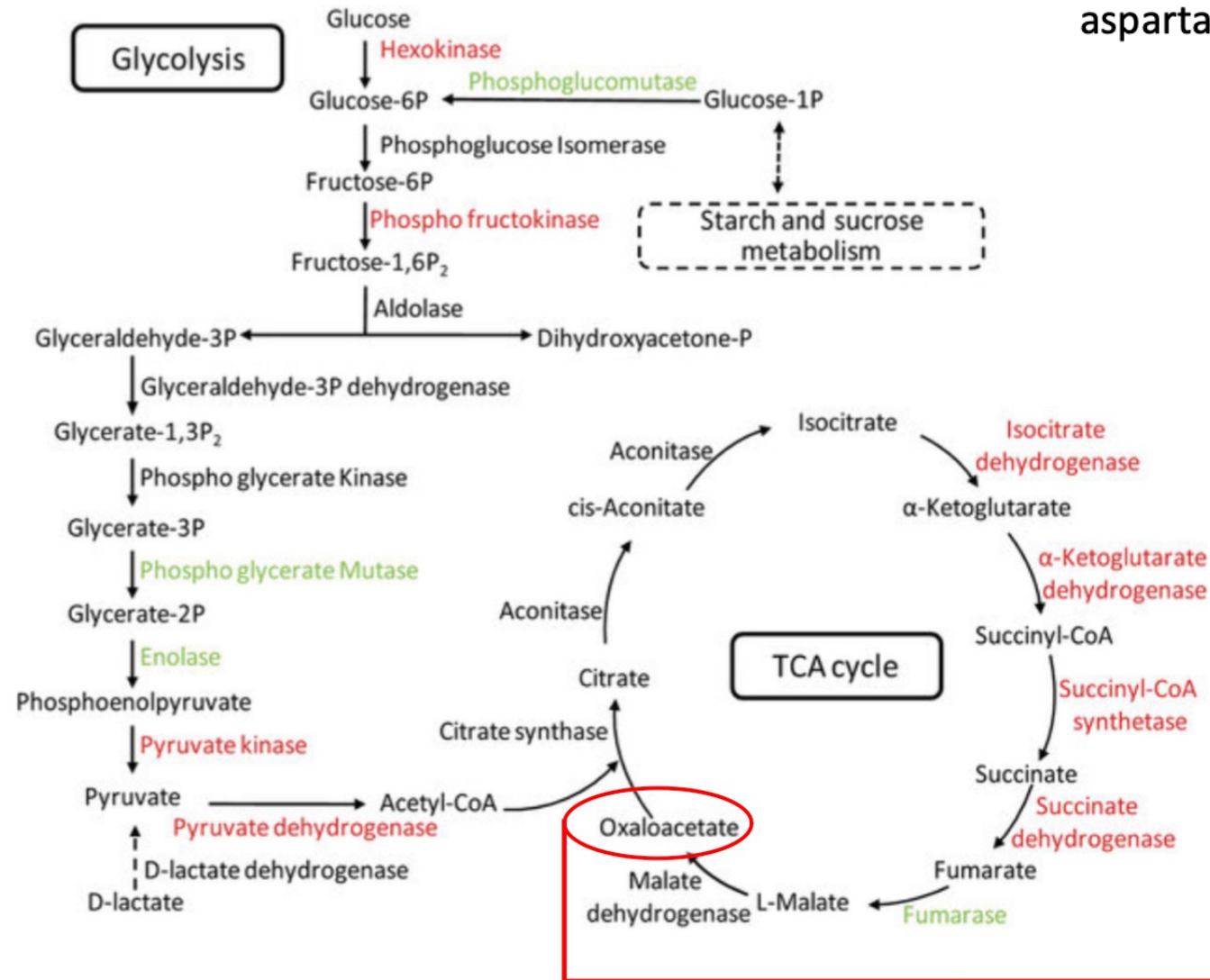
Biological Chemistry II

Question 1

Write the entire series of reactions that lead from glucose to aspartate in presence of glutamate

Answer

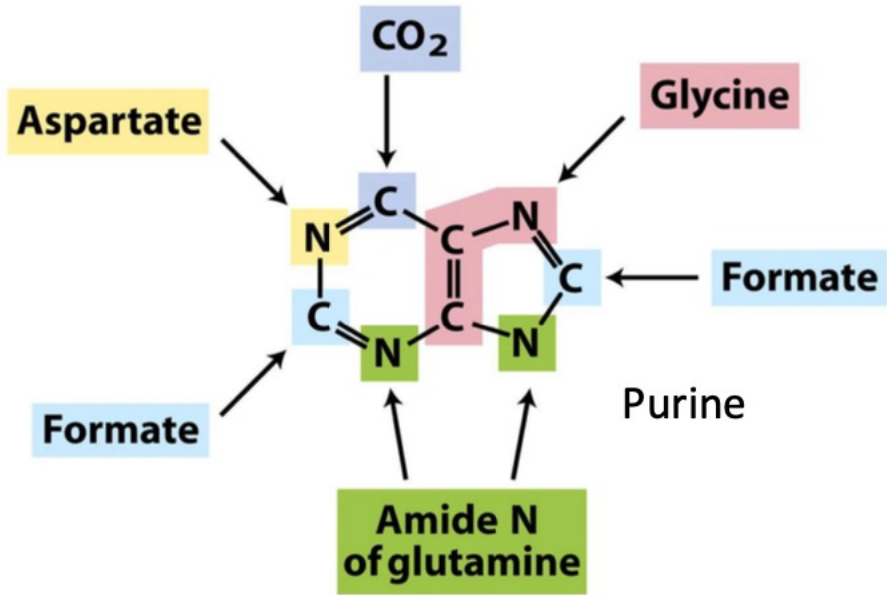
- We need to go through glycolysis and the TCA
- Aspartate is produced by transamination of oxaloacetate in a reaction catalysed by aspartate transaminase (AST).



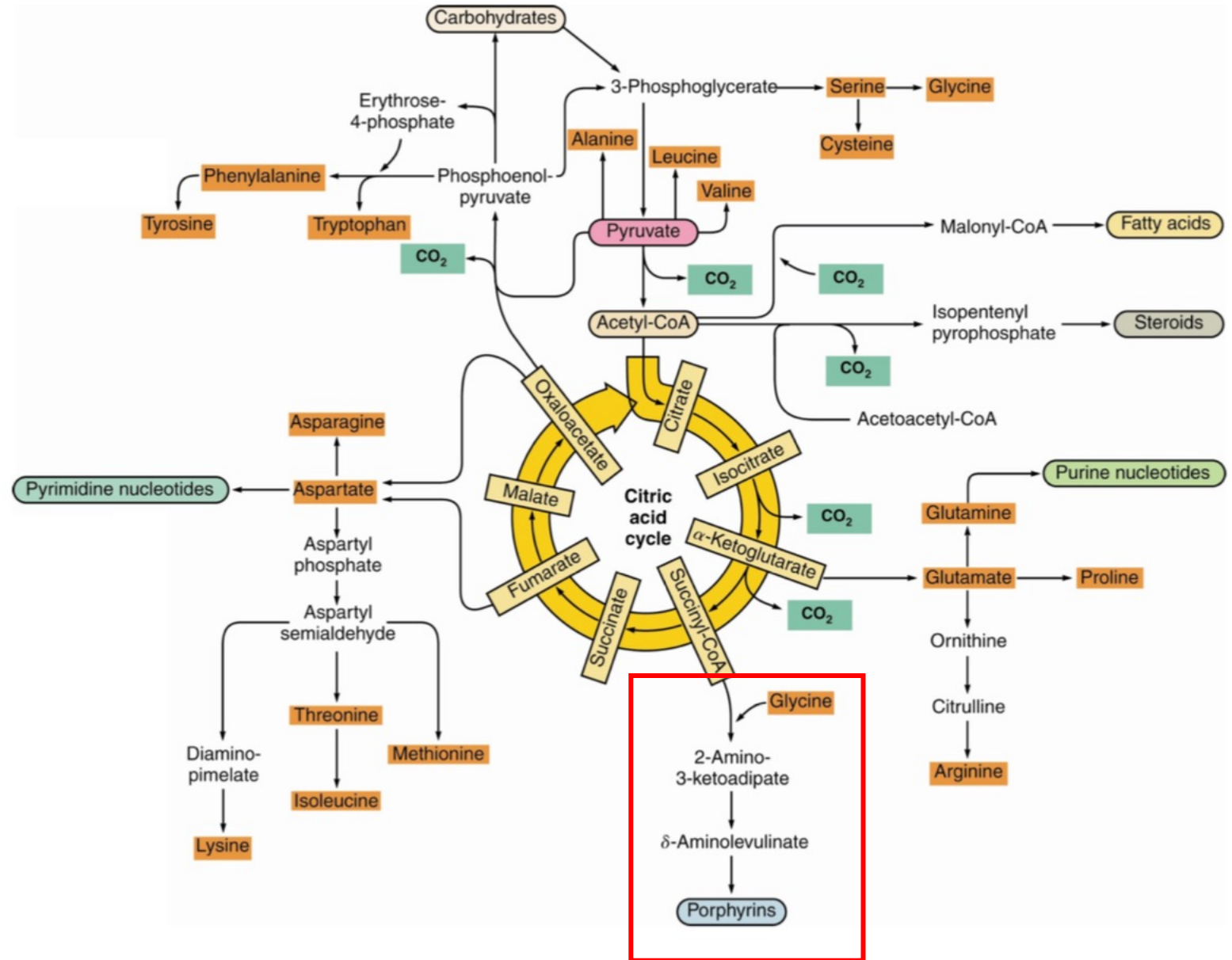
Question 2

E. Coli is able to synthesise all the amino acids. Some mutant bacteria nevertheless have defects in specific enzymes and are said *auxotroph* towards some specific amino acids (i.e., they cannot synthesise a given amino acid and need to take it up from the environment to grow). Consider three *E. Coli* auxotroph strains in glycine, glutamine and aspartate. Apart from proteins (that need all amino acids to be synthesised) what other compounds cannot be produced by each of these bacterial strains? Explain your answer

Answer



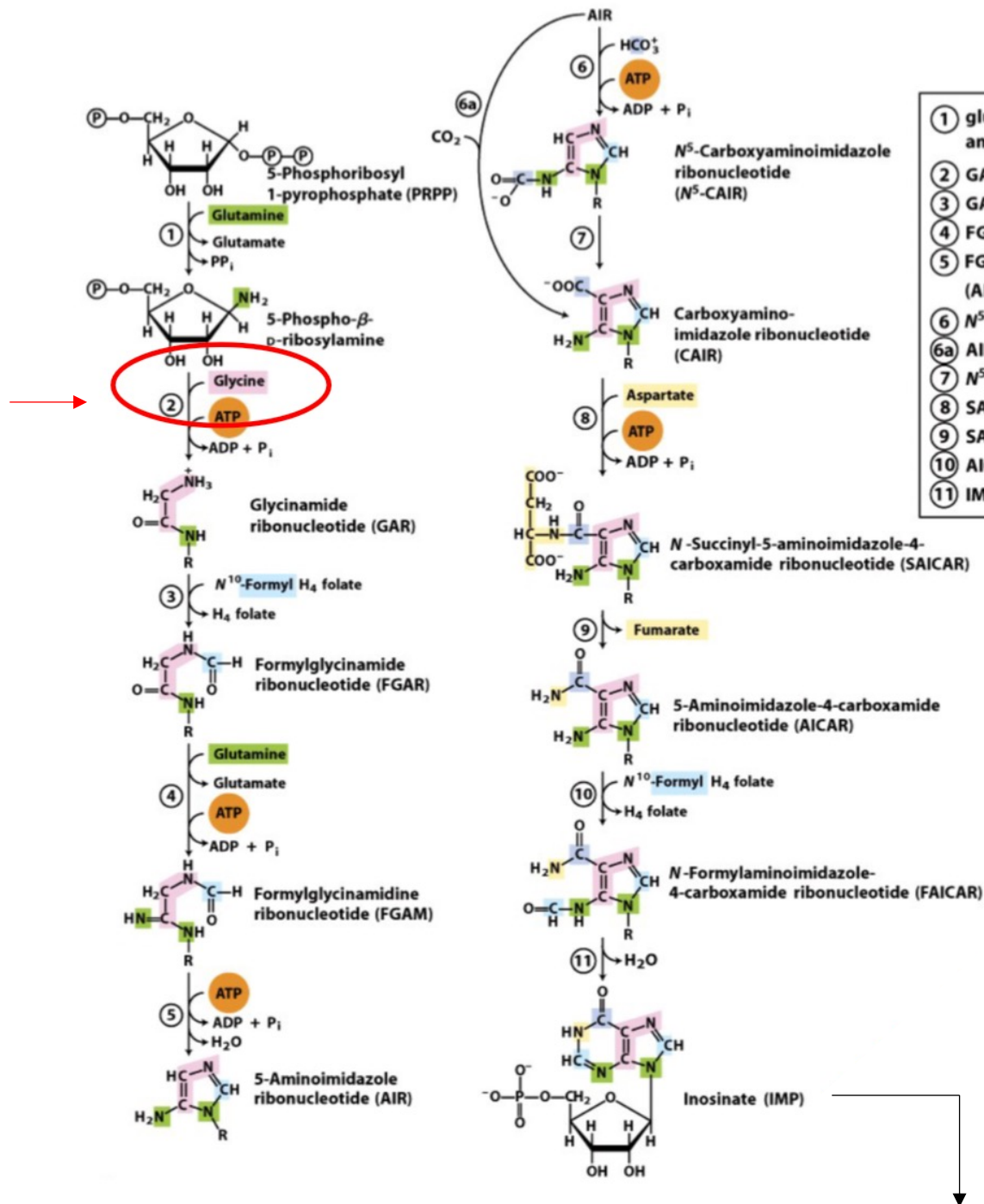
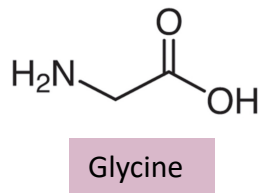
- Auxotroph in GLY:
 - Porphyrins
 - Purines
- Auxotroph in GLN:
 - Purines and pyrimidines
- Auxotroph in ASP:
 - Pyrimidine and purines



Question 3

What is the ^{14}C labelling of AMP in cells grown in the presence of uniformly ^{14}C labelled glycine?
explain your answer.

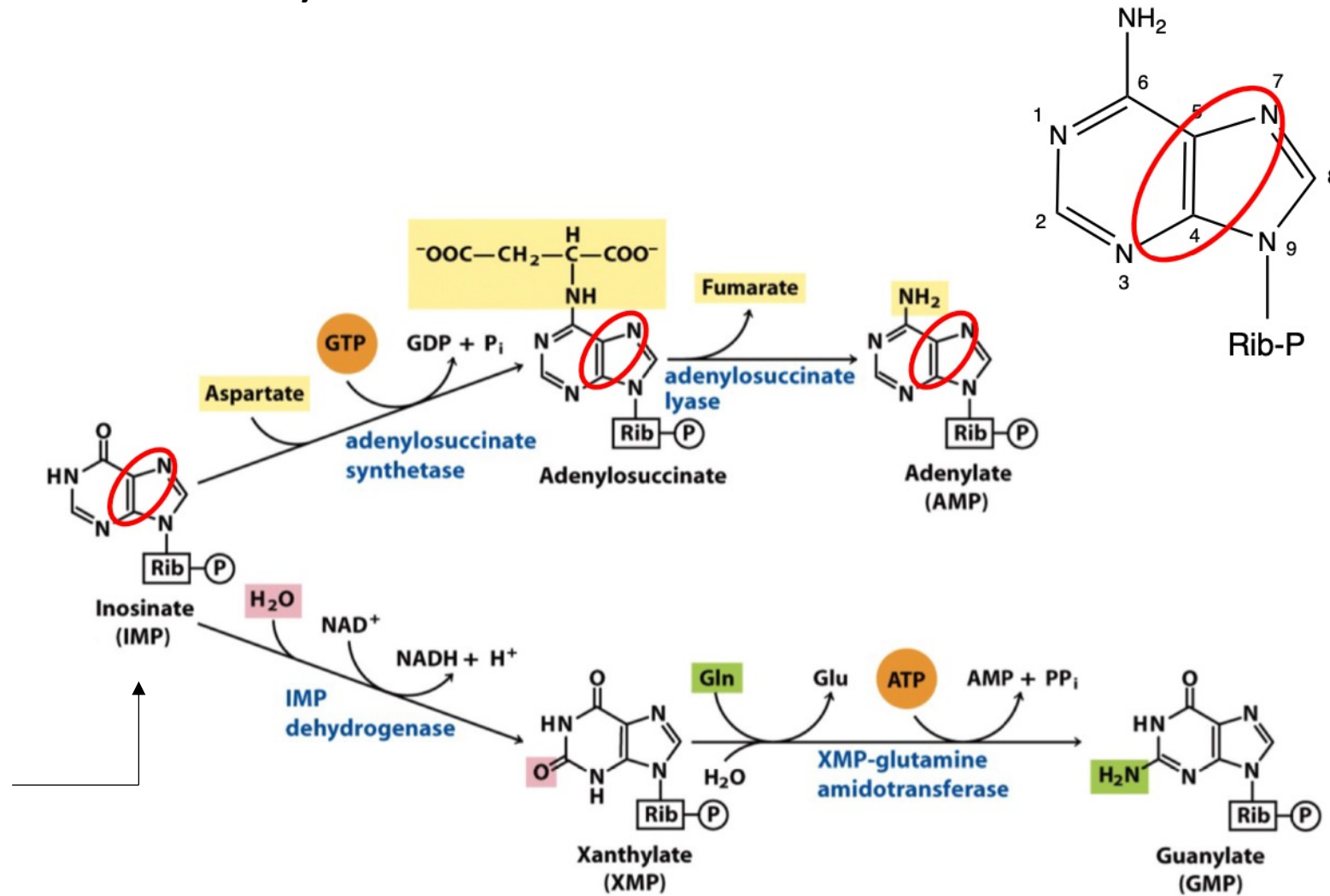
Answer



- ① glutamine-PRPP amidotransferase
- ② GAR synthetase
- ③ GAR transformylase
- ④ FGAR amidotransferase
- ⑤ FGAM cyclase (AIR synthetase)
- ⑥ N^5 -CAIR synthetase
- ⑥a AIR carboxylase
- ⑦ N^5 -CAIR mutase
- ⑧ SAICAR synthetase
- ⑨ SAICAR lyase
- ⑩ AICAR transformylase
- ⑪ IMP synthase

Answer (continue)

C4, C5 on AMP

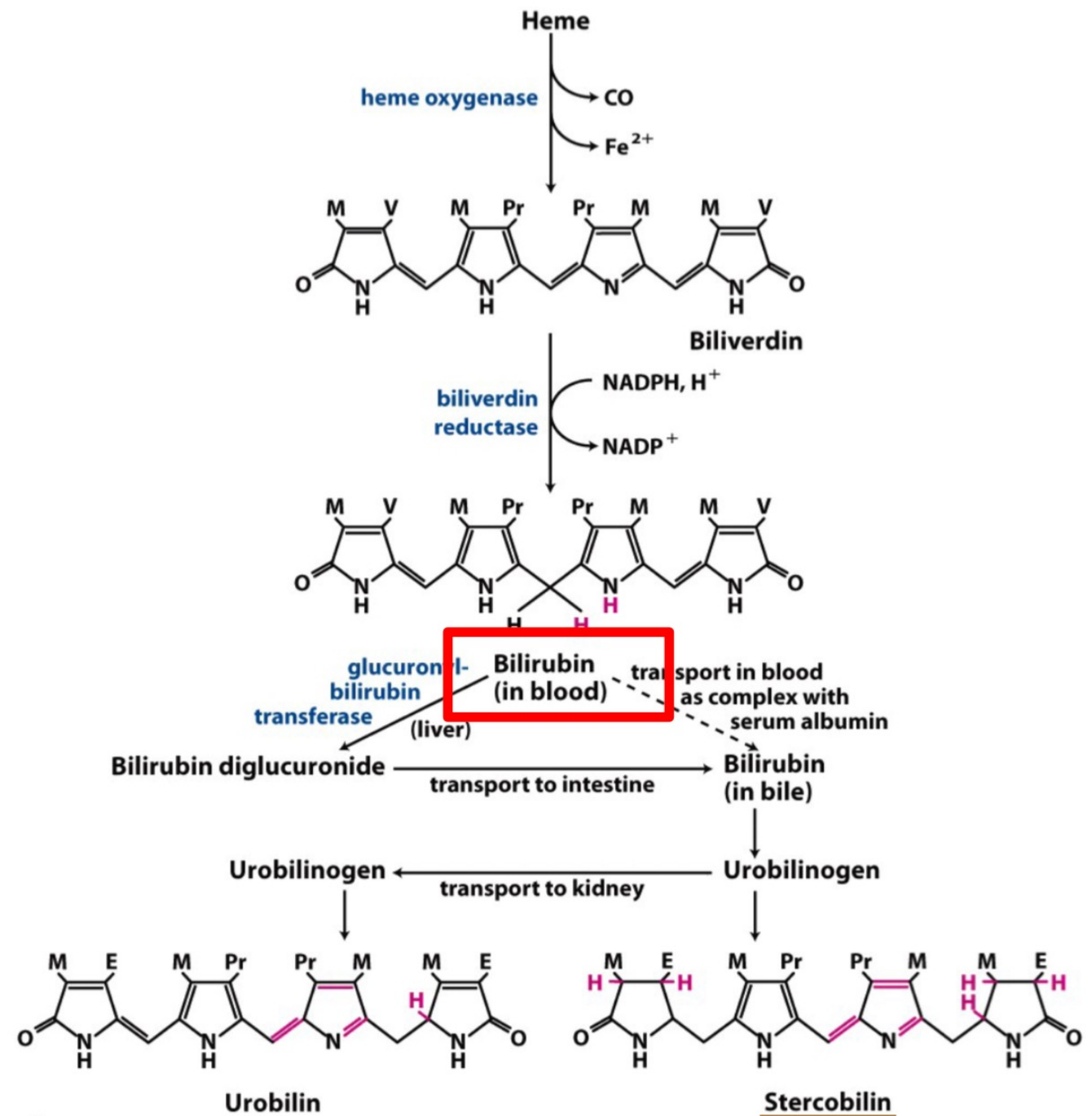


Question 4

Obstructive gallbladder stones cause (among other things) jaundice and white stool. Can you explain this phenomenon?

Answer

- Gallbladder stones block the bile duct.
- Bilirubin can not be excreted.
- Hence, high bilirubin levels in the blood.
- Bilirubin is yellow, which explains jaundice (yellow skin).
- In the intestine, bilirubin is converted to stercobilin (brown pigment). If bilirubin does not reach the gut, the lack of brown pigment will yield pale stool.



Question 5

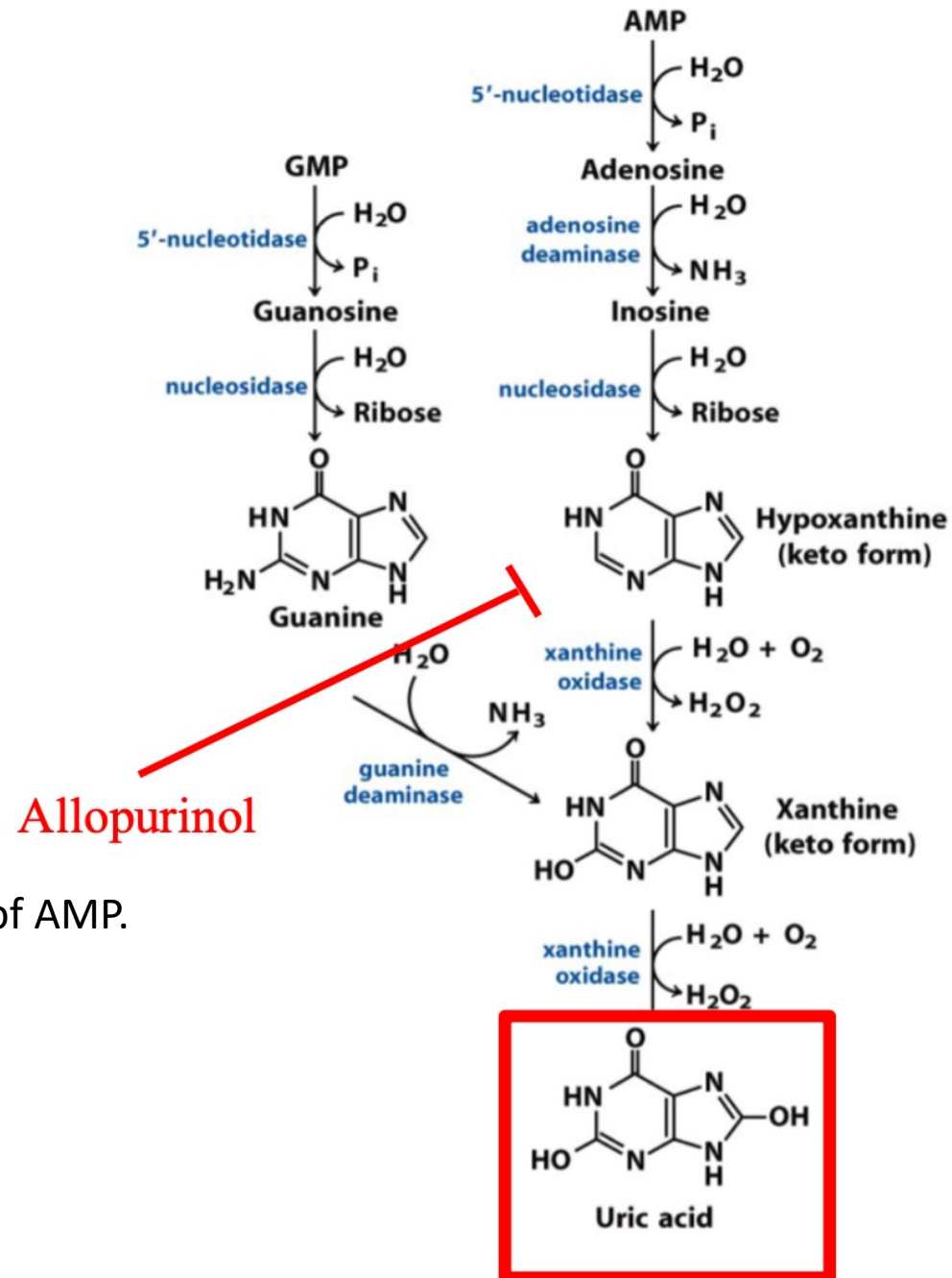
Gout is a common form of arthritis that occurs when urate crystals accumulate in your joint, causing the inflammation and intense pain of a gout attack.

- 1) A wrong diet can be a triggering cause of gout. Can you tell what substances should a food be rich in to be promoting gout.
- 2) Allopurinol (an inhibitor of xanthine oxidase) is used to treat gout. Can you explain the biochemical bases of the treatment?
- 3) Allopurinol treatment often causes the formation of kidney stones (crystals) but the incidence of kidney damage of this treatment is way less severe than that caused by gout. Can you explain this phenomenon (tip: the solubility of uric acid in urine is 0.15 g/L, that of xanthine is 0.05 g/L, that of hypoxanthine is 1.4 g/L)

Answer 5.1

- Purines are degraded to uric acid.
- Purine-rich food promotes gout (liver, seafood, alcohol).

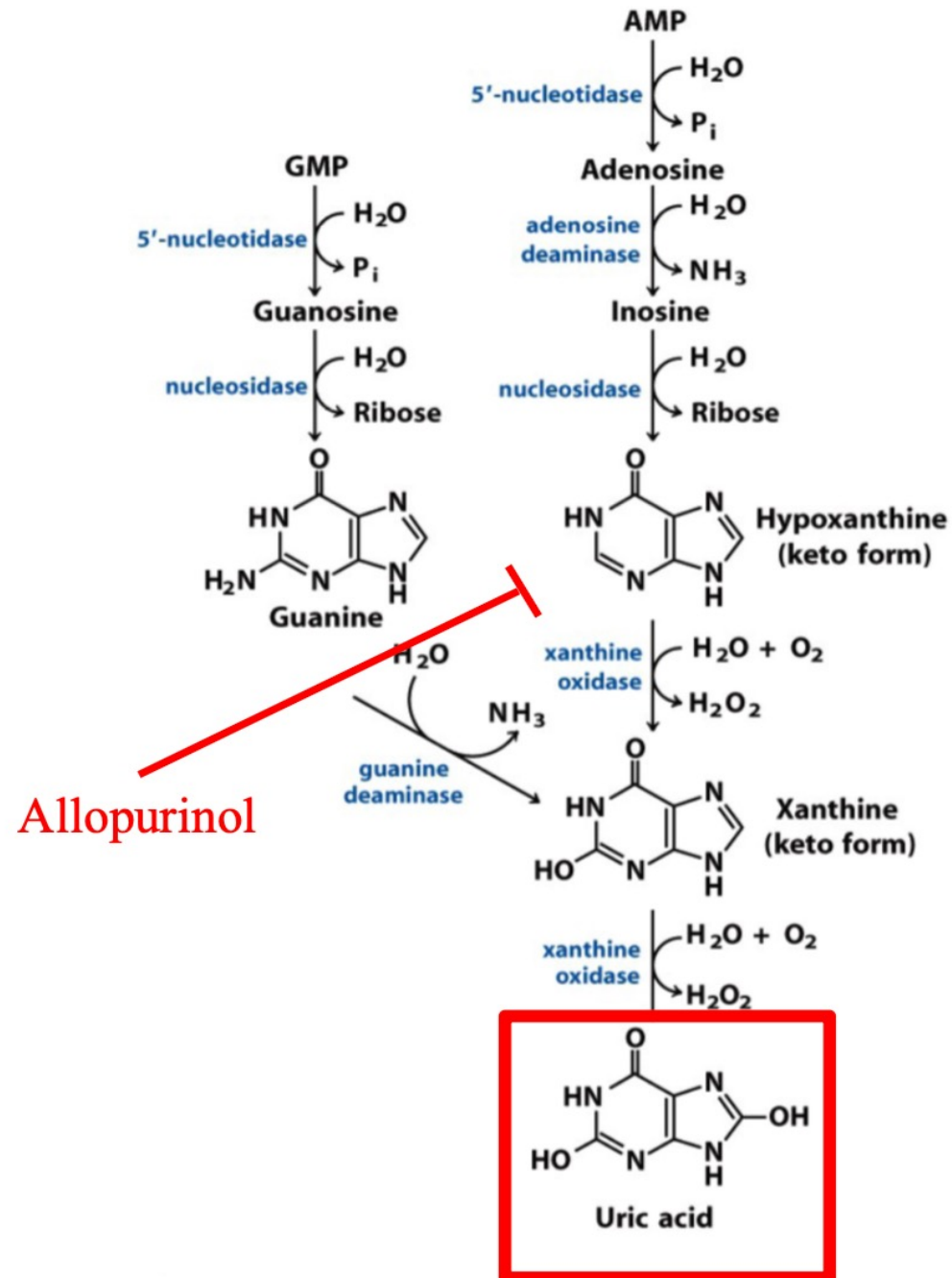
Answer 5.2



Allopurinol inhibits the degradation of AMP.

Answer 5.3

Accumulation of hypoxanthine, along with its higher solubility in urine compared to uric acid and xanthine, leads the formation of kidney stones,



Question 6

Methotrexate side effects include hair loss, diarrhea, low blood cell levels, increased risk of infection, liver damage.

Can you explain the common cause of these problems?

Answer

Methotrexate competitively inhibits with dihydrofolate reductase(DHFR), and blocks the formation of tetrahydrofolate and the activity of thymidylate synthase.

Folic acid is as a cofactor to various methyltransferases involved in serine, methionine, thymidine and purine biosynthesis. Because methotrexate inhibits tetrahydrofolate synthesis, folic acid bioactivation is blocked. By affecting de novo synthesis of the nucleoside thymidine, it interferes with DNA synthesis.

All these effects on DNA and protein synthesis have an impact on healthy cells too, especially the fast dividing ones.

