A. General questions

1. (5) Enriching flour with folic acid at a level of 140mg per 100g has decreased neural tube closure defects in the USA yet it is evident that further reduction could be achieved by higher levels of supplementation. What would be the most logical argument against a further increase in the amount of folic acid added to enriched flour? (not cost).

   The problem would be that higher folic acid intake could mask the symptoms of pernicious anemia.

2. (15 pts) Using a diagram, equation or metabolic scheme (structures not necessary), explain why:
   a. Methyl malonic acid appears in the urine in a B12 deficiency.

   \[
   \text{methylmalonyl CoA} \rightarrow \text{succinyl CoA} \rightarrow \text{fumarate or }
   \text{malate or }
   \text{without adequate B12, methylmalonate acid builds up}
   \]

   b. Homocysteine levels may be elevated in a B6 deficiency.

   \[
   \text{HCS} \rightarrow \text{cystathionine}
   \]

   In low B6, hence low PLP, HCS becomes elevated

   c. Symptoms of pellagra could result from isoniazid therapy if niacin intake was low.

   deficiency of niacin results in pellagra

   tryptophan \( \rightarrow \rightarrow \rightarrow \) niacin

   PLP is involved in several steps, most notably in the tryptophan synthase enzyme in the pathway.

   converting tryptophan to niacin. Another isoniazid form

   a Schiff base with PLP to tie up PLP with resulting low niacin
3. (10) Explain why a patient with age-related achlorhydria will benefit from oral B12 supplements whereas those with classic pernicious anemia will not. For the latter group list two B12 dosage forms that would be helpful.

HCl is needed to break covalent links with B12 in food. If a has low HCl, then oral supplements of B12 will be absorbed. In pernicious anemia, (not bound) will be absorbed. In pernicious anemia, the problem is lack of intrinsic factor, a glycoprotein carrier. PO B12 will not be absorbed in this case. One can give an IM injection, sublingual tablets or a nasal spray or gel to bypass the need for intrinsic factor.

4. (4) Explain using the concept of Km, the reasons why very high doses of thiamin can relieve the inborn error of metabolism called hyperpyruvate aciduria.

In this case the error is a pyruvate dehydrogenase which has a high Km (low affinity) for TPP. High thiamin is needed to restore activity.

5. (8) What two independent disease consequences could logically result from a 65 year old man not taking in enough folic acid? Explain how these diseases arise.

- megaloblastic anemia due to failure to generate DNA RNA precursors for RBC turnover.
- elevated HCS which could lead to CVD, CHD or Alzheimer's disease risk.

6. (8) You have a patient come in with a shoulder rotator cuff injury. Explain why vitamin C might speed up the healing process. What biochemical reaction is involved?

C is needed for collagen synthesis needed for injury repair.

C is needed for hydroxyproline formation to convert procollagen to collagen.
7. (5) The patient with the torn rotator cuff is a scientist and buys your suggestion but wants to take 1500mg of vitamin C per day because that is what she takes for the common cold. Draw a saturation curve to convince the patient of a more appropriate dose. What would be that dose?

![Saturation Curve](image)

8. (5) Heating meats can result in substantially decreased bioavailability of vitamin B6 due to Schiff base formation between pyridoxal in meat and the N-terminal amino acids. Draw the structures of A and B below where A is any N-terminal amino acid.

![Chemical Structures](image)