Pellagra results from the deficiency of niacin (vitamin B3). It was first described by Don Casal, a Spanish court physician in the 1700s, where thickened skin was noted in peasants. However, it was not until the 1900s that the cause and treatment of pellagra was determined. [1]

Niacin can be derived from:

- Dietary sources: include nicotinic acid, nicotinamide and other biologically active derivatives. High bioavailability is in food products such as beans, milk and eggs. Flour is enriched with niacin and has an excellent bioavailability.
- Conversion of the amino acid tryptophan to niacin: an increased rate of turnover is seen in niacin deficiency states - eg, pregnancy and with the oral contraceptive pill - and conversion is inhibited by isoniazid.

Nicotinic acid and nicotinamide are precursors of two important co-enzymes: nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP).

NAD and NADP are crucial to a number of oxidative and reductive reactions - eg, steroid formation, fatty acid synthesis, protein metabolism and DNA repair.

Absorption of vitamin B3

Both nicotinic acid and nicotinamide are absorbed from the stomach and small intestine. At low doses absorption depends on facilitated diffusion and at higher doses the absorption is passive. Some storage occurs in the liver.

Recommended dietary allowance (RDA)

The RDA is 13-19 NE/day for adults. NE is 'niacin equivalent', in which one NE = 1 mg niacin or 60 mg tryptophan.

Epidemiology

- Vitamin B deficiency is rare in the UK.
- Prior to food fortification with niacin, epidemics of pellagra were seen. However, sporadic cases are still occasionally seen.
- Niacin deficiency is seen in the following groups:
  - Diets based mainly on corn (low in tryptophan and niacin) - eg, China, Africa and India.
  - Alcoholics - usually deficient in other vitamins also.
  - Eating disorders - eg, anorexia nervosa. [2]
  - Hartnup's disease - congenital malabsorption of tryptophan from the intestine and kidney.
  - Carcinoid syndrome - tryptophan is increasingly converted to serotonin.

There is concern that the number of cases of pellagra will be likely to increase with increasing fad diets. [3]

Presentation

Classically described as '3 Ds':

- Dementia
- Diarrhoea
- Dermatitis
Some add a fourth D - Death.

Early symptoms include:

- Loss of appetite
- Generalised weakness
- Irritability and aggression
- Abdominal pain
- Vomiting

Continued deficiency leads to epithelial changes leading to:

- Stomatitis.
- Bright red glossitis.
- Vaginitis.
- Oesophagitis.
- Dermatitis - classically, a pigmented, scaly rash prominent in sun-exposed skin - eg, the back of the hand, called 'gauntlet of pellagra' or on the neck where it can form a ring called 'Casal’s necklace'. The rash begins as itchy erythema and then looks similar to a tan and may vesiculate.\[4, 5\]

Other features include:

- Diarrhoea - due to a combination of proctitis and malabsorption.
- Dementia - may present as depression, followed by memory deficits and hallucinations or psychosis which may occur.
- Seizures.
- Paraesthesia - may occur.
- Malabsorption.

**Diagnosis**

After niacin has been processed it can be excreted in the urine. The products detected in the urine include nicotinic acid, niacin oxide and metabolites including 2-pyridone and 2-methyl nicotinamide.

The latter two metabolites can be measured to assess niacin deficiency (low levels will be present).

RBC levels of NAD/NADP can also be useful in the diagnosis.

**Management**

- Oral supplementation with nicotinamide is usually used (eg, 100-200 mg three times a day until symptoms remit).
- Nicotinamide is used in preference to nicotinic acid, as side-effects relating to vasodilatation are fewer - eg, flushing.\[6\]
- Cutaneous lesions begin to resolve in 24-48 hours after starting treatment.

**Adverse effects of treatment**

- Nausea, vomiting and abdominal pain.
- Dry skin and pruritus.
- Headache.
- Flushing - mediated by prostaglandin release and seen with high doses of nicotinic acid - eg, above 50 mg per day.
- Glucose intolerance.
- Macular oedema and cysts.
- Hepatotoxicity - very rarely, jaundice with a rise in transaminases is seen. Fulminant hepatitis has been reported with very high doses (>3 g per day).
High doses of nicotinic acid (>3 g per day) are used in the treatment of certain types of hyperlipidaemia (it lowers both cholesterol and triglycerides) and toxic effects, such as flushing and hepatotoxicity, are seen more frequently at these dose ranges.

No toxic effects are seen with food sources of niacin.

It is unclear whether sustained forms of nicotinic acid are associated with more or less toxicity.

Prognosis and prevention

Prompt diagnosis and treatment of cases lead to an excellent recovery.

Prevention involves adequate niacin intake and dietary advice to vulnerable groups - eg, pregnant women.

Further reading & references

6. British National Formulary, NICE Evidence Services (UK access only)

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