**L8** **30/4/2019**

**Niacin (vitamin B3)**

Niacin **encompasses** nicotinic acid and nicotinamide. Nicotinamide is an essential part of the two pyridine nucleotides, nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP), which play a key role as hydrogen acceptors and donors for **many enzymes**.

Niacin can be synthesized in the body in limited amounts from the amino **acid tryptophan**.

**Deficiency – pellagra**

Pellagra was formerly endemic among poor people who subsisted chiefly on **maize,** which contains niacytin, a form of niacin that the body is unable to utilise.

Pellagra can develop in only **8 weeks** in individuals eating diets that are very deficient in niacin and tryptophan.

**It remains a problem in :-**

* Parts of Africa, and is occasionally seen in
* Alcoholics
* Patients with chronic small intestinal disease in developed countries.
* Hartnup’s disease, a genetic disorder characterised by impaired absorption of several amino acids, including tryptophan.
* Carcinoid syndrome when tryptophan is consumed in the excessive production of 5-hydroxytryptamine (5-HT, serotonin).

***Pellagra has been called the disease of the three Ds:***

* **Dermatitis.** Characteristically, there is erythema resembling severe sunburn, appearing symmetrically over the parts of the body exposed to sunlight, particularly the limbs and especially on the neck but not the face (Casal’s necklace). The skin lesions may progress to vesiculation, cracking, exudation and secondary infection.
* **Diarrhoea.** This is often associated with anorexia, nausea, glossitis and dysphagia, reflecting the presence of a non-infective inflammation that extends throughout the gastrointestinal tract.
* **Dementia.** In severe deficiency, delirium occurs acutely and dementia develops in chronic cases.

**Treatment** is with nicotinamide, given in a dose of 100 mg 3 times daily orally or parenterally. The response is usually **rapid**. Within 24 hours the erythema diminishes, the diarrhoea ceases and a striking improvement occurs in the patient’s mental state.

**Toxicity**

Excessive intakes of niacin may lead to **reversible hepatotoxicity**.

Nicotinic acid is a lipid-lowering agent but at doses above 200 mg a day gives rise to vasodilatory symptoms (‘flushing’ and/or hypotension).

**Pyridoxine (vitamin B6 )**

Pyridoxine, pyridoxal and pyridoxamine are different forms of vitamin B6 that undergo phosphorylation to produce pyridoxal 5-phosphate (PLP).

 **PLP** is the co-factor for a large number of enzymes involved in the metabolism of amino acids.

Vitamin B6 is available in most foods.

Deficiency is **rare**, although certain drugs, such as isoniazid and penicillamine, act as chemical antagonists to pyridoxine.

Pyridoxine administration is effective in isoniazid-induced peripheral neuropathy and some cases of sideroblastic anaemia.

 **Large doses** of vitamin B6 have an **antiemetic effect** in radiotherapy-induced nausea.

 Although vitamin B6 supplements have become popular in the treatment of nausea in pregnancy, carpal tunnel syndrome and pre-menstrual syndrome, there is no convincing evidence of benefit.

Very high doses of vitamin B6 taken for several months

**can cause a sensory polyneuropathy**.

**Biotin**

Biotin is a co-enzyme in the synthesis of fatty acids, isoleucine and valine, and is also involved in gluconeogenesis. Deficiency results from consuming very large quantities of raw egg whites (> 30% energy intake) because the avidin they contain binds to and inactivates biotin in the intestine. It may also be seen after long periods of total parenteral nutrition.

The clinical features of deficiency include scaly dermatitis, alopecia and paraesthesia.

**Folate (folic acid)**

Folates exist in many forms. The main circulating form is 5-methyltetrahydrofolate. The natural forms are prone to oxidation. Folic acid is the stable synthetic form. Folate works as a methyl donor for cellular methylation and protein synthesis. It is directly involved in DNA and RNA synthesis, and requirements increase during **embryonic development**.

Folate deficiency may cause three major birth defects (spina bifida, anencephaly and encephalocele) resulting from imperfect closure of the neural tube, which takes place 3–4 weeks after conception.

 The UK Department of Health advises that women

who have experienced a pregnancy affected by a neural tube defect should take 5 mg of folic acid daily from before conception and throughout the first trimester; this reduces the incidence of these defects by 70%.

All women planning a pregnancy are advised to include good sources of folate in their diet, and to take folate supplements throughout the first trimester.

**Liver** is the richest source of folate but an alternative source **(e.g. leafy vegetables)** is advised in early pregnancy because of the high vitamin A content of liver.

Folate deficiency has also been associated with **heart disease, dementia and cancer.**

There is mandatory fortification of flour with folic acid in the USA and voluntary fortification of many foods across Europe.

 There are now concerns that this may contribute to the increased incidence of colon cancer through promotion of the growth of polyps.

**Hydroxycobalamin (vitamin B12**)

 Vitamin B12 is a co-factor in folate co-enzyme recycling and nerve myelination. Vitamin B12 and folate are particularly important in DNA synthesis in red blood cells.



**Vitamin B12** , but not folate, is needed for the integrity of myelin, so that vitamin B12 deficiency is also associated with **neurological disease**

**Neurological findings in B12**

Peripheral nerves

 • Glove and stocking paraesthesiae

 • Loss of ankle reflexes

Spinal cord

* Subacute combined degeneration of the cord
* Posterior columns – diminished vibration sensation and proprioception
* Corticospinal tracts – upper motor neuron signs

Cerebrum

* • Dementia
* • Optic atrophy

Autonomic neuropathy deficiency

**Neurological consequences of vitamin B12**

In older people and chronic alcoholics, vitamin B12 deficiency arises from insufficient intake and/or from malabsorption.

 Several drugs, including neomycin, can render vitamin B12 inactive.

Adequate intake of folate maintains erythropoiesis and there is a concern that fortification of foods with folate may mask underlying vitamin B12 deficiency.

In severe deficiency there is insidious, diffuse and uneven demyelination. It may be clinically manifest as peripheral neuropathy or spinal cord degeneration affecting both posterior and lateral columns (‘subacute combined degeneration of the spinal cord), or there may be cerebral manifestations (resembling dementia) or optic atrophy.

 Vitamin B12 therapy improves symptoms in most cases.

**Vitamin C (ascorbic acid)**

Ascorbic acid is the most active reducing agent in the aqueous phase of living tissues and is involved in intracellular electron transfer.

It takes part in the hydroxylation of proline and lysine in protocollagen to hydroxyproline and hydroxylysine in **mature collagen.**

It is very easily destroyed by heat, increased pH and light, and is very soluble in water; hence many traditional cooking methods reduce or eliminate it.

 Claims that high-dose vitamin C improves immune function (including resistance to the common cold) and cholesterol turnover remain unsubstantiated.

**Deficiency – scurvy**

Vitamin C deficiency causes defective formation of collagen with:-

* Impaired healing of wounds
* Capillary haemorrhage
* Reduced platelet adhesiveness (normal platelets are rich in ascorbate)

**Scurvy – vitamin C deficiency**

 **Precipitants**

 ***Increased requirement***

• Trauma, surgery, burns, infections

• Smoking

• Drugs (glucocorticoids, aspirin, indometacin, tetracycline)

***Dietary deficiency***

• Lack of dietary fruit and vegetables for > 2 months

• Infants fed exclusively on boiled milk

**Clinical features**

 • Swollen gums that bleed easily

• Perifollicular and petechial haemorrhages

• Ecchymoses

• Haemarthrosis

 • Gastrointestinal bleeding

• Anaemia

 • Poor wound healing

A dose of 250 mg vitamin C 3 times daily by mouth should saturate the tissues quickly.

 The deficiencies of the patient’s diet also need to be corrected and other vitamin supplements given if necessary.

 Daily intakes of more than 1 g/day have been reported to cause **diarrhoea** and the **formation of renal oxalate stones.**

**Other dietary organic compounds**

There are a number of non-essential organic compounds with **purported** health benefits, such as reducing risk of heart disease or cancer.

Groups of compounds such as the flavonoids and phytoestrogens show bioactivity through their respective antioxidant and oestrogenic or anti-oestrogenic activities.

**Flavonoids** (of which there are a number of different classes of compound) are found in fruit and vegetables, tea and wine; **phytoestrogens** are found in soy products (with higher intakes in parts of Asia compared to Europe and the USA) and pulses.

**Caffeine from tea** and coffee and carbonated beverages affects the nervous system and can improve mental performance in the short term, with adverse effects seen at higher intakes. Intake of non-carbonic organic acids (which are not metabolised to carbon dioxide), e.g. oxalates, may be **restricted** in individuals prone to kidney stones.