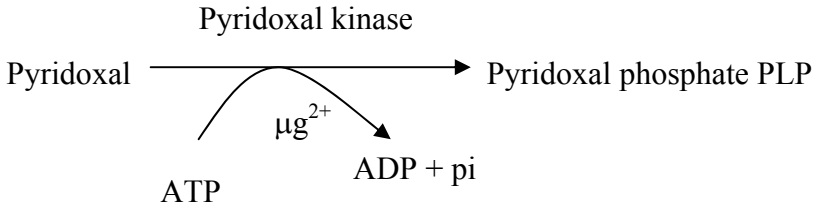
Water soluble vitamins

BCH 282 (Lec 14)

Vitamin B_6 pyridoxine:

- Vitamin B6 consists of 3 closely related pyridine derivatives: pyridoxine, pyridoxal and pyridoxamine.
- All three compounds are efficiently converted to the biologically active form of vitamin B_6 pyridoxal phosphate.



- Vitamin B_6 is called a "sleeping giant" of vitamins. Unlike other water-soluble vitamins, vitamin B_6 is stored extensively in muscle tissue.

Metabolic role of vitamin B_6:

1. Protein and amino acids metabolism, involved in transamination reaction
   (alanine + αKG ↔ pyruvate + Glu
   α amino acid + α keto acid ↔ α KA + αaa)
   αaa αKA
2. Converts tryptophan into niacin (hence pellagra is a frequent accombination of PLP deficiency).
3. Play important role in hemoglobin synthesis.
4. Regulation of blood glucose, release stored glucose from glycogen (cofactor for glycogen phosphorylase, the enzyme that breakdown glycogen).
5. Vitamin B_6 has a role in immune function and hormone response.
6. Required for synthesis of some neurotransmitters.

The association between vitamin B_6 and immune function is related to the role of the vitamin in protein metabolism. (Immunoglobins are proteins).

Sources: As B_1

Requirement: 2mg/day

Vitamin B_6 Deficiency:

1. B_6 deficiency can impair immune response, may be by way of impaired antibody production.

2. Being energy releasing, vitamin, some of the symptoms of severe B_6 deficiency are similar to those of other energy-releasing vitamins (skin lesions resembles those of B_2 and Niacin deficiency).
3. Being essential for synthesis of some neurotransmitters, these effects are though to explain:
    - Irritability, nervousness and depression with mild deficiencies.
    - Peripheral neuropathy and convulsions with severe deficiencies.
4. It's essential for heme biosynthesis → its deficiency cause sideroblastic anaemia (a microcytic anaemia seen in the presence of high serum iron).

Vitamin B_6 Toxicity:

- For years it was believed that vitamin B_6, like other water-soluble vitamins. Could not reach toxic concentrations in the body.
- Toxic effects of vitamin B_6 became known in women who had been taking more than 2g/day of vitamin B_6 for 2 months of more.
- Most of these women had been attempting to relieve premenstrual syndrome (PMS), the cluster of physical, emotional, psychological symptoms that some women experience before menstruation.
  PMS occur due to hormonal changes.

Hematopoietic Water Soluble Vitamins:

1. Folic acid
2. Cobalamin (B12)

1. Folic Acid

Pteroyl glutamic acid

(Pteridiine + para-amino benzoic acid)

PABA

- Animal cells are not capable of synthesizing PABA or attaching glutamate to petroic acid, but bacteria and plants can. Thus animals require folic acid in their diet.

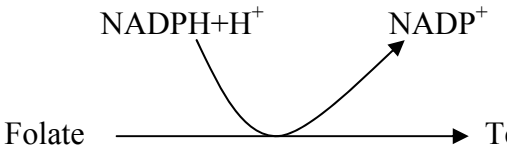
Requirement: 0.2 mg/day

Sources:

The major source is leafy vegetables. Other good sources are yeast, cauliflower, liver and kidney.

Function:

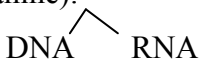
- Formation of the important coenzyme – tetrahydrofolate (FH_4).



(Folate reductase) → (Required reduced CoII as a hydrogen donor)

N.B.: NAD^+ = Coenzyme I $NADP^+$ = Coenzyme II

- The "one carbon" moiety is carried on FH4, which may be methyl ($-CH_3$), methylene ($-CH_2-$), formyl (-CHO) or forminino (-CH = N1+) moiety.
- One carbon tetrahydrofolate derivatives are used in biosynthetic reactions e.g.
    1. Metabolism of some amino acids e.g. methionine
    2. Purine biosynthesis (adenine, guanine):



    3. Synthesis of deoxythymidylic aicd (dTMP) → DNA
- Folate is active in cell division.

There is increased need of folate during periods of rapid growth and cell division such as pregnancy and adolescence. So folate deficiency may occurs during this periods of rapid growth.

If deficiency occur cell division of the blood and gastrointestinal tract (GIT) are impaired.

- So the first symptoms of folate deficiency are:
    1. Macrocytic anaemia (due to inhibition of DNA-synthesis as a result of ↓ available purines and dTMP → slow down the maturation of RBCs → abnormal large "macrocytic" RBCs + fragile membrane) + Megaloblastic changes in bone marrow. (Folate deficiency may be true (1 rg) or it may be secondary to B_{12} deficiency).
    2. GIT disturbances
- Alcohol, drugs, smoking have a –ve effect on folate status. They impair folate's absorption and increase its excretion.

Folate and Neural Tube Defect:

- Folate is very important in preventing neural tube defect.
- The brain and spinal cord develop from the neural tubes defect in its formation during early weeks of pregnancy may result in various central nervous system disorders and death.
- Folate can be taken before and continuous throughout the first trimester (1^{st} 3 months) of pregnancy. This can prevent neural tube defect.

Folic acid antagonist:

These are substances used in treatment of malignant diseases (cancer) e.g. methotrexate. They block synthesis of nucleic acids in malignant cells by preventing the reduction of folic acid to tetrahydro folic acid (FH_4).