1. Why might covalently linked (multifunctional) enzymes, such as those of the pyrimidine and fatty acid biosynthetic pathways of mammals, be advantageous to an organism?

2. Elevated levels of ammonia in the blood can be caused by a deficiency of mitochondrial carbamoyl phosphate synthetase or a deficiency of any of the urea cycle enzymes. These two types of disorders can be distinguished by the presence of orotic acid or related metabolites in the urine.
   a. Why is it possible to determine the basis of hyperammonemia in this way?
   b. Why would a deficiency of cytoplasmic carbamoyl phosphate synthetase not cause hyperammonemia? What problems would such an enzyme deficiency cause? How would you treat a patient who has a deficiency in cytoplasmic carbamoyl phosphate synthetase?

3. You wish to prepare $^{14}$C-labeled purines by growing bacteria in a medium containing a suitably labeled precursor. The only precursors available are amino acids that are all uniformly labeled to the same specific activity per carbon atom. Which of the amino acids would you use to obtain purine rings that are labeled to the highest specific activity?

4. Hydroxyurea, potent chelator of ferric ions, has been shown to interfere with DNA synthesis, and it is used as an antitumor agent. What is the likely target enzyme for hydroxyurea?

5. Many multivitamin preparations contain nicotinamide. Most mammalian cells contain cytosolic enzymes that convert nictinamide directly to NAD$^+$. What other substrates are required for the formation of NAD$^+$ from nicotinamide? How could PRPP and ATP be used as source of those substrates?

6. Hypoxanthine-guanine phosphoribosyl transferase (HGPRT), a salvaging enzyme of nucleotide metabolism, uses 5'-phosphoribosylpyrophosphate (PRPP) to convert hypoxanthine to IMP and guanine to GMP. A deficiency of this enzyme can lead to an increased level of purine synthesis, excess formation of uric acid, and hyperuricemia, or gout.
   a. How might a deficiency in HGPRT stimulate purine synthesis?
   b. Under what conditions might one expect a deficiency of hypoxanthine-quanine phosphoribosyl transferase to affect the rate of pyrimidine nucleotide synthesis?